



## SCIENCE AND TECHNOLOGY SELECT COMMITTEE

### Genetically Modified Insects

#### Oral and Written evidence

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## **Advisory Committee on Releases to the Environment (ACRE) – Written evidence (GMI0014)**

### **Summary**

- Our response to this inquiry reflects ACRE's remit i.e. GMO regulation and environmental risk assessment.
- Ideally the regulatory framework should capture organisms based on the novelty of their characteristics i.e. use a trait based approach. This is not the EU's current method (or that of the vast majority of countries); instead, organisms are captured based on how they were produced and the nature of their genetic alterations. A trait-based approach would facilitate greater consistency in applying potential solutions (novel and existing) to challenges facing the EU and its Member States.
- In addition to adopting similar regulatory triggers, countries are also consistent in their approaches to regulatory assessment. The EU, like most countries, does not have a formal process for considering benefits. The legislation sets out how to carry out an environmental risk assessment and lists questions that are designed to identify and characterise the risk of harm but not potential benefits. Our view is that a consideration of benefits would improve the evidence base for decisions.
- Decision endpoints for these regulatory assessments should be established from the outset. If this is not the case, it will be difficult for applicants and decision-makers to know if, and under what conditions, a GM insect might be authorised. It is likely that this will be achievable for research trials, at least in some EU Member States. The current political situation in the EU is likely to make this very difficult to achieve for commercial releases.
- Regulators and risk assessors will need to gain experience in dealing with applications to release GM insects into the environment. Discussing issues well in advance of plans to release a GM insect into the environment will be particularly important. It is also important that the EU/ UK learns from the experience of other countries.
- Selection pressure acting against the persistence of novel traits in the environment will be an issue. From a regulatory point of view, the stability of the genetic modification has to be addressed in the risk assessment. Applicants must propose measures to manage and monitor resistance evolution. An understanding of the mechanisms involved and the use of standard mathematical models and quantitative data will be central to the risk assessment (as it has been in assessing resistance in insect pests targeted by GM plants).
- The idea that gene drives could counter this negative selection pressure is not new and researchers have explored the use of different approaches. The discovery of the

CRISPR/Cas system in bacteria and its application as a gene drive system in insects has provoked a great deal of interest. There are technical challenges including the evolution of gene-drive resistant DNA sequences but there have been successes under laboratory conditions. It has also provoked discussion about regulatory issues. Scientific (as opposed to social and economic) issues associated with adverse impact human health and the environment will be captured by the risk assessment. However, the challenge will be to establish what information will be required to identify and characterise these risks and how it can be generated prior to environmental release.

## Introduction to ACRE

1. We are the Advisory Committee on Releases to the Environment (ACRE). We are a statutory, independent committee that provides scientific advice to UK Government on the release of GMOs into the environment. This includes advising on GM microorganisms, GM animals and GM plants. We provide scientific advice to UK Ministers on (1) applications to carry out research and development trials in the UK and on (2) applications involving the commercial release of GMOs in the EU.
2. Our response to this inquiry reflects ACRE's remit i.e. GMO regulation and environmental risk assessment. We have not commented on the potential for GM insects to help in addressing global and UK challenges or on funding mechanisms associated with their development. We have focused on regulatory issues and not discussed wider, non-scientific concerns associated with the adoption of GM technologies.
3. In 2013, we published a series of reports based on our experience of working within the EU's regulatory framework for GMOs. One of our reports, which considered whether the current regulatory framework is fit for purpose<sup>1</sup>, included the regulation of GM insects in our considerations. A second report, which considered how environmental risk assessments could be improved within this framework<sup>2</sup>, focused on the assessment of applications for the commercial cultivation of GM plants. However, as our conclusions relate to fundamental aspects of the EU's approach to GMO assessments, these are very likely to apply to the assessment of GM insects.
4. To date, we have not assessed any applications to release GM insects into the environment. The only Member State (MS) in the EU that has is Spain. It is currently assessing an application for the trial release of GM olive flies. As it is a trial release, the Spanish authorities will carry out the assessment. This will be in accordance with the EU's legislation on the deliberate release of GMOs (Directive 2001/18/EC) but the assessment and decision will be made unilaterally by the Spanish authorities. Experience of GM plant trials in the EU suggests that there will be inconsistencies in the approach that different EU MS will take in regulating field trials of GM insects, making it important for potential applicants to discuss their plans with individual MS as early as possible.

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<sup>1</sup>Towards an evidence-based regulatory system for GMOs (2013):  
<https://www.gov.uk/government/publications/genetically-modified-organisms-review-of-current-eu-regulations>

<sup>2</sup> Towards a more effective approach to environmental risk assessment (2013).  
<https://www.gov.uk/government/publications/genetically-modified-organisms-improving-risk-assessments>

The first part of our response to the inquiry is based on the conclusions of our 2013 reports.

### **Do the current EU and UK genetically modified organisms (GMOs) regulatory frameworks work for GM Insects**

5. UK regulations implement EU legislation. The first iteration of EU legislation controlling GMOs was adopted in 1990; UK regulations<sup>3</sup> transposing this Directive came into force in 2002. The legislation established that organisms would be considered GMOs depending on how they were produced and the nature of the alterations made to their genetic material.

6. As the definition of a GMO in EU legislation has this ‘process-based’ component, it means that the methods used to develop insects are significant in determining whether they are GMOs or not. Consequently, some insects developed for population suppression or population replacement strategies will be captured by the GMO legislation and some will not. For example, insects sterilised using traditional mutagenesis (i.e. radiation) and released to suppress a wild population will not be captured by the legislation whereas insects ‘sterilised’<sup>4</sup> using recombinant DNA techniques will. Similarly, pest insects infected with a bacteria (*Wolbachia*) that compromises their ability to transmit disease between are unlikely to be captured by the GMO legislation because the genetic material of the insects has not been altered.

7. The adoption of a regulatory approach based on how the genetic material of an organism has been modified rather than on the novelty of the organism has led to a number of problems. These include lack of regulatory clarity (are organisms produced using non-traditional mutagenic techniques GMOs?) and inconsistency (some insects with a novel characteristic are captured by the GMO legislation, whilst others with the same, or similar trait, are not). These issues could conceivably affect innovation, which is a serious concern given the threat to humans and other animals from insect borne diseases and the challenges facing agriculture over the coming decades.

8. Another fundamental problem with the current regulatory framework for GMOs is that it does not explicitly take benefits into account. Implicit in an approach that takes benefits into account, is the idea that a particular level of "harm" might be tolerated when the benefits are high, whereas they might not be if the product had much more restricted value. A regulatory system that both takes account of potential benefits and includes compensatory measures (where appropriate) has the potential to deliver greater net benefits. We have discussed the principle components of a framework that takes a more holistic approach to assessing novel organisms in our 2007 report: *Managing the Footprint of Agriculture: Towards a Comparative Assessment of Risks and Benefits for Novel Agricultural Systems*<sup>5</sup>.

9. Ideally the regulatory system should capture organisms based on their novelty and take benefits into account in the decision-making process. This is not the case in the EU but

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<sup>3</sup> GM is a devolved matter in the UK and as such, the different nations have separate (but identical) GMO deliberate release regulations.

<sup>4</sup> The GM insects die before reaching sexual maturity.

<sup>5</sup> <http://webarchive.nationalarchives.gov.uk/20080727101330/http://www.defra.gov.uk/environment/acre/fse/widerissues/pdf/acre-wi-final.pdf> (2007).

neither is it the case in most of the countries outside the EU<sup>6</sup> that do have functioning GMO regulatory systems<sup>7</sup>. The nature of the EU's regulatory framework does not explain all the problems affecting the functioning of the GMO regulatory system. In addition to our 2013 reports and those of the CST and EASAC, the last mandatory evaluation of the EU legislative framework for GMO cultivation concluded that '*the legislative framework as it is operated today is not meeting.... its own objectives* (EPEC, 2011<sup>8</sup>).

10. Our particular interest is in the efficacy of the environmental risk assessment of GMOs. We held an evidence-gathering meeting in 2013 to discuss environmental risk assessment. It was apparent from this that the current GMO legislation in the EU could be implemented more effectively.

### **Environmental risk assessment**

11. The regulation of GMOs is divided into two parts. The first is 'risk assessment', which is a scientific evaluation based upon a dossier of information provided by the applicant. The second element comprises 'risk management', which is the responsibility of the European Commission, and the various national ministries. Whereas the former procedure should be based on objective scientific principals it is to be expected that the second element may be influenced by non-scientific and often political considerations.

12. It is apparent that the distinction between the two parts of the GMO regulatory process in the EU is becoming blurred and there is clear political pressure to add additional burdens to the risk assessment process. For example, there is now a formal requirement to conduct animal feeding trials as part of the assessment of GMO applications. This requirement was imposed in law in 2013 despite lack of evidence to support such a change and the objection of the European Commission's scientific expert panel.

13. The policies that different EU member states have adopted on GMOs over the past 18 years are often based on factors other than scientific evidence. The Cultivation Directive was adopted earlier this year and it allows MS to opt out or ban GM crop cultivation on non-scientific grounds. This amendment to the Deliberate Release Directive does not apply to GM insects. It is yet to be determined whether the Cultivation Directive will facilitate decision-making on GM crop cultivation in the EU.

14. Even if the decision-making system is improved in the EU, there are issues with the approach to the scientific risk assessment, which underpins such decisions. Risk assessments should test plausible, clearly defined hypotheses of how a characteristic of a GMO or its use could result in harm to human health or the environment. Instead, the EU has a tendency to focus on academic detail and standardising methodologies, which adds to the regulatory burden without adding value. It also makes it difficult for applicants to understand what is required. A more coherent understanding of what constitutes unacceptable environmental

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<sup>6</sup> Canada has the only regulatory framework that captures organisms based on their novelty (and potential to cause harm) rather on how they were produced.

<sup>7</sup> James, Clive. 2014. Global Status of Commercialized Biotech/GM Crops: 2014. ISAAA Brief No. 49. ISAAA: Ithaca, NY.

<sup>8</sup> [http://ec.europa.eu/food/food/biotechnology/evaluation/docs/gmo\\_cultivation\\_report\\_en.pdf](http://ec.europa.eu/food/food/biotechnology/evaluation/docs/gmo_cultivation_report_en.pdf)

harm from the outset, applied consistently across regulatory frameworks, would significantly aid transparency.

15. The inquiry refers to EFSA's guidance on the environmental risk assessment of GM insects. As this guidance is directed at those dealing with applications under the current GMO legislation, it addresses information requirements for risk assessment only. There is no facility for efficacy or benefits to be taken into account within the scientific assessment set out in the legislation. The EFSA guidance refers specifically to population replacement and population suppression approaches where this is appropriate, but generally does not distinguish between the two for risk assessment purposes. This is because both approaches cover a range of different strategies, each of which must be assessed in a case by case manner and it is difficult to generalise. An issue that ACRE has with the guidance is that it attempts to cover all eventualities/ hazards (for a range of potential uses of the technology in insects) rather than providing a practical framework that will help applicants identify and characterise risks on a case by case basis.

16. The EFSA guidance is helpful in highlighting the fact that the EU Directive dealing with the 'Deliberate Release of GMOs' was drafted with GM plants in mind (including sections dealing with non-plant GMOs). This means that some of the questions will have to be interpreted for GM insects. Another important message to be taken from the guidance was the need for careful consideration to be given to the selection of comparators in environmental risk assessments. The legislation requires a comparison with a non-GM equivalent (with very similar genetic backgrounds) but this does not preclude additional comparisons, which will provide decision-makers with a more informed/ contextualised risk assessment.

17. The WHO guidelines on testing GM mosquitoes compile information on a range of issues that researchers should consider when developing GM mosquitoes. Whilst it does not propose a regulatory framework, it is a clear, practical document that discusses elements that could be part of a regulatory framework i.e. case by case assessments, increasing environmental exposure in incremental steps, risk/ benefit, efficacy and stakeholder engagement. The guidelines describe regulatory regimes and discuss risk assessment frameworks. In the case of the latter, the authors conclude that 'because of the breadth of different genetic approaches that are under consideration and the conditions under which they might be used, it is not possible to provide an exact formula for the evaluation of all GM mosquito technologies'. We agree with this conclusion and it explains why the EFSA guidance would be difficult to use in practice. This conclusion also applies to the guidance on the risk assessment of GM mosquitoes in accordance with the Cartagena Protocol<sup>9</sup>.

18. An important conclusion reached in the WHO guidelines is that developers of these technologies should discuss potential applications as soon as is practical with regulators. Defra encourages applicants planning research trials to meet with regulators pre-submission. Up until recently, it has not been possible for applicants to discuss individual applications pre-submission at EU-level. We are aware that EFSA now provides this facility and this is welcomed.

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<sup>9</sup> The Cartagena Protocol applies to transboundary movements of Living Modified Organisms (LMOs). There is specific guidance on GM mosquitoes available at:  
[https://bch.cbd.int/onlineconferences/guidancedoc\\_ra\\_mosquitoes.shtml](https://bch.cbd.int/onlineconferences/guidancedoc_ra_mosquitoes.shtml)



### Resistance management

19. It is inevitable that there will be an evolutionary response to genetic changes resulting in altered characteristics in organisms (irrespective of the method by which the alterations occurred). This phenomenon is assessed and risk managed in applications to market GMOs in the EU (even where there is no link between resistance occurring and environmental harm or risk to human health). We have developed a great deal of experience in using standard mathematical models and quantitative data when assessing the potential for insect resistance to evolve as a consequence of the cultivation of GM insect-resistant plants. In general, we will need to harness our understanding of the mechanisms involved and apply this knowledge on a case by case basis. Where GM insects are used for biological control, integrating different approaches for controlling pest populations will be essential for a durable and resistant outcome.

### Gene Drives

20. The aim of population replacement strategies is to spread a novel trait through a target population. It is likely that such traits will impose a fitness cost; therefore, in order for them to persist (and spread) through a population, they will need to be linked to a system that increases the frequency of the associated genetic modification. These so-called gene drive systems may also be used in population suppression strategies e.g. to drive lethal mutations through a population. The idea of using gene drives to control insects or their capacity to transmit disease is not new. However, their application has been technically challenging<sup>10</sup>.

21. The discovery of the CRISPR/Cas system in bacteria and its application as a tool for gene editing in a range of species has very rapidly become the focus of research in a number of areas. Directing Cas9 nuclease to cut/ nick the DNA at specific sites in insect genomes has provoked a great deal of interest. Last year, Esvelt *et al*<sup>11</sup> published a feature article designed to provoke discussion about this technology. This was followed up by an article by the same group<sup>12</sup> about perceived 'regulatory gaps' associated with the use of gene drives (notably the robustness of the gene drives over time and the potential for these elements, and associated traits, to spread beyond the target population). These sort of issues are considered in GMO risk assessment more generally (there is a requirement to consider genotypic and phenotypic stability and to characterise vertical and horizontal gene flow). Whilst the communication of new technologies and their risks to a wider audience is important, a recent article by Laura DeFrancesco in Nature Biotechnology<sup>13</sup> highlights how a lack of context may misrepresent the actual risks posed by a technology.

The challenge is to establish how to address questions about the risk of harm and to establish what is acceptable and not acceptable. Data produced to address risk-based

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<sup>10</sup> There have been successes under laboratory conditions but there have been no field trials e.g. in *Drosophila* and mosquitoes. Bassett AR, Tibbit C, Ponting CP, Liu J-L. (2013). Highly efficient targeted mutagenesis of *Drosophila* with the CRISPR/Cas9 system. *Cell Reports* 4:220–228. Windbichler N., Menichelli M, Papatathanos PA., Thyme SB., Li H. et al., (2011). A synthetic homing nuclease-based gene drive system in the human malaria mosquito. *Nature* 473: 212 -215.

<sup>11</sup> <http://elifesciences.org/content/elifesciences/3/e03401.full.pdf>

<sup>12</sup> <https://www.sciencemag.org/content/345/6197/626>

<sup>13</sup> Laura DeFrancesco (2015). Gene drive overdrive. *Nature Biotechnology* (advanced online publication): [http://blogs.nature.com/tradesecrets/files/2015/09/Gene\\_Drive\\_Overdrive.pdf](http://blogs.nature.com/tradesecrets/files/2015/09/Gene_Drive_Overdrive.pdf)

questions will need to be generated throughout the process of development. The EU/UK's GMO regulation forsee a step by step approach whereby environmental exposure is increased if uncertainties about risk of harm are satisfactorily addressed. We note that the USA's National Academies of Sciences, Engineering and Medicine is funding a project on 'Gene Drive Research in Non-Human Organisms: Recommendations for Responsible Conduct':

22. A key message from our 2013 report is the importance of establishing what constitutes unacceptable harm from the outset. This can be informed by scientific evidence/ knowledge but it also has a social dimension (e.g. the acceptability of introducing genetic systems that are designed to persist in populations). There is a tendency for assessors/ regulators in the EU to attempt to address this lack of consensus on what constitutes harm by collecting more data / focusing on hazards, which is potentially an open-ended exercise. The WHO guidelines emphasise the need for such endpoints at every stage in the development of a GM mosquito (insect). Establishing regulatory endpoints is important if the EU's regulatory system for GMOs is to work efficiently. It will help determine whether different applications of this technology have the potential to achieve authorisation for commercial use in the EU (and thereby in the UK).

*18 September 2015*

**Advisory Committee on Releases to the Environment (ACRE), Dr Jeremy Sweet, Sweet Environmental Consultants, and Oxitec Limited – Oral evidence (QQ 26-38)**

*Evidence Session No. 3*

*Heard in Public*

*Questions 26 - 38*

TUESDAY 20 OCTOBER 2015

Members present

Earl of Selborne (Chairman)  
Lord Hunt of Chesterton  
Lord Kakkar  
Baroness Manningham-Buller  
Lord Maxton  
Duke of Montrose  
Baroness Morgan of Huyton  
Baroness Neville-Jones  
Lord Patel (co-opted)  
Lord Peston  
Viscount Ridley  
Lord Vallance of Tummel

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**Examination of Witnesses**

**Professor Rosemary Hails**, Chair, Advisory Committee on Releases to the Environment (ACRE); **Dr Jeremy Sweet**, Environmental Consultant, Sweet Environmental Consultants; and **Ms Camilla Beech**, Head of Regulatory Affairs, Oxitec Limited

**Q26 The Chairman:** Good morning. We are most grateful to the three of you for giving evidence to this session in our inquiry into GM insects. We are being broadcast on the web. First, would you introduce yourselves for the record? If any of you would like to make an introductory statement, do feel free to do so.

**Ms Camilla Beech:** Good morning. Thank you for having me at the inquiry. I am Camilla Beech. I am head of regulatory affairs for Oxitec in the UK. We are the only company in the UK and probably the world dealing with GM insects and consequently we have quite a lot of knowledge. We can hopefully help your inquiry today.

**Dr Jeremy Sweet:** Good morning. My name is Jeremy Sweet. I am an environmental consultant. I am a member of the EFSA GMO panel, which is relevant to this discussion. I see in the questions for today there is a lot of discussion about regulation and I am not a regulator; I am a risk assessor. I was also involved with a group in EFSA in developing the

Advisory Committee on Releases to the Environment (ACRE), Dr Jeremy Sweet, Sweet Environmental Consultants, and Oxitec Limited – Oral evidence (QQ 26-38)

EFSA guidance documentation for the environmental risk assessment of GM insects, together with a number of other independent scientists.

**Professor Rosemary Hails:** Good morning. I am Rosemary Hails. My day job is science director for biodiversity and ecosystem science at the Centre for Ecology & Hydrology. I am here because I have been a member of ACRE, the scientific advisory committee for the UK on releases into the environment of GM organisms. I have been a member since 2006 and the Chair since 2013. I was also an ad hoc expert for the Environment Working Group of EFSA from 2006 to 2010.

**Q27 The Chairman:** As Dr Sweet said, we hope to concentrate on the regulatory framework. Here we have represented, of course, those who are being regulated, those who assess the regulation and those who help set it, so I think that gives a good balance from which to discuss the regulatory framework. Can I ask a general question to start with? We are familiar from the written evidence with the role of ACRE within the United Kingdom and EFSA within the European Union. Can you give us your thoughts on the current regulatory environment in the UK and indeed in Europe? How do such regulations differ for non-EU countries that are members of the European Economic Area?

**Professor Rosemary Hails:** I shall summarise the legislation briefly. There are two EU directives on contained use and deliberate release and then there are three sets of national regulations to implement them on contained use, deliberate release and the Environmental Protection Act. ACRE is a statutory advisory committee set up under the Environmental Protection Act and it advises Ministers in the UK and the devolved Administrations. EFSA is the scientific advisory body at EU level that advises the EU Commission. We implement the deliberate release regulations through two parts. Part B is for research trials, which are assessed nationally, so ACRE would assess those for the UK. Part C is for commercial release and that is assessed at the EU level. EFSA leads on that with input from the member states. Also, ACRE advises the UK Government on the position to take from a scientific perspective at an EU level. The most notable thing from non-EU countries in the EEA relates to Norway. Norway has some additional legislation—the Gene Technology Act 1993—where it considers the benefits also of a particular element to the community and the contribution to sustainable development, but that is in addition to the other regulations.

**The Chairman:** On that subject, I note that in the written evidence from ACRE you refer to the benefits issue and how it is not taken into sufficient consideration perhaps. Are we inhibited in the UK from taking this approach that Norway has because of our membership of the EU or would we be free to take a view also?

**Professor Rosemary Hails:** Certainly we would be free to take a view. ACRE does have a view on this. Also we have some thoughts on how benefits could be taken more into account even within the existing framework. For example, in the whole risk assessment process, the very last question is to characterise the overall risk of a GM organism. Additional information could be provided on context under that question and that context could include benefits also. The reason why that does not happen routinely is the questions leading up to that final question do not put in the building blocks for benefits in the same way as they do for risks. There is scope within the existing framework.

**The Chairman:** Would the other two witnesses like to add anything at this stage on the regulatory framework?

Advisory Committee on Releases to the Environment (ACRE), Dr Jeremy Sweet, Sweet Environmental Consultants, and Oxitec Limited – Oral evidence (QQ 26-38)

**Ms Camilla Beech:** I would like to broaden it out. We have heard how the GM aspect is regulated but we are regulated also under the quarantine regulations because we work with insect pests, either for human health or agriculture. There are quarantine regulations that apply. Also, as insects are animals, there is an intersection with the animal feed and animal by-products regulations. There is a potential here that these regulations may be misapplied for insects because these regulations were intended for animal feed and food-producing animals. I would like to broaden the overall scope regarding the regulatory environment. The other regulation with which we have to comply is the Cartagena Protocol transboundary movement regulation, as we are the only exporter of GM materials outside of Europe.

**The Chairman:** That is the international legal framework for cross-border movement of GMOs.

**Ms Camilla Beech:** Correct.

**The Chairman:** You have practised that, have you not, and moved GMOs across boundaries.

**Ms Camilla Beech:** We have already undertaken several movements of that, yes.

**The Chairman:** The directive from Europe that would affect you most, were you to release genetically modified insects into the environment in Europe, which I do not think you have done yet, would be Directive 2001/18/EC, which covers the deliberate release of GMOs.

**Ms Camilla Beech:** That is correct, 2001/18/EC on deliberate release, as Rosie says, either Part B for a field trial at national level or a Part C application which is for “commercial”. Commercial also meaning placing on the market or giving to third parties.

**The Chairman:** I think that helps us explain the regulatory framework in which we are operating.

**Q28 Lord Maxton:** Is the European regulation very different from the international and, if so, why?

**Ms Camilla Beech:** There is no international regulation as such for GM insects.

**Lord Maxton:** For other countries then.

**Ms Camilla Beech:** Yes, in Europe the regulation specifies field trials and then commercial release. It is difficult to generalise, but for other countries it is a bit more seamless.

**Dr Jeremy Sweet:** There are regulations in different countries based largely on the principles of the Cartagena Protocol but with lots of different interpretations. Starting at what I would call the desirable end, there are the Canadian regulations, which are based on novelty, novel organisms or novel traits, so they do not discriminate GMOs from other types of engineering or manipulation or technologies. They look at the novelty of a product and say, “Are we concerned about this and do we need to look at it and regulate it?” It is very much a science-based approach of looking at whether a new organism could have an impact on human health and the environment, through to the much more rigid systems that apply in Europe and many countries elsewhere, which is very much based on the technology approach. I think you had some discussions about this last week.

This is a big problem because now there are tremendous debates about what the technology is and what GM is and what GM is not. We have new technologies coming through such as synthetic biology and various others which people are unable to put into a neat box and say, “Yes, it is GM”, or, “No, it isn’t GM”. We are getting into a bigger and bigger mess by basing

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the regulation around the technology. Many people, particularly scientists, feel that moving towards a trait-based approach, the Canadian approach, would be much more desirable.

**The Chairman:** We will come back to the trait-based approach in a later question.

**Lord Kakkar:** Just listening to the conversation so far, I would like to be clear on your views about the current European and UK regulatory environments and whether they are really fit for purpose, as that is fundamental to this issue.

**Professor Rosemary Hails:** I would like to separate this into about three parts. The first is that, if you were designing the regulatory system from scratch, you would design it differently. Jeremy has talked already about what actually triggers regulation. The second element is the scope, and we have already talked a little bit about the extent to which benefits are not explicitly included and perhaps we could make a little bit more of that. Thirdly, ACRE feels we could take the current regulations and interpret and implement them more effectively. Other countries have very similar frameworks and they have functioning systems. In the EU we do not have a functioning system for GM crops. In fact, the last mandatory evaluation of GMO cultivation for crops concluded that the EU legislative framework is not meeting its own objectives as it is operated today.

If we turn to medicinal and veterinary products, it is working somewhat better. For example, there have been 10 applications for commercial release of veterinary products. Nine of them have been authorised and one is still pending in the system. The picture for medicinal products is better than it is for crops. I think there have been about 10 commercial applications: two have been authorised, four have been withdrawn and four are still in the system.

**Viscount Ridley:** Can you clarify what you are talking about there? Are you talking about bacteria?

**Professor Rosemary Hails:** Largely I am talking about vaccines.

**Viscount Ridley:** But not in plants.

**Professor Rosemary Hails:** No. I am making the distinction that in that case it is working. They are also governed by 2001/18/EC for the environmental risk assessment part and it is working somewhat better than it is for GM crops, which is where the problem really is. The big issue for GM crops is that so many applications have been stuck in the system for so long that in many cases they are being withdrawn by companies because they are no longer commercially relevant.

**Lord Kakkar:** Just to be clear, the regulations around GM insects are an extension of those for crops.

**Professor Rosemary Hails:** Yes.

**Lord Kakkar:** For crops they are working very badly; for insects there may be capacity for them to work better.

**Professor Rosemary Hails:** Yes.

**Lord Kakkar:** Overall, how bad is it that there is this link between crops and insects, in perception and in regulation? To pick up on a point to which you have already alluded, when you talk about regulations working better in other countries, is that other European countries that have decided to interpret the European regulations in a different way or is it

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countries outside Europe? What genuine capacity in UK regulation do we have to look at the application of what the European directives and regulations tell us?

**Professor Rosemary Hails:** I was talking about countries outside Europe. Within Europe we are all part of the same system for GM crops that is not currently working. If you look at other countries such as the United States and Australia, I would say that their risk assessments follow very broadly a similar process and they have more effective systems.

**Lord Kakkar:** You mentioned in the previous answer the question of incorporating benefits into the equation. To be clear about it, are you saying that the current EU regulation will prevent that, whether it is crops or insects?

**Professor Rosemary Hail:** There is no explicit consideration of benefits but in the structured risk assessment process the last question is to characterise the overall risk and in doing that applicants could be encouraged to provide more information on context that would also include benefits.

**Lord Kakkar:** That would not be open to challenge at a European level.

**Professor Rosemary Hails:** Surely more information for decision-makers must be a better thing.

**Ms Camilla Beech:** As an applicant we believe that the European system does not work because it is just not predictable. You put an application in and you can never predict when you are going to receive a response. That is bad for innovation and it is bad for companies.

**Lord Kakkar:** Why is it not predictable? Is there not clear guidance to the regulators on the time they have to look at an application and respond to the applicant?

**Ms Camilla Beech:** There is some guidance, but it is routinely ignored.

**The Chairman:** Honoured in the breach.

**Lord Patel:** Can I be clear? From what you said, the European regulation relating to GM insects performs on the same basis as the regulation relating to GM crops. If that is the case, what discussions took place at the time when the regulation for GM insects was being considered, or was it just rubber-stamping that this was the same GM?

**Dr Jeremy Sweet:** To come back to the original discussion, the framework covers all GMOs. It was initiated originally because of microbes and because people were genetically engineering bacteria for various reasons. The original regulations were established around microbes and then developed for plants and now have been developed for animals. All GMOs in Europe come under the same regulatory framework and, as you have heard, the problem with that is not so much at the scientific level, the risk assessment process and so on; it is what happens after that. For example, in EFSA we produce scientific opinions which go to the Commission and to the member states, and that is where they are lost. They disappear into a black hole. There is never a qualified majority vote and so nobody will make a decision on whether or not to commercialise a GM crop. There are several GM crops on which we have given favourable opinions for cultivation in Europe that have been sitting there for up to eight years purely because the political process is not allowing decision-making to take place.

**Baroness Morgan of Huyton:** In essence, are you saying that the process is significantly more difficult than the regulation itself?

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**Dr Jeremy Sweet:** As Rosie said earlier, the regulation in principle is workable.

**Baroness Morgan of Huyton:** Is it doable?

**Dr Jeremy Sweet:** There are problems with the definition of GMOs and so on with the new technologies. In principle it should work, because similar ones are working in other countries, but in practice its application is the big problem. This is why in Europe there has been this discussion to have opt-outs so that countries that want to cultivate GM crops can do so and other countries can say they will not. This was to try and get through this logjam to allow some countries to proceed and not be blocked by other countries which said that they were not going to have any GMOs.

**Q29 Viscount Ridley:** Can I probe further on the question of stifling innovation, which has already been mentioned? A surprising number of the written submissions we have had have mentioned this point. Oxitec Limited said, “If we over-regulate we alienate entrepreneurial innovations and value creation”. Even ACRE said, more guardedly perhaps, that these issues could conceivably affect innovation, which is a serious concern given the threat to humans and other animals from insect-borne diseases. Is this really happening? Can you give real examples? Of course it is hard to give an example of somebody who did not start a company because they could not, but could you flesh this out?

**Ms Camilla Beech:** Maybe I can help you with an example. We have a product for olive fly which is a very destructive pest in Europe. We would like to field-test it in a cage to start with, not in the open environment, and we applied to Spain under the deliberate release directive 2001/18/EC for a caged trial with a security fence in a research environment at a research station. The Spanish authorities felt they could not authorise that trial without additional significant containment measures in place. We said, therefore, we would withdraw the dossier because we have other strains coming along on which we can better spend our money. We cannot even get to the first hurdle of getting a genetically modified insect in a field cage.

**Viscount Ridley:** That is you as an existing company with a track record.

**Ms Camilla Beech:** Correct.

**Viscount Ridley:** What would the effect be if there was a research group in a university where one of the professors was thinking of spinning out a company and starting this because he could see an opportunity? What would it be like for him to do that today?

**Ms Camilla Beech:** The bottom line is probably they would not start, certainly in Europe. To take an example, we have just had a release in the USA of a diamondback moth, because at the very least they could see the benefits of testing it. That is the next step forward. We have had people saying, “We cannot use your technology because Europe will say no”.

**Viscount Ridley:** To be clear, if I was to start a company tomorrow to suppress the Scottish midge, for example, using the old-fashioned sterile insect technique—ie irradiating midges—that would be no bother, I could do that straight away.

**Ms Camilla Beech:** Correct. It would be no bother at all.

**Viscount Ridley:** But that is (a) less effective and (b) possibly a more risky technology than if I was to do it with a specific GM version.



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**Ms Camilla Beech:** You are introducing mutations into the whole genome in that midge by irradiation whereas we are specifically putting one or two genes into our insect.

**The Chairman:** Is it not evident within Europe that there is a great suspicion about the concept of genetically modified organisms and as such the public expect a different regulatory regime?

**Ms Camilla Beech:** I think it is an appetite and an attitude and the attitude is precautionary. It is based on the precautionary principle that you do not know enough about it. The regulators do a thorough assessment of the product.

**Lord Maxton:** You may have answered my question already. You mentioned Spain. Was it a Spanish authority regulation that they were applying or was it a European one?

**Ms Camilla Beech:** It was the same directive, 2001/18/EC, the deliberate release directive. It is the same in the UK and it has been implemented into Spanish law. It is exactly the same set of questions.

**Lord Patel:** Could I have some clarification on what you said about the European law regarding germline mutations? Does that arise out of the regulations relating to human genome manipulation and is it directly applied therefore to any insects or animals?

**Ms Camilla Beech:** I do not believe so. I am not very familiar with that law. I apologise but I do not think I know the answer to your question.

**Q30 Baroness Neville-Jones:** My question follows from the current conversation. One has rather a strong sense that there is an impasse here, from what Ms Beech was saying about not being able to start a field trial. Is it possible then to start thinking ahead to try and get proposals on the table which get ahead of the current situation—in other words, instead of waiting on and on for a field trial that may never happen, because you cannot get to that post, actually start initiating a dialogue on a new regime? If you did that, what would you like to see as its salient characteristics?

**Professor Rosemary Hails:** I think we should be proactive in trying to solve these problems on two fronts. As you say, we should look to the long game about designing a system that my committee would feel is more scientifically defensible. A key feature of that system and the trigger for regulation would be around novelty rather than around a particular method that has been used to produce the organism, as Jeremy has already alluded to, because that is more scientifically rational now.

**Baroness Neville-Jones:** The trait?

**Professor Rosemary Hails:** Yes, that is right. When the regulations were first produced, recombinant DNA technology was very new and they could see the potential to produce very different sorts of organisms. This is why we have our current regulatory system now. Yes, we should play that longer game and seek to set up a new system that is more defensible and more future-proof. We have this bizarre debate now where new techniques are being developed to manipulate genomes and you have people scrutinising the legislation to try to decide whether technically it is captured by it or not. That is a bit of a nonsense.

In designing that new system, we would like to see one where benefits are very explicitly included. However, I think we ought to be proactive on another front as well, because that is a very long game. We ought to be proactive on trying to make the current system work more

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effectively. In essence, we have the evidence that it works more effectively in other countries. We have this big issue to which we have alluded where politics is being conflated with the scientific process. It is really embodied in the position of GM crops where we have these applications in a suspended state. I have pointed to the fact already that for medicinal and veterinary vaccines we have had more success.

The cultivation proposal is where countries can opt out of growing GM crops and that is an attempt to separate the science from the politics to some extent. It is early days yet. It remains to be seen whether that will be effective. Also there are other issues of detail about how the risk assessment is conducted in the EU. ACRE is one of several voices across Europe which promote the problem-formulation approach. Risk assessment should test plausible, clearly defined hypotheses. There is some pressure within the EU to focus on harmonising data requirements and standardising methodologies and we feel that that acts a little bit in opposition to the case-by-case approach to risk assessment. There are some issues of detail that we can work on with EFSA to improve the efficiency of the environmental risk assessment. Whether this will solve the big issue is quite another matter.

**Baroness Neville-Jones:** As a practical matter, how do you think you could start a debate on changing the approach?

**Professor Rosemary Hails:** That is a very good question. EFSA would be the place where the dialogue would need to start, as leaders of the process in Europe.

**Q31 Lord Hunt of Chesterton:** I was going to ask whether you can model this. You have risk assessment and then you have regulations, but the question is whether there are models both of the biological and the physical process of the effect of different kinds of regulation. You do experiments and you examine those in the laboratory and conceptually, but then how do you study the effects of different kinds of regulation, to put the question another way?

**Professor Rosemary Hails:** I guess the evidence is in whether or not the regulation is effective, in that applications that have been deemed to be safe or even beneficial for human health and the environment are then allowed to reach the market. I would say that would be the hallmark of success for a regulatory system.

**Lord Hunt of Chesterton:** I am thinking of the example of this box in Spain in which you were going to do the experiment. The way the question was answered was whether it does or does not fit within the regulation, rather than a scientific study of what would be the consequences if something went wrong and all the possibilities and how that would affect the decision. The decision would be made with a rich knowledge of all the possibilities that might emerge from a particular trial or experiment or whatever.

**Ms Camilla Beech:** That is included in the risk assessment process that the authorities undergo. When you apply you have to envisage all the potential scenarios that are both direct, indirect, short term and long term that could be a consequence of an organism being in the environment.

**Lord Hunt of Chesterton:** Do you think the risk assessors do that job very completely? It sounds as if in your olive fly experiment you did all your calculations but, before the decision was made, did the Government or European side look at your science and your calculations and did they test them?

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**Ms Camilla Beech:** I agree very much with Rosemary and Jeremy that the risk assessment process itself works scientifically. The problem that we face in Europe is a political overlay of the implementation of the regulations.

**Dr Jeremy Sweet:** Can I come back to your previous issue? One of the things that has been looked at in Europe, particularly by EFSA, which is taking a lead on this, is to try and switch the focus of risk assessment away from looking at whatever is regulated, whether it is a pesticide or a GMO, towards what we are really concerned about, which is the environment. We want to protect the environment, so whatever we put in it is a stressor on that environment and we need to look at it and see what the impact is. There are now discussions in EFSA and at other levels to try to harmonise the approach to risk assessment taken by the pesticide people, by the invasive species people—and maybe John can say something about this later—and by those dealing with GMOs. We are all trying to address the same concern that you are putting something new into the environment and, therefore, what is the environmental impact, how do you assess it and how do you come to a conclusion? There is a move to try and harmonise this approach and to move the focus away from looking at all the different technologies and saying the issue is environmental protection and let us build a framework that is focused on environmental protection. This is the way we are trying to move things in Europe at the moment, but it is very difficult because there are very strong political forces who say immediately, “You’re trying to hide the fact that it is GM by wrapping everything up into an umbrella framework”. I would like to see a one-stop shop, so that you produce something new and you say, “Let’s do an environmental risk assessment”, and everybody is following the same, agreed process. This would be the ideal solution, but that is too simple for regulators.

**Baroness Neville-Jones:** In your view, that would improve the risk assessment process. Would it actually deal with the issue of benefits or would that still lie outside?

**Dr Jeremy Sweet:** The risk assessments are always comparative. You are asking what the situation is now and how it will change when you put the GM organism or pesticide out there. In the case of GMOs, therefore, the baseline is the current situation. If what you are dealing with is a pest or a mosquito or whatever, then the baseline is pretty horrendous. What you are saying is that you have this really bad baseline and what happens when you put the GM mosquito or the GM olive fly out there, where does it move from the baseline? Of course it moves upwards and you can then assess across a whole range of environmental areas and see in most areas that it is moving up from that baseline. There may be one or two particular ecological issues that need to be ironed out but, on the whole, if you are comparing with the appropriate baseline, then to a certain extent you are looking at the benefit of what you are putting out there.

**Baroness Neville-Jones:** You are saying it would emerge from the process.

**Dr Jeremy Sweet:** This is what we do in the risk assessment.

**Q32 Lord Kakkar:** We have heard a lot about the regulatory framework and we have just heard that it could be improved, but also that it is reasonably good in comparison to those in other nations in the world. There is a political overlay beyond that where, once the scientific advice is provided based upon the regulatory framework, it goes into some system and is lost there. First, I would like to understand a bit more about the stage beyond the scientific assessment and the approval for a particular approach. Where does it go after that?

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Secondly, how would you propose dealing with that political roadblock beyond the independent scientific opinion to ensure that things move?

**Baroness Morgan of Huyton:** Can I ask a supplementary on exactly the same issue? To what extent do you think that Defra and probably BIS as well are sufficiently proactive in trying to move this forward at the EU level?

**Dr Jeremy Sweet:** You are the closest one to Defra!

**Ms Camilla Beech:** That is the second question. Do you want to start with the first question?

**Dr Jeremy Sweet:** I am not an expert on what happens in the political environment in Europe, but I have observed it for a long time. There are big political constraints in different European countries which are holding them back. The other thing that is not helpful is many European countries do not even have independent scientific committees. We are fortunate in the UK that we have ACRE and other committees and of course Europe has EFSA. There are a number of countries that have pseudo-scientific committees where all the scientists are directly employed by the Government or there are committees which will produce an opinion but then it is entirely overruled by Ministers, as happens just across the Channel from here. You have a very tricky situation where either the scientists are not able to express themselves or, if they do express themselves, they get overruled by politicians. That works its way up to the political decision-making process in Europe by the majority of states. There are a large number of states, such as the UK, which give scientifically based opinions, but unfortunately they do not carry a lot of political weight across Europe as a whole.

**Ms Camilla Beech:** A lot of countries take the opinions of some of the NGO groups and regard them with the same scientific weight that the opinions of EFSA and Defra are given, without the rigorous scientific evaluation of those comments. If you wanted to change the system in some way, it would be useful to level that playing field so that the scientific weight is equal on both parties.

**Q33 Lord Peston:** Most of the questions I was going to ask have already been asked by colleagues, which makes me quite fed up, but could I ask a more general question? To take an example, we regulate the financial sector because financial institutions have done enormous damage in our economy. Are there any examples at all of anybody in this field—GM or specifically insect GM—doing any damage at all up until now? Can you cite me an example of someone who has done some damage and therefore needs regulation?

**Professor Rosemary Hails:** If the regulatory system is working, that would not be the case. I would turn that question round and say that in the past agriculture has had an impact on the environment and some of those impacts have been very undesirable. GM crops are a part of that agricultural picture, so I think we should regulate them, but we should regulate them robustly and proportionately. One of the reasons why I feel we should move to a different trigger for regulation is that there may well be new farming practices in the future that are not captured by regulation which could further damage the environment. We need robust but proportionate regulation to protect the environment and human health.

**Lord Peston:** I must say, wearing my economics hat, that that sounds like regulation for the sake of regulating. You have not made any case to me as to why we need to regulate. It is always, "It might be and therefore we had better regulate". If I could add to that, if you construct some regulations and you get some regulators, what are they going to do to earn their income? They are going to regulate. How will they interpret regulation? They will

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interpret it as stopping things. That seems to me to be a way of destroying an economy, not a way of giving us the world we want.

**Professor Rosemary Hails:** We are an independent scientific committee.

**Lord Peston:** You are independent, yes.

**Professor Rosemary Hails:** We are not actually regulators. I would contest that what I was stating was regulation for the sake of it. I am also a member of the Natural Capital Committee, which has just finished and produced three reports that illustrate that the natural capital—the state of the environment—is in decline because of pressures on the environment. This is just one of the potential environmental drivers. We need to be better stewards of the environment.

**Dr Jeremy Sweet:** Just to add to that, one of the few good things about the European system is that, as well as looking at the impact of GMOs, we also look at the impact of the management of GMOs. That distinguishes Europe from other countries such as the United States of America. For example, within EFSA we have been looking very carefully at herbicide-tolerant crops because here you have two stressors, the GM crop itself and the fact that the herbicide regimes are changed by the management. You therefore have to look holistically at the impact of these and come to a conclusion. We have seen already in some areas of North and South America where there has been an extensive move to some of these herbicide-tolerant crops that there have been consequences for agricultural systems which we would not want to see in Europe. To a certain extent this came out experimentally in the farm-scale evaluation studies with which I think some of you are familiar, which showed that certain herbicide regimes could reduce botanical diversity and therefore biodiversity in farmland. If we introduce those systems, they have to be managed appropriately and not make the situation in farmland worse. These are the sorts of issues that need to be looked at very carefully. I come back to my original comment that regulation is there to protect the environment and therefore I think that it is justifiable. That would be my response to saying that we are overregulating, because we need to protect our environment.

**Ms Camilla Beech:** Perhaps I could add a little to that. When we are talking about genetically modified insects specifically, not GM crops necessarily, a lot of these species are invasive. They have come into our environments and they should not really be there. When you are considering—Jeremy was saying what the baseline is—regulating these, you have to decide what you want to protect in the environment and that is where we have political goals, because we do not really know what we want to protect. You say, “Protect the environment”, but what is it in the environment that we want to protect? Is it naturalness? Is it farmland? What are the end points that we want to protect? I would ask you to consider that point strongly when you are considering this inquiry.

**Lord Peston:** Do you not want to protect all the people dying of malaria in the poorest countries in the world? Should that not be the thing you focus on first and foremost?

**Ms Camilla Beech:** Absolutely and that is exactly what we are doing in Brazil where we have had very high success in reducing the amount of vectors in the environment with our technologies.

**The Chairman:** We are coming back to the benefits and disadvantages equation.

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**Viscount Ridley:** To follow on from that, we are not necessarily talking about protecting the environment but improving it in many cases. We have a damaged environment in all sorts of ways and we want to bring it back to something better. Surely we are not after the status quo in many of these cases.

**Professor Rosemary Hails:** Absolutely I would agree.

**Viscount Ridley:** I hope I am not treading on someone else's toes but, on the point about how we want to bring benefits into the regulation as well as risks, is this a general problem with the way the precautionary principle has been adopted in the European Union, that it essentially compares any new technology to Utopia rather than comparing it with the existing system?

**Professor Rosemary Hails:** I would say that the precautionary principle properly applied would also take into account the risks of not developing a particular technology and the benefits forgone. It is a misuse of the precautionary principle that has led us to this place.

**Viscount Ridley:** The way it has been specifically defined in the European Union does not include that.

**Professor Rosemary Hails:** No, that is right.

**Q34 Baroness Morgan of Huyton:** We are clear that you all think that, were we starting from scratch, a trait-based approach would be a better way of effective regulation. If we take that as a given, can you give us a little bit more explanation of why that works and where it works? You mentioned Canada. Why does it work better? If we did that, could GM insect technologies be separated from GM crops? Would that be helpful in your view or would that not be necessary if we had a different form of regulation?

**Professor Rosemary Hails:** The reason why I think it would work better is partly because it is more scientifically defensible. I can give you a crop and an insect example. We can produce herbicide-tolerant crops by different methods and some are captured by the regulations and some are not. It is the same with insects. We are producing sterile insects by different methods. Some are captured by the regulations and some are not. Moving to a trait-based system would not separate insects from crops; it would separate some insects from other insects and some crops from other crops. That is the first point. Also it would be more future-proof because the technology is developing rapidly and it would be very hard to word legislation in a way that would capture all potential new techniques. We might try and do it for now and we might be back here in five or 10 years' time with us having the same discussion. It would be more future-proof. That is why I think it would work. Of course, the Canadian system does appear to work well.

**Q35 Lord Patel:** My question is more general but I am also asking you to do a bit of crystal-ball gazing. It sounds from the evidence we have heard so far as if the current regulation is restrictive or even prohibitive, to the extent that it might prohibit development in science, let alone the application of that science. If this continues with the science now, where do you think the UK would be placed in 10 years' time? On the other hand, if the regulation was not so prohibitive and allowed for science and its application to flourish, where do you think we might be in 10 years' time?

**Ms Camilla Beech:** With our existing frameworks and the existing politicisation of the process, the EU and the UK are unlikely to benefit from GM insect technologies. We have

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tried in Europe already and have been knocked back in trying to achieve that. It is not that it is not going to happen, but it is going to be very difficult for a company to put forward applications in the current environment. If you change the environment and move to maybe a trait-based one, then it is untested of course, but we may have more opportunity for success. It is like reviewing a book as to whether it has been written on a typewriter or a computer and not on its content.

**Baroness Neville-Jones:** You paint a very powerful picture of interference with the system and none of you gives us any hope that that is going to change in short order, for all sorts of institutional reasons which you have set out. Can the opt-out system get us anywhere?

**Professor Rosemary Hails:** That remains to be seen.

**Baroness Neville-Jones:** What would be the nature of the opt-out that is likely to be developed and how far would it provide a basis, at least for field trials, in the UK?

**Professor Rosemary Hails:** Currently the opt-out system is just for the cultivation of GM crops.

**Baroness Neville-Jones:** If the legislation is for all varieties of genome, why could the principle not be extended?

**Professor Rosemary Hails:** The opt-out is to opt out of a decision made at the EU level. If a decision was made at EU level that a crop could be commercialised, a country could then opt out. That is my understanding.

**Q36 Lord Patel:** My question also had the science development component to it, because even if we were developing insect modification in mosquitoes to prevent the spread of malaria, we could not do it under the current regulation because the science would fall foul of the genome modification regulation. Am I correct?

**Ms Camilla Beech:** The genetic modification regulations work very well in the UK for contained use—for example, science in laboratories. A lot of laboratories in the UK are doing that and I believe we are a world leader in that area. That process is not subject to the same political constraints as releasing into the environment and therefore I do not think the UK would suffer if we continued to use GM insects in the laboratories. The concern is when we want to go to a wider scale in the environment.

**Lord Patel:** That takes me to a comment that Professor Hails made earlier about vaccine development. If you go to using reverse vaccinology to develop vaccines, which involves genome sequencing and then manipulating the genome side of that to produce vaccines, we can do the science but we cannot do the application of the development of vaccines by that process in the United Kingdom. Is that correct?

**Professor Rosemary Hails:** I do not see why we could not do it, because the regulatory system seems to have worked more effectively particularly for veterinary vaccines.

**Lord Patel:** But not for human vaccines.

**The Chairman:** I am concerned that we have the opportunity for Lord Vallance to ask his question.

**Q37 Lord Vallance of Tummel:** Turning to the commercial side of this—and perhaps this is one for Ms Beech—Oxitec Limited, a UK company, is the world leader in this technology and

Advisory Committee on Releases to the Environment (ACRE), Dr Jeremy Sweet, Sweet Environmental Consultants, and Oxitec Limited – Oral evidence (QQ 26-38)

it was acquired by Intrexon, which is a larger American company. What are the implications of that for the UK, if any? It would help us to understand it if we knew a little bit about how the acquisition developed. Who approached whom? The assumption might be that the Americans approached a smaller UK company, but there would be good reasons for a smaller UK company to approach the Americans.

**Ms Camilla Beech:** When you work in this space, you know the other people who work in this space. We knew about each other for a long time—two or three years—and it became obvious there would be some synergies if we got together. That is how the acquisition arose.

**Lord Vallance of Tummel:** A spontaneous transatlantic meeting of minds and no commercial side.

**Ms Camilla Beech:** No. You meet in scientific conferences. They are a leader in synthetic biology and we are a leader in the genetic modification of insects, so the minds meet—hopefully not mid-Atlantic. They are looking at a whole range of sectors as well—food, consumer, environment applications—and, knowing each other, it became obvious to share our common goals. It is securing funding for inward investment into the UK as well. We will remain in the UK and, while previously we had lots of small shareholders as a private company, we now have just one large shareholder. We will remain in the UK and we are increasing our footprint in the UK, so there will be inward investment into the UK as a result of this acquisition.

**Lord Vallance of Tummel:** In effect, you are saying that this is a benefit to the UK rather than having an independent UK company.

**Ms Camilla Beech:** It is a little early to tell because it is very fresh—the deal was only completed in September—but we believe that that will be the approach.

**Lord Vallance of Tummel:** Did the differential regulatory regimes in the UK, Europe and the United States play any part in the acquisition?

**Ms Camilla Beech:** No, not at all.

**Lord Vallance of Tummel:** You were not looking for reach beyond Europe.

**Ms Camilla Beech:** No. We have an application for mosquitoes in the US at the moment. That is one of the regulatory regimes that works well, but even then it has taken them quite a long time—five years—to work out what to do with mosquitoes.

**Q38 Lord Hunt of Chesterton:** Lord Patel asked about what the position might be 10 years from now. I am afraid to say that a lot of my European continental colleagues always look at the downside, but the fact is that there are dangers; we have lost elm and chestnut trees. Therefore it seems to me that the danger over the 10 years concerns what aspects of our biodiversity we will lose. Nobody seems to be playing this card as a way of preserving European biodiversity through this kind of technique. Nobody in Europe on the political green side addresses the dangers of just carrying on as we are. Is that something that you are pushing in your own discussions and presentations?

**Professor Rosemary Hails:** That is a very interesting point and for any one application that would be an element that would be brought in, both in the wider context and in the consideration of benefits. These potential benefits also extend to GM crops. If you use GM



Advisory Committee on Releases to the Environment (ACRE), Dr Jeremy Sweet, Sweet Environmental Consultants, and Oxitec Limited – Oral evidence (QQ 26-38)

crops that are insect-resistant, how does that compare with the spraying of insecticides? It might greatly reduce the non-target effects.

**Lord Kakkar:** Let me just come back to the opt-out system. If I understand it correctly, if some poor application manages to get itself all the way through European political bureaucracy and gets a positive opinion, the scheme will be for member states to opt out of that particular GM organism technology or whatever. Is there a way of a negative decision coming from Europe and a country such as ours opting in to use it nevertheless?

**Professor Rosemary Hails:** I am not aware of any such mechanism.

**The Chairman:** That brings us to the end of this session. We could have continued much longer. Thank you very much, particularly for the help in exploring the regulatory framework and the developments you would like to see us propose in the report. You have given us many leads. Thank you all very much.

## **Agricultural Biotechnology Council (abc) – Written evidence (GMI0018)**

The views expressed in this submission are those of abc – the umbrella organisation for the agricultural biotechnology industry in the UK. Comprising of six member companies, abc works with the food chain and research community to invest in a broad range of crop technologies – including conventional and advanced breeding techniques, such as GM. These are designed to promote the sustainable intensification of agriculture by tackling challenges such as pests, diseases and changing climatic conditions, whilst reducing water usage, greenhouse gas emissions and other inputs. The companies are BASF, Bayer, Dow, Monsanto, Pioneer (DuPont) and Syngenta.

### **Executive Summary**

abc welcomes the inquiry of the House of Lords' Select Committee on Science and Technology consultation on GM insects, particularly its recognition that "an important use of GM insects is in protecting crops, livestock and native species." abc believes that all GM technologies have a role in this regard, and that to succeed, integrated pest management needs as many tools in its toolkit as possible. The dysfunctional EU approvals process must be addressed if the UK, and Europe, intend to modernise and compete with at the world level on equal footing.

The focus of abc is on the promotion of innovative agricultural biotechnology and advanced breeding products. As such, this response is only concerned with the agricultural crop applications of genetically modified (GM) insects.

### **Call for evidence – questions**

**1. Which human diseases, across the world, could be addressed through GM insect technology? Are there any human disease risks in Europe, particularly the UK, for which GM insects are under development?**

n/a

**2. What are the possible livestock and agricultural crop applications of GM insects across the world? Of current livestock disease risks and agricultural insect pests that could be addressed through GM Insects, which should be the highest priority for Europe?**

n/a

**3. Opportunities and complementarity**

**a) Are there likely to be opportunities provided by GM insects that cannot be provided by other approaches, such as biological control methods?**

n/a

**b) How could GM insect approaches be complementary to existing Integrated Pest Management (IPM) programmes?**

- i. The global population is expanding rapidly – there are forecast to be 9 billion people on the planet by 2050, and critical resources such as land, water and energy will become scarcer. The challenge posed to the global food supply by climate change and the increasing population means that we need as many tools as possible to help us grow more food in a sustainable way.
- ii. Integrated pest management involves mixing and matching new and old technologies to achieve an appropriate control of insects with a minimal environmental footprint.
- iii. IPM also has an important role in preventing or delaying the build-up of resistance in the environment, known as resistance dilution. As such the use of GM insects could be a major new tool in the armoury of farmers; it will not obviate the need for others but could be used alongside insecticides, bio-pesticides, natural predators and GM insect-resistant plants.

#### **4. Regulatory frameworks**

##### **a) How appropriate are current EU and UK GMOs regulatory frameworks in addressing the issues raised by GM Insects?**

- i. Defra and its Advisory Committee on Releases to the Environment oversee the control and deliberate release of GMOs in England.
- ii. In terms of GM, abc believes that ACRE, the Food Standards Agency (FSA) and its Advisory Committee on Novel Foods and Processes (ACNFP) adequately oversee the application of EU regulation on GM in the UK.
- iii. However, the dysfunctional EU approvals process and its continued vulnerability to political interference by Member States mean that independent scientific evidence is not being utilised to inform the current authorisation framework.
- iv. This bottleneck at EU level means that Britain, and the EU, are falling behind in terms of food security and agricultural research, whilst countries such as China and Brazil set targets for greater proportions of their GDP to come from agricultural biotechnology.
- v. The inability to register GM products and difficulties in conducting field trials in the EU is pushing the UK-based biotechnology companies and research base to leave overseas.
- vi. For the use of GM insects to become a reality, as with GM crops, a higher political priority should therefore be given to increasing the efficient processing of applications for GM authorisations. GM products should be put to vote without delay, recognising that any safety concerns associated with a product have already allayed with the scientific evaluation carried out by the European Food Safety Authority.

- vii. The European Commission should also continue to seek a reasonable science-based path forward to resolve this gridlock, which is accepted by a majority of Member States, but ensures a freedom of choice for farmers.
- viii. The current plan devised by the Commission to nationalise market authorisations of GM crops for feed and food use is not a solution, and demonstrates a lack of understanding of where in the regulatory approval system the problems lie. It risks jeopardising our farming and import industries, destabilising the UK's agriculture and food sector, our largest manufacturing sector while also undermining the single market, one of the EU's fundamental principles. The near unanimous opposition expressed by the Member States in ongoing discussion at the European Parliament and Council shows that these flaws are evident. Quite simply, such an undermining does nothing to improve the confidence within the science fraternity that Europe is the best place to invest in biotechnology solutions to the many problems that exist in agriculture.

**b) Are there lessons to be learnt from the regulation of GM insects in other countries such as Brazil?**

n/a

**5. Do the World Health Organisation (WHO) guidelines on the release of GM mosquitoes provide the basis of an effective regulatory framework? How should issues regarding the emergence of resistance be considered?**

n/a

**6. Do the European Food Safety Authority (EFSA) guidelines on the environmental risk assessment of GM Insects for commercial use sufficiently address the different risks from population suppression and population replacement approaches? How should the ecological risks and human benefits that might arise from the application of gene drive techniques to population replacement approaches be assessed?**

n/a

**7. How is research into the development of GM insects currently funded? Are there opportunities to attract more private investment into this area?**

n/a

**8. Given the possible public health benefits of GM insects, should the Government be funding their commercialisation? Would this result in a conflict of interest with regard to regulation of releases? If so, how might this be managed?**

n/a

**9. How could the UK benefit economically from both developing GM insect technology and its use within the UK?**

- i. While abc cannot comment on the economic benefits of GM insects, the economic value of the entire agricultural biotechnology sector is significant. Research teams across the UK are global leaders in this field. They are developing agronomic systems and technologies that combat pests and disease, help crops to respond to

a changing climate and increase agricultural productivity per hectare using fewer resources like water, fertilizer and fuel.

- ii. From laboratory discovery through to farm-scale cultivation, crops go through a typical technology development cycle. The UK has a particular strength at the early discovery stage of R&D. This success drives private and public investment in the UK which is relatively high compared to other EU countries. For example, the Biotechnology and Biological Sciences Research Council (BBSRC) spends around £445 million per year on biotechnology and biological sciences.
- iii. However, under the current system, UK innovations are not able to benefit the UK – since the majority cannot be commercialised in Europe, and in many cases nor imported back into Europe. Not being able to fully realise the benefits of research has an inevitable impact on future investment and undermines the stability of our academic success in the sector.
- iv. To quantify the contribution of the agricultural research base, abc commissioned a report titled *Going for Growth* on the potential economic opportunity presented to the UK by agricultural technology research and innovations. It received significant support and input from across the agricultural technology sector, including the NFU, National Institute of Agricultural Botany (NIAB) and public research institutes including Rothamsted Research and The Sainsbury Laboratory.
- v. Through the report, abc was able to engage very positively with the Government and is fully supportive of its Agricultural Technologies Strategy. However, the worsening authorisation delays are further slowing UK innovation, a situation likely to deteriorate should the EU review into GM decides to impose even greater restrictions.

## 10. Public concern

### a) How can the gap between regulatory approaches and public concerns over GMOs be addressed?

- i. According to the most recent biannual public attitudes tracker by the Food Safety Authority, only 7 per cent of responses listed GM foods as a concern when unprompted, down 1 per cent from 8 per cent in the previous tracker. The level of concern is still low when prompted, finding that just 24 per cent are worried about GM foods (FSA, 2015).
- ii. Attitudinal surveys have consistently shown that British consumers worry less and less about GMOs in food and drink (Eurobarometer, 2005-2010).
- iii. An EU funded study of public perceptions of agricultural biotechnologies (CSEC, 2001) carried out in five European countries showed that participants did not react so much to genetic modification as a specific technology. Their main concern related to the institutional context in which *innovations in general* are developed,

evaluated and distributed. Indeed, respondents expressed a deep distrust in regulators, scientists, media and commercial actors' ability to anticipate or monitor risks once the product or technology is on the market.

- iv. The erosion of public confidence in the decision-making process has been widely acknowledged. Regarding agricultural GM technology, abc believes that greater transparency and a reliance on sound scientific evidence will help to stem public distrust. As will the strict application of existing regulation.
- v. Despite falling consumer concern, regulation in many ways is going in the opposite direction, as demonstrated by the current plans by the European Commission to nationalise authorisation process of GM crops for import.
- vi. abc strongly opposes this approach as it will inevitably lead to arbitrary, ideology-based, disproportionate and discriminatory decision-taking.
- vii. abc also firmly believes that all those involved in food production and distribution have a role in alleviating public concerns over GMOs. By providing factual information to consumers on GM and other forms of agricultural technology, the food and feed chain hopes to give UK consumers greater confidence in the science and safety of agricultural technologies so that informed decisions can be taken on the future role for such innovations in the UK.

**b) Is there a role for 'responsible innovation' approaches?**

- i. abc considers that all stakeholders share a co-responsibility for innovation. However we believe that once a product is deemed to be safe to the consumer and the environment, it should be the consumer who should decide the future of a product through purchasing decisions. In the case of GM insects, since the insect is not the "product" to be consumed, there is not the need to convince a consumer to eat the product, but conversely, the consumer therefore does not have the "purchasing" to pronounce their views on the subject.
- ii. In the end, all EU-authorized GMOs have been proven safe before their placing on the EU market. This has been concluded by the European Food Safety authority (EFSA) in collaboration with Member States for each individual GMO present on the market, on a case-by-case and step-by-step basis.
- iii. There have been two European Commission reports on the effects of GM crops on health and the environment. Representing more than €300 million of investment in research over 25 years, the studies have shown no scientific evidence associating GMOs with higher risks than conventional plants and organisms.
- iv. GM crops bring vast benefits to the environment. With the advent of technology, farming has become more efficient in its use of inputs such as plant protection products, water, fertilisers and energy. GM technology has significantly contributed to optimising pesticide application (by up to 37 per cent) and increasing yields on the same amount of land by up to 22 per cent. Other

environmental benefits include reduced ploughing and tilling which are crucial for combating soil degradation and erosion, and are facilitated by herbicide tolerant GM crops. Reduced ploughing, tilling and optimised pesticide use practices are widespread and increasing in countries where GM crops are cultivated, while still very rare in the EU. In 2013 alone, GM crops cultivated around the world contributed to saving greenhouse gas emissions equivalent to taking 12.4 million cars off the roads for one year.

- v. Despite this, the malfunctioning GM approvals process continues to put the UK and Europe at a significant disadvantage and current plans to nationalise import authorisations for food and feed have will a devastating effect on the agricultural biotechnology sector and the UK's agriculture sector more widely.
- vi. Choosing to allow individual Member States or regions to ban safe products based on undefined criteria is a clear signal that the EU Commission no longer stands by science and evidence-based decision-making, a critical precondition for growth, innovation, investment, as well as consumer confidence and safety.

**c) What are the critical factors in effective public engagement from lab to final release?**

n/a

*18 September 2015*

## **Agricultural and Horticultural Development Board (AHDB) – Written evidence (GMI0015)**

The Agriculture and Horticulture Development Board (AHDB) is a statutory levy board, funded by farmers, growers and others in the supply chain and managed as an independent organisation (independent of both commercial industry and of Government).

Our purpose is to make agriculture and horticulture industries more competitive and sustainable through factual, evidence-based advice, information and activity

AHDB has a position statement on the Genetic Modification of Crops and Crop Protection Agents which can be found at <http://www.ahdb.org.uk/news/documents/AHDB-GMpositionv504Nov12updated.pdf>

### **1. Which human diseases, across the world, could be addressed through GM insect technology? Are there any human disease risks in Europe, particularly the UK, for which GM insects are under development?**

Potentially any insect transmitted human disease could be addressed through the use of GM insect technology, however, the current modifications have only been applied to a limited number of species in a few genera so it is by no means certain that all species would be suitable targets.

### **2. What are the possible livestock and agricultural crop applications of GM insects across the world? Of current livestock disease risks and agricultural insect pests that could be addressed through GM Insects, which should be the highest priority for Europe?**

AHDB feels that globally there are many potential opportunities to exploit GM insects to address a range of livestock disease risks and crop pests. For livestock an important target would be the control of a range of Culicoides species which vector bluetongue and Schmallenberg virus infecting livestock in the UK and throughout Europe. Other potential targets related to livestock would be flies in buildings and also blowflies in sheep where in field trapping has been tried in the past. Area-wide treatment with GM flies could be used to depress populations below damaging levels.

The range of potential targets for crop pests is significantly greater and could deliver benefits not only in crop production but potentially in the protection for the wider environment against non-native species e.g. pine and oak processionary moths. Introduced species such as *Tuta absoluta*, a pest of tomatoes in glasshouses or *Drosophila suzukii* (spotted wing drosophila) a recently introduced pest affecting a wide range of soft fruit crops that are causing significant crop damage and financial losses would be key targets for this technology. Other high priority pests that could benefit from the application of this technology are cabbage stem flea beetle, cabbage root fly, pollen beetle and brassica pod midge and diamond back moth. Some of these targets have already been genetically modified for sterility or are currently under development. These suggested targets assume that the technology which has been developed in Diptera, Coleoptera and Lepidoptera can be reliably applied to other species in these orders.



**3. Are there likely to be opportunities provided by GM insects that cannot be provided by other approaches, such as biological control methods? How could GM insect approaches be complementary to existing Integrated Pest Management (IPM) programmes?**

Spotted wing drosophila (SWD) is currently causing major issues for the soft and tree fruit industry and despite the investment of many millions of pounds globally there are a limited number of chemical controls available and as yet no effective biological controls. The UK and other countries rely heavily on biological controls for the majority of pest control for soft fruit in polytunnels but with no suitable biological solutions for SWD means the use of conventional crop protection chemicals can severely disrupt these programmes leading to significant extra cost (typically in the order of thousands of pounds per hectare) . Given that SWD is an alien species in many regions of the world, it is particularly suited to a Sterile Insect Technique (SIT) GM insect approach, since its eradication would restore the correct ecological equilibrium rather than disturb it as it would if it were a native species. Conventional SIT would also potentially provide the same solution although would probably be slightly less efficient and costly due to impact of irradiation on the competitiveness of the treated flies and the additional infrastructure required to produce them.

The use of GM insects may also provide other opportunities for development of less impacting IPM approaches than would otherwise be possible with conventional chemical control currently used against pests such as diamondback moth and flea beetle etc.

**4. How appropriate are current EU and UK GMOs regulatory frameworks in addressing the issues raised by GM Insects? Are there lessons to be learnt from the regulation of GM insects in other countries such as Brazil?**

The broad regulatory framework used within the EU and the UK appears to be sufficient to assess the human health and environmental risks that could result from the use of GM organisms. Clearly the original framework was developed for the assessment of organisms other than insects but it is sufficiently robust to provide a meaningful assessment of the risks although for “public good” releases there is no requirement to comment on the benefits that may accrue from the release. Regulations and frameworks developed in other countries such as Brazil and Australia could provide useful additional thinking in this area. Any assessment would need to be tailored to the specific modification and the application of the insect along with the potential risks arising from it. As with all assessments it is not just the framework but the way in which it is carried out, such as the provision of robust, publicly available evidence and data that would provide additional reassurance that the process was as thorough as possible.

**5. Do the World Health Organisation (WHO) guidelines on the release of GM mosquitoes provide the basis of an effective regulatory framework? How should issues regarding the emergence of resistance be considered?**

The WHO Framework provides a well-considered approach to the risk assessment, analysis and management of the release of GM mosquitoes. The framework has the benefit of considering not only the costs and benefits of the releases but also addresses the issue of efficacy of the organisms in achieving the desired goal. Another interesting approach to evaluating the desirability of the release suggested in the WHO framework is to look at whether the GM insect approach has a greater or lesser impact than the current control being implemented i.e. the relative impact rather than an absolute one. The approach that

is promoted is a phased approach to the risk assessment each building on the last phase with a “go, no-go” decision being made at each stage

The approach to community engagement is dealt with in some detail and highlights the need for appropriate ethical practice in engaging with individuals and communities. As with many other interventions it is likely that the final decision to implement a field trial or full scale implementation will be taken by a government agency rather than the local population since that will be the relevant authority for the regulatory approval.

Whilst the Framework appears adequate in covering a very large number of issues it will ultimately depend on how well the evidence is gathered and whether suitable tests are developed, undertaken and ultimately deliver high quality data and evidence. One of the key parts will be the development of a suitable test for the type of modification in question and whilst there are currently only two main types, it is highly likely this will increase in number in the future. The framework is a starting point and there is therefore still much to be done before an adequate assessment could be completed.

Resistance is covered in the framework both on the part of the mosquito but also the pathogen. As with insecticide resistance, the development of resistance to the transgene will be very difficult to predict, so a rigorous programme of monitoring of both native and released populations is suggested in the framework. This will enable any change in the frequency (or rate of change in frequency) of any resistance to be detected and used an indicator to prompt appropriate action within any programme.

**6. Do the European Food Safety Authority (EFSA) guidelines on the environmental risk assessment of GM Insects for commercial use sufficiently address the different risks from population suppression and population replacement approaches? How should the ecological risks and human benefits that might arise from the application of gene drive techniques to population replacement approaches be assessed?**

The EFSA guidelines for GM Insects (and other animals) provide a robust framework for the assessment of risk potentially associated with the release of these organisms and take account of the risks posed by either population suppression or replacement especially with regard to potential ecological disturbance in food chains. Population replacement poses its own potential problems but the scope of the risk assessment appears to adequately capture those in the guidelines. The assessment of ecological risks for population replacement activities will differ depending on the species in question and its origin i.e. native or alien although the bulk of the assessment is likely to be common. At its simplest the ecological impacts and human benefits could both be assessed on an economic basis although it would be important to capture non-market values of the environment that may be affected too, however results using this approach would be likely to have a high degree of uncertainty attached to it. Any impact would of course need to be made against a baseline so thorough knowledge and understanding of the current situation is vital before any intervention is made. For insects acting as vectors of either plant or health diseases modification to prevent transmission could deliver significant value to human health or crop production without a significant wider impact on the environment i.e. the species could continue to exist and therefore there could be little or no ecological disturbance. Any organism so modified would of course need to be assessed to see that its behaviour and/or fitness was not unduly

affected by the modification, something that might lead to significant non-target ecological changes. Capturing the benefits of population suppression and reduction would be an important step towards providing a cost benefit assessment rather than just a risk assessment. A comparative assessment of the risks and impacts of using existing management techniques with those associated with the introduction of the GM organism would potentially provide a better measure whereby the use of one technology might be favoured over another. If the impacts of introducing a GM organism were less than the existing methods then it would seem logical to favour the GM approach assuming that it was still able to deliver the same or greater benefits.

**7. How is research into the development of GM insects currently funded? Are there opportunities to attract more private investment into this area?**

Our current understanding is that development of GM insects and related technologies is achieved through a mixture of private, public and charitable funding including RCUK studentships and research grants, Innovate UK grants, Gates funding of GM mosquito research and implementation and companies such as Oxitec. Private investment is a possibility but probably works best for population suppression, where there are continued sales to keep populations below damaging levels. Gene drive approaches may be more appropriate for a public funding approach where a single release may achieve the desired outcome into the future. Currently investment into the area is targeted on GM organisms that address issues in those countries where it is possible to use GM approaches without undue public concern and can offer significant human health or commercial benefits.

**8. Given the possible public health benefits of GM insects, should the Government be funding their commercialisation? Would this result in a conflict of interest with regard to regulation of releases? If so, how might this be managed?**

As an organisation we are not in a position to say whether government should or should not fund the commercialisation of GM insects. However, the important question here relates to whether government can both fund and regulate without a conflict of interest. Government does already fund development of technologies through the Biomedical Catalyst that will develop therapies for patients where the regulatory body is the government. There is scope for conflict of interest but using the same safeguards used for other regulatory bodies i.e. arm's length approach using independent members and declaration of any conflicts of interest should mitigate any risks in this area. Inevitably many of those most able to understand the technology and inform the process are likely to have interests in the field either in academia or industry. Managing the risks associated with those having a vested interest in the process is important so the inclusion of independent specialist and lay members may go some way to providing balance and transparency.

**9. How could the UK benefit economically from both developing GM Insect technology and its use within the UK?**

The benefits to the UK accruing from the use of GM insects are potentially very large. To give an example it is estimated that the potential losses from spotted wing drosophila in the fruit industry (strawberries, raspberries, blueberries, blackberries, cherries, blackcurrants etc.) are between £80-120 million pounds per year at current levels of production and given current trends in production could rise to £135-235 million in 5 years. Whilst these losses are not realised because of existing control operations these compromise the use of

biological control for other pests in fruit systems and can result in the need for repeat releases of biocontrols resulting in an additional cost of thousands of pounds sterling per hectare.

The potential for the UK to benefit from the development and deployment of GM insects is already in the early stages with Oxitec exploiting the commercial potential of GM mosquitoes for dengue control in Brazil. With the very large range of potential targets for this technology the constraint for economic benefits is likely to exist around the regulation and public acceptability than the potential deployment of the technology

**10. How can the gap between regulatory approaches and public concerns over GMOs be addressed? Is there a role for 'responsible innovation' approaches? What are the critical factors in effective public engagement from lab to final release?**

A good first step would be to clearly explain the rationale for the approach being taken i.e. the problem being addressed is particularly intractable or difficult to solve using existing approaches and a novel solution offers the only prospect for progress. It is important that this is not developed as a solution looking for a problem! Credible, evidence-based communication is key the factor, which openly acknowledges public concerns and seeks to address them. The development of public engagement throughout the process, from the early stages of discussions around using the technology, programme planning and design right through to implementation, is very important as is a clear assessment of the relative risks and costs and benefits to all stakeholders.

The careful selection of targets i.e. by focussing on the right problems first such as non-native species where the ecological impacts of eradication are much reduced would appear to be preferable to selecting endemic species where impacts on food webs could be far greater. Targets that offer significant benefits to the general public (disease vectors) are also likely to be more acceptable targets.

*18 September 2015*

Dr Marcia Almeida de Melo, Federal University of Campina Grande, Dr Professor Paulo Paes de Andrade, Federal University of Pernambuco and Dr Amaro de Castro Lira Neto, State Institute for Agronomy (IPA) – Written evidence (GMI0006)

**Dr Marcia Almeida de Melo, Federal University of Campina Grande,  
Dr Professor Paulo Paes de Andrade, Federal University of Pernambuco and  
Dr Amaro de Castro Lira Neto, State Institute for Agronomy (IPA) – Written  
evidence (GMI0006)**

[Written evidence to be found under Dr Professor Paulo Paes de Andrade](#)

**Professor Luke Alphey, The Pirbright Institute, Professor Paul Eggleston, Keele University, and Professor Austin Burt, Imperial College London – Oral evidence (QQ 48-55)**

*Evidence Session No. 5*

*Heard in Public*

*Questions 48 - 55*

TUESDAY 27 OCTOBER 2015

Members present

Earl of Selborne, Chairman  
Lord Cameron of Dillington  
Lord Fox  
Lord Hennessy of Nympsfield  
Lord Kakkar  
Lord Krebs (co-opted)  
Baroness Manningham-Buller  
Lord Maxton  
Duke of Montrose  
Baroness Morgan of Huyton  
Baroness Neville-Jones  
Lord Patel (co-opted)  
Lord Peston  
Viscount Ridley

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Lord Taverne

**Examination of Witnesses**

**Professor Luke Alphey**, Head of Arthropod Genetics Group, The Pirbright Institute, **Professor Paul Eggleston**, Professor of Molecular Entomology, Keele University, and **Professor Austin Burt**, Professor of Evolutionary Genetics, Imperial College London

**Q48 The Chairman:** Welcome to our three professors who have kindly joined us today. We are most grateful to you. I am sure you are aware of the inquiry we are conducting on GM insects. Today we hope to hear particularly from you about the science behind GM insect technologies. You need to be aware that we are being broadcast on the web camera. Would you like to introduce yourselves and if anyone would like to make an introductory statement, please feel free to do so?

**Professor Luke Alphey:** Thank you for inviting me to your inquiry. I am Luke Alphey. I lead the arthropod genetics group at The Pirbright Institute. I know from previous hearings that you are aware of Oxitec. I co-founded that company in 2002. I was the research director

Professor Luke Alphey, The Pirbright Institute, Professor Paul Eggleston, Keele University, and Professor Austin Burt, Imperial College London – Oral evidence (QQ 48-55)

there until early last year, and then a board member until the recent acquisition by Intrexon. Also, I have been involved in regulatory affairs and public engagement in various countries, including in the recent EFSA and WHO deliberations.

**Professor Paul Eggleston:** Good morning and thank you for inviting me as well. My name is Professor Paul Eggleston; I am professor of molecular entomology at Keele University and currently faculty research director. My background is very much in genetic engineering technologies for insects, predominantly mosquitoes.

**Professor Austin Burt:** Good morning. I am Austin Burt, professor of evolutionary genetics at Imperial College. I am also the principal investigator for Target Malaria, which is a not-for-profit research consortium trying to develop novel approaches for malaria control.

**Q49 The Chairman:** Thank you for that. If none of you wishes to make an introductory statement, I will start with a very general question. I am sure you will have noted from earlier evidence sessions that we have been informed of some of the underpinning science. Could each of you give us your understanding of the underpinning science behind population suppression? We will come to population replacement later, but if you could give us your version, in as clear a way as you can, as to how population suppression GM insect strategies might be underpinned by science?

**Professor Luke Alphey:** In the underpinning science there is a great deal of overlap between suppression and replacement. In each case you need to be able to make modified insects using transformation technology. Associated with that is the ability to rear the insects, sometimes in quite large numbers, and handle them in the lab, which is not the case for all insect species.

Of course, for population suppression you are trying to impose some sort of fitness load. You are trying to put some sort of lethal, sterile or perhaps sex ratio-distorting factor into the target population.

On the underpinning science for using these sorts of systems, what I have talked about there is more on the molecular biology/synthetic biology side—what sort of modification you want, what trait and how you are going to construct that. You could turn that around and look at it more from the field point of view, and say it is applied ecology, population genetics and population dynamics and how you are going to interfere with the target population, and that the synthetic biology aspect is merely the nuts and bolts, or cogs for the machine that is going to do that. So there are a number of ways of looking at it, and the underpinning science for all of that is pretty general. Most of it was developed not for these particular applied purposes but drawn from fundamental science carried out for other reasons.

**The Chairman:** Could you give us an indication as to how long ago this might have been implemented originally?

**Professor Luke Alphey:** Radiation-based sterile insects have been used for at least 50 years. There is a paper on population replacement from 1968, long before molecular biology, so these ideas have been around for a long time. It is one of the areas perhaps where theory is somewhat ahead of practice in synthetic biology, which is not that common.

**Lord Fox:** Turning to the other side, population replacement, what is there in addition, or that is different, and how will the effect of gene-editing techniques change the game for you?

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**Professor Paul Eggleston:** On population replacement, as Luke has already mentioned, a lot of the basic underpinning science is the same. The intention with population replacement is to make a change to the insect and then try to force that altered insect into the natural environment to replace what was there before. The idea would perhaps be that you change a population of mosquitoes that was capable of transmitting disease for one that was not. A key difference here is that the insects would remain within the environment.

A key difference in the underpinning science here is that when you make the sorts of changes that we are talking about in a genetically modified insect, the end product is likely to be less fit, in a Darwinian sense, than what was there before. There is an argument that we may well need to alter the strategy for the release of these modified insects by using something that has become known as a gene drive system. Put very simply, that means, instead of having normal genetic inheritance, you bias the inheritance in favour of retaining the modified insects as opposed to the natural ones. By doing that you can change the nature of the population and, in theory, cause the modified insects to spread.

There are fundamental differences in the genetics and the ecology, but one key difference is that you would not end up with an empty ecological niche. You will have insects there at the beginning and at the end, and therefore food supplies for organisms that eat those insects.

**Lord Fox:** Do gene-editing techniques change what you can do and give you more things you can change?

**Professor Paul Eggleston:** It provides another set of tools we can use. There will be applications in which it might be particularly useful and there may be other applications where, I hesitate to say, more traditional genetic engineering techniques might still be preferable.

**Lord Fox:** It opens up more opportunities?

**Professor Paul Eggleston:** It opens up more opportunities, yes.

**Professor Austin Burt:** I want to clarify, this distinction between suppression and replacement is orthogonal to the issue of whether you drive something through or you inundate a population. You can do inundation with either replacement or suppression, and you can do inoculative drive with either replacement or suppression.

**Lord Fox:** In one case you flood the population.

**Professor Austin Burt:** Yes, inundate.

**Lord Fox:** In the other, you weigh the balance in favour of the genetics and the trait you want.

**Professor Austin Burt:** In the other one, you release a relatively small number and then over a period of generations that triggers a response.

**Lord Fox:** Because you bias the survival rate or whatever.

**Professor Austin Burt:** Each of those implementation modes—inoculation versus inundation—can be used for suppression or replacement, although I think a better term would be modification.

**Professor Luke Alphey:** To expand on what Austin was saying, you think of the outcome you are trying to achieve, whether you are trying to reduce or eliminate the number of the target population—that is suppression—or you are trying to modify them in some way, such as



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spreading a trait through the population that makes them less likely to bite humans and less able to transmit malaria or insecticide resistance; any trait that you may want to spread, short of killing them. The one we talk about most is to make the mosquitoes less able to transmit a pathogen, for example dengue virus.

Replacement looks similar: you still have mosquitoes out there filling their ecological niche, biting people, but less able to transmit disease. In suppression, the outcome is there are far fewer mosquitoes, perhaps none, and that is how you control the disease. How do you go about doing that? As Austin said, in either one you could have a so-called self-limiting genetic system that only stays out for a relatively short period of time, unless you supplement it by releasing more, or you could have a more invasive, or self-sustaining genetic system that will persist for a long time, perhaps increase in frequency locally and spread geographically of its own accord.

**Lord Krebs:** Following up on Professor Burt's comment, as we look over the next decade or so, do you feel that the two approaches you describe—inundation and inoculation—are going to be pursued in parallel or do you think that eventually, one will come to be shown to be more effective than the other?

**Professor Austin Burt:** I imagine there will be different purposes for each one. For malaria in rural Africa, an inoculative approach would be very powerful. In other more confined settings that you want to target, an inundative approach would be fine too. It depends on the goal, the disease, the setting and the target.

**Baroness Neville-Jones:** I want to be clear, in these various techniques you have been talking about—inundation and inoculation—are we talking about actual use already or field trials or laboratory experiments? I want to know exactly what is happening and how far these things have been taken in practice.

**Professor Austin Burt:** Oxitec has carried out field trials of inundative releases of mosquitoes. No inoculative release has been done. There have been proof-of-principle experiments in the lab but no field release.

**Viscount Ridley:** Are there some insects for which population suppression will not work? As I understand it, it is based on the Sterile Insect Technique, whereby once an insect has mated it cannot reproduce, as it were, or the female would not go back and try again to reproduce. Are there some for which that technique will not work?

**Professor Paul Eggleston:** There are some for which it would be more difficult. It highlights something we have touched on a little bit. All of these strategies depend on insects breeding. If you are planning any release of this kind, you need a pretty good understanding of what the breeding structure of those populations might be. For example, mosquitoes that are transmitting malaria in Africa exist in nature in ways which might make population suppression quite a difficult route to take and may favour the choice of a population replacement strategy. It depends very much on the biology, the breeding patterns and the population structure of the insects you are working with.

**Viscount Ridley:** Can you give us an idea how much more effective at suppressing populations GM insects could be than the conventional irradiated Sterile Insect Technique?

**Professor Luke Alphey:** Compared with conventional approaches as well—it is hard to make a direct comparison with radiation. The radiation Sterile Insect Technique worked very well in some particular species—New World screwworm, Mediterranean fruit fly—and these are

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ones where it has been possible to find a sterilising dose of radiation that does not weaken or incapacitate the insects too much. That has proven difficult with mosquitoes. With some insects it would be very difficult to run an effective, or at least economic radiation-based sterile insect programme at all. Compared with other conventional methods, an expert mosquito control district estimated that, with the best of current methods, they could suppress *Aedes aegypti* by 30%; if they hit it with absolutely everything, maybe 50%.

**Viscount Ridley:** This is using pesticides?

**Professor Luke Alphey:** Yes, using pesticides, chemicals, breeding site restriction and that sort of thing. All of Oxitec's field trials, even on a relatively small scale, have shown more than 90% suppression of the target mosquito populations.

**Lord Maxton:** Is it very largely mosquitoes you are talking about, or have you done trials with other insects as well?

**Professor Luke Alphey:** It is certainly not only mosquitoes, although they get most of the attention. A range of agricultural pests is certainly in development and either in or approaching trials. In fact, the first Oxitec collaborative field trial of GM insect release anywhere in the world was in Arizona, of a pink bollworm, which is a moth that attacks cotton, so it is not just mosquitoes.

Of course, that also comes back to which approach is more useful. As I said, for population replacement the most commonly talked about modification is something which will make a mosquito less able to transmit disease, and clearly that is appropriate for plant disease vectors, and animal as well as human ones. You can imagine doing that. If you think about the caterpillars which eat your cabbages, the damage they are doing is from direct feeding and it is not obvious what trait you would try to spread which would reduce that harm. Population suppression seems a more obvious approach to take in that case than for something that is transmitting a disease. Again, the nature of the insect and the harm it does might point you more to one strategy than another.

This comes back to what Austin said earlier. There are some cases where you want to treat a particular population and not another one, perhaps even nearby, and there a spreading system would be less appropriate. There are others where you have a very diffuse population and the economics point towards something that will spread itself. So all of these approaches will likely co-exist going forwards.

**Q50 Lord Krebs:** If I could change tack slightly, I want to ask the witnesses about the evolution of resistance and whether they think that is a significant concern with any of the techniques that we have been discussing and, if so, what consequences it might have for efficacy or the environmental risks.

**Professor Paul Eggleston:** Can I just clarify what you mean by resistance in this context?

**Lord Krebs:** I will give you an example. The Wellcome Trust says: "Resistance would be expected to evolve both to the drive mechanism (eg mutations in the genomic region you were targeting making the drive mechanism ineffective) and towards any genetic trait you were modifying (eg the ability to resist a particular pathogen)."

**The Chairman:** Target malaria, too, identified that resistance to the gene drive mechanism might arise.

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**Professor Luke Alphey:** Resistance is an issue for any technique—and you can finish the sentence there—not just the ones we are discussing here.

**Lord Krebs:** Yes, but obviously we are particularly interested in the ones we are discussing.

**Professor Luke Alphey:** My point is, yes, certainly it is an issue for these methods but in no way uniquely to these methods. Clearly, it is also an issue for chemicals or whatever. *Aedes aegypti* breeds in a particular type of container and you could fill it with concrete and it would evolve resistance to that, not by breeding in concrete but by changing its breeding sites and so on. It is a very wide issue. If you think about engineered sterile insects, you could imagine a situation where you are putting some sort of fitness-reducing gene—lethal, sterile or whatever—into the population, and that is generally the case for population suppression. You could imagine ways in which an emerging genetic factor in the wild population could make that sterilising or fitness-reducing effect less effective. You could also imagine more of a behavioural response. If the wild females, let us say, can differentiate between modified and unmodified males, there would be strong selection for ones that preferred to mate with the unmodified ones.

**Lord Krebs:** Certainly, I recognise your comment that the evolution of resistance applies to any technique that is used to control pests in the natural environment or elsewhere. Do you have any insight as to whether evolution of resistance is more or less likely to occur in, let us say, RIDL technology or in the kind of technology that Austin Burt has been developing using genetic drive, or can one not say at this stage?

**Professor Luke Alphey:** The fewer moving parts of a sterile insect method, the less prospect of resistance. Because you are releasing new batches repeatedly, you can monitor and also change things relatively easily.

With population replacement, where you have a drive and then separately a beneficial trait that you are trying to spread through the population, you have more separate parts that could become detached or stop working. One of the really elegant things about what Austin has been doing is using the drive directly so there is no additional beneficial trait to it, which reduces the number of working parts and reduces the possibilities for resistance, but Austin can talk about that better than me.

**Professor Austin Burt:** Overall, I would say it is too early to say whether resistance is more or less likely to evolve compared to a chemical. What I would say is that when you get resistance to a chemical, often it is a whole class of chemicals that they become resistant to, so that takes them off the table. There is a possibility that the genetic approaches will lead to resistance to a specific construct, and by tweaking the construct it would be able to get around the resistance. However, that is a hunch, not something we have proved.

**Professor Paul Eggleston:** In some ways we have talked about two different kinds of resistance there. The first is the breakdown of genetic technology, which could happen in a variety of ways. If you think instead, for example, of engineering an insect with a molecule that is designed to kill a parasite or a virus, then the parasite or the virus can evolve through natural selection and develop resistance to that particular intervention. The way that we might need to get around that problem is thinking of slightly more complex strategies. I usually think of them as multi-hit approaches so that you do not have all of your eggs in one basket. It would be more difficult for an insect to evolve a resistance mechanism to. It is analogous to using combination drug therapy for pathogens.

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**Lord Krebs:** Could you unpack that a little bit further and tell us what the complementary approaches might be?

**Professor Paul Eggleston:** I will use my own work as an example. If you are trying to engineer an insect to introduce a molecule that will kill malaria parasites, for example, there are a variety of ways you could do that, but if you chose just a single way and built your engineered insect with a single trick that killed parasites, then those parasites are really quite adept at evolving ways around blockages in their transmission. A single intervention such as that may be something that parasites could work their way around. If you engineered your insect with two or three independent approaches that tackled the parasite or the pathogen from a number of different angles, it would be more difficult for those parasites or pathogens to evolve resistance. It is similar to combination drug therapy.

**Lord Peston:** Could you clarify one thing? The fact that resistance develops, it does not follow logically, or for that matter ethically, that you should not do it, does it?

**Professor Paul Eggleston:** No, as scientists we would all agree.

**Lord Peston:** It simply makes the problem more difficult and there may be different ways of dealing with it. I understand from the drugs that most of us take—a drug such as penicillin was the greatest boon, and if it had only come earlier it would have saved George Orwell's life. But it is the bacteria that develops the resistance, so the pharmaceuticals have to go on spending tons of money inventing new antibacterials, but that is what they are supposed to do. Does the same logic apply to your field?

**Professor Paul Eggleston:** Absolutely.

**Lord Peston:** You would not like to leave the message, “Let all these people die because resistance develops”?

**Professor Austin Burt:** Quite the contrary, resistance evolves because you are having an effect.

**Lord Peston:** I just wanted you to say it.

**Lord Fox:** Professor Eggleston, you were touching on what I wanted to speak about. It seems that inoculation gives you more and different tools. If you are going to have a multiple set of things within your organism, rather than inundation, it is inoculation where you have multiple choice, in a sense; is that wrong?

**Professor Paul Eggleston:** I do not think that is necessarily true. The strategy you adopt is worked up in the laboratory. You develop an insect with a range of attributes that you think might be useful for controlling that disease, for example. Part of that strategy has to be to make a decision on how you intend to deploy it. If you intend to deploy it as an inundative release, you would not need to couple it necessarily with a drive mechanism, although that might help, but I do not think it makes a difference in the way you have suggested.

**Lord Patel:** While it is interesting to go into this debate, we are now indulging in pretty speculative science. The science of resistance on population reduction is understandable because we know where the science is, but when we talk about trying to change the genome of an insect in several different ways to increase its resistance or ability to be an effective vector, let us say for malaria, the amount of genome you are changing is so great that you are creating a completely new organism. Can you give us some examples that will work?

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**Professor Paul Eggleston:** If you wanted to, you could build a piece of DNA in the laboratory that was designed to do two things. It could express a protein in the mid gut that damaged parasites or you could have a different protein that was expressed in the salivary glands. These are key regions where malaria parasites, particularly, are moved around. This could all be engineered as part of a single construct. It might be a relatively large construct.

**Lord Patel:** Exactly.

**Professor Paul Eggleston:** Then it could be introduced at one particular place in the genome of the insect, so that it does not change the rest of the biology of the insect.

**Viscount Ridley:** What do you mean by relatively large—1% of the genome?

**Professor Paul Eggleston:** No, tiny—tens of kilobases of DNA. Small in relation to a genome.

**Professor Luke Alphey:** You are talking about 10,000 or 20,000 bases for an organism such as *Aedes aegypti*, which has 1.4 billion bases, something like that.

**Professor Paul Eggleston:** A tiny fraction.

**Professor Luke Alphey:** Another way of looking at it would be, two or three functional genes in organisms that have tens of thousands of functional genes.

**Professor Paul Eggleston:** We already introduce multipart cassettes, and so you could have an effector gene designed to kill malaria parasites, for example, and a different part of that construct would be a marker gene designed to produce fluorescence so you could identify the modified insects. It is a relatively straightforward path.

**Lord Patel:** Can you explain to me about a vector, let us say, for carrying malaria? You are altering its gene to kill the bacteria or virus, for any disease but let us say malaria. An insect is just a vector and it is not affected by the disease itself, so you modify the insect to be not just a carrier or a vector but to deal with the disease-carrying parasite.

**Professor Austin Burt:** There are two approaches that have been taken here. One is to put in an effector gene, so an antiparasitic peptide that will put a hole in the membrane or a single-chain antibody that will coat the parasite in a particular way and which will impede its progress through the mosquito. That is to put something additional into the mosquito which disrupts the parasite. Alternatively, you can remove or try to knock out a gene in the mosquito that is useful but not essential for the mosquito but is essential for the parasite to get through the mosquito. For example, there could be a receptor in the mid gut that is recognised by the parasite and is needed to get through the mid gut, or a receptor in the salivary glands that is recognised by the parasite to get through into the salivary glands. You could add something to the mosquito and work on that and see what can be found, or you can try and knock out a gene in the mosquito which then renders it unable to transmit the malaria.

**Professor Paul Eggleston:** Either way the insect would cease to be a vector. In the case of malaria, if you have an intervention that stops sporozoites getting into the salivary glands, when that mosquito bites someone they will not get malaria. You are tackling what is a very complex parasitic disease with stages in insects and in humans by tackling it in the insect, which is possibly a better way of doing it than by tackling it in people, where you have billions of circulating parasites. There are much smaller numbers inside a mosquito and it is perhaps easier to kill them off there.

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**Q51 The Chairman:** There is public concern about resistance. Everyone is familiar with the concept of chemical insecticides becoming ineffective and whole classes of compounds no longer being effective. What you are proposing is recoded, modified interventions, whereas perhaps a vector develops resistance so you remodify, as I understand it. Is this not yet another version of the arms war? Should we not be as concerned?

**Professor Paul Eggleston:** It is absolutely a version of the arms war but any kind of intervention against vector-borne disease is an arms war. None of us working in this area would think of these technologies as being the sole solution or a magic bullet. They are always going to be part of an integrated set of approaches which, for example with malaria, will include bed nets and insecticide treatments and everything else we can throw at it, but GM technologies might just add another range of tools. However these things are deployed, there is going to need to be monitoring and surveillance of how the genetic changes are faring in the natural environment. If there is evidence of some kind of breakdown, or a deletion or some kind of rearrangement that stops it working, I do not think that makes it necessarily any more risky; it just stops it working, so you have to have another release strategy in train to bring forward and help with the disease transmission.

**Q52 Viscount Ridley:** Can I change the subject to commercialisation? Professor Alphey, you have built up a very successful business around population suppression. How far away is the prospect of doing the same around population replacement? As a corollary to that, is there even a business model that works because one of the problems, as I understand it, with population replacement is that you only have to do it once. If you release it once you have solved the problem and you can go home. Is there a viable business model there?

**Professor Luke Alphey:** I doubt that we will do it once and solve the problem and go home. That does not mean there is not a viable business model—I do not think any of us is claiming that—I think there is, but in particular circumstances or for particular types of insect. Where you are looking at the more extreme invasive genetic systems where you are seeding them across an area and then they will spread through the whole species or species complex—Austin can talk about this better—it is hard to see anything other than a philanthropic or government basis for that. It is hard to see a conventional revenue-generation business model for that. There are other population replacement or gene drive-type systems which are anticipated to be more local, so you can treat one area and not another area, and it will persist in one area but not spread to another, at least in simulation models. There you might easily see a more conventional business case and therefore more private sector involvement. As you say, the one-time release big impact will still need monitoring and maintenance and perhaps the development of replacements and so on for it, if and when it breaks down, but I think it is hard to see a commercial business case for those more invasive genetic systems. However, that is not every case.

**Viscount Ridley:** Is someone going to be selling gene drive population replacement at some point, even if only for the Gates Foundation to apply or whatever? Is that going to be at the point where we are using it in the near future?

**Professor Austin Burt:** For those of us working on gene drive for population suppression for malaria, we do not see a business model where there can be a profit generated from it. We are not going down that route at all.

**Viscount Ridley:** But you do see application in the near future?

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**Professor Austin Burt:** Yes.

**Viscount Ridley:** Give us a timescale, if you can.

**Professor Paul Eggleston:** Five to 10 years.

**Professor Austin Burt:** I think our Gantt chart gives a timeframe of 2028-30, something like that, when we might get rollout in a country. There is huge uncertainty on this. A lot of it is over the regulatory aspect and how long that is going to take. This is a long-term thing. It is not happening tomorrow.

**Q53 Lord Patel:** I will take my question in stages and it relates to safety issues. I am sure you are all familiar with the kind of concerns that are raised on safety issues, including horizontal gene transfer, damage to ecosystems, the production of virulent strains, et cetera. Which ones do you think should be of most concern?

**Professor Luke Alphey:** They are all legitimate issues to look at and all of these have to be looked at on a case-by-case basis. Not just in the case of a regulatory agency but, as developers of these technologies, we would ourselves look at as wide a range of risks, or potential hazards I should say, as we can imagine, and go through them one at a time and think how feasible they are and to what extent we can get around them by design. Resistance relates to that. Some designs would be less amenable to resistance evolution than others. One of the good aspects of some groups opposed to these kinds of technologies is that you get an external, sceptical eye cast on this which can potentially provide things that people who are more favourable to the technology may not have thought of, at least in principle. You get as large a list of these things as you can, which will include all the ones you have suggested and more, and then for your particular case or application go through them and think how feasible they are—if they are feasible—what you can do to mitigate them and how that relates to the benefits and so on. To go through such a list here is inevitably going to be rather superficial.

Horizontal gene transfer, which has been talked about a lot, is probably not such a big concern. A lot is known about natural horizontal gene transfer and it seems unlikely to be a major issue for any of the technologies that we are talking about here.

The impact on the ecosystem is probably the biggest area of discussion—and that is, “What if it works?” as well as “What if it does not?”, but especially, “What if it works?”

For population suppression, if you eliminate the target species from a particular location, is that a good thing? It is probably a good thing in some ways, such as reducing disease transmission, but does it open a niche for another intake to come in? Does it have some disruptive effective on the ecosystem? The answer could be dramatically different, even for the same species, in one place than in another. If you imagine an island over here where it is an alien invasive species relatively recently introduced, you might imagine eliminating it to be an environmental benefit, in addition to any reduction in disease transmission there might be. However, in this other place over here, in its native range where perhaps the same species is a more integrated part of the ecosystem and is providing some ecosystem functions, eliminating it might be much more of an issue from an ecosystem point of view than over there. It is very case-by-case for those things. You mentioned the evolution of virulence, and to my mind the suppression approach, where you are trying to take out the vector, will have only an indirect effect on the pathogen and is unlikely to cause issues in that direction, which is not to say we should not think about them. Certainly, where you are

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trying to modify the insect in a way that makes it less able to transmit, that brings in a third player in these multiple evolutionary responses, being the pathogen, and you certainly have to think about those issues.

**Professor Paul Eggleston:** The pathogens are very able to modify the virulence themselves, whether we are talking about normal or genetically modified insects. It does not change the risk profile there at all.

The other thing I would like to add is all of this is tied up with some of the regulatory issues that we might touch on later. My own view is that all of this is about a balanced approach to risk versus benefit, and people's perceptions of risk versus benefit differ depending on where they live. In the work I did in Mali, for example, local people and scientists there had a slightly more balanced view than you tend to get in western Europe. The current regulatory system does not put enough emphasis on what the potential benefits might be. There is a risk that worrying overly about all of these risks means we will never ever be able to do anything. That is a personal view, but I think it is pertinent.

**Professor Austin Burt:** I would just reiterate that it has really got to be taken on a case-by-case basis.

**Lord Patel:** Can you put these worries about safety issues in the context of using alternative methodologies such as insecticides?

**Professor Paul Eggleston:** In the longer term they will not work.

**Lord Patel:** Do we not have examples of using insecticides, chemicals, to reduce the population?

**Professor Paul Eggleston:** Yes, but if you throw a poison at any natural population, in time it will develop resistance. We have populations of mosquitoes now that are multiply resistant to virtually everything that we have, and that situation is not going to get any better. It is one of the drivers for thinking about developing technology of this kind. Insects will become resistant to insecticides. Parasites will become resistant to the drugs you try to treat them with. We need more tools, not fewer, to be able to tackle the problem of disease transmission.

**Professor Luke Alphey:** One of the differences and perhaps benefits of genetic insect approaches relative to chemicals is specificity. Most chemicals have a relatively broad spectrum effect. In other words, they will be toxic to quite a wide range of insects. That varies from one to another, but they are unlikely to be specific to a single species, whereas for GM insect approaches, the control agent is now not a chemical; it is a modified insect, and it interacts with the wild population through mating. Modified males will only mate with females of the same species, so that initial contact and effect is very species-specific. That feature of these technologies is a real strength from an environmental point of view. When you go back to the question, "Where are they good and where are they not?", it is a potential limitation in other areas. If you were a farmer whose crop was being eaten by a dozen different pests, you might prefer something a bit more broad spectrum than a dozen different species-specific interventions. That species-specific nature means that GM insect methods are likely to be more useful where you have a single dominant pest species—whether that is in agriculture, conservation, human health or wherever—than where you have whole slew of different things doing the same kind of damage, where something more broad spectrum might be more appropriate.



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**Lord Hennessy of Nympsfield:** How difficult is the science that lies behind the forecasting of unintended consequences in your specialist fields? Is it the same as it is for most other scientific activities or are there particular perils here? As you said earlier, it goes to the heart of the confidence question on the spectrum of public confidence/public anxiety, around which the question of regulation always swells. Is it particularly difficult in your trade, because it still strikes me that what you are doing is wonderful stuff but it is very early days?

**Professor Luke Alphey:** It is relatively early days for gene drive systems, although even there, by analogy, there are some things you can look at. We know quite a lot about natural selfish DNA systems that have these sorts of properties. For sterile insects it is a little simpler because we have a 50-year history of the use of radiation-sterilised insects which are extremely similar operationally, so we perhaps know rather more about that. One of the big advantages when we started developing genetically modified sterile insects—although, obviously, we were going on a rather cautious step-by-step basis of lab, cage, small field trial—was that we could see these very large programmes using radiation-sterilised insects which told us about the operational issues, also some issues about resistance and managing that. For example, the New World screwworm was eliminated from a continent by a rolling programme of release of radiation-sterilised insects so we have vast experience of the field use of sterile insects.

**The Chairman:** Professor Eggleston, you make the observation that it is a question of assessing risks against benefits. Would it be more accurate to say it is a question of assessing potential benefits against potential disbenefits?

**Professor Paul Eggleston:** Yes, that is fair.

**The Chairman:** I think that is an important distinction.

**Professor Paul Eggleston:** It is, but most of the regulatory issues that we all battle with focus on perceived risks, many of which the scientists think are negligible, and there is not often that much emphasis put on what the benefits might be. As I was saying, if you are living in a disease-endemic country you might have a slightly different view on that balance of risk versus benefit.

**Viscount Ridley:** Following up on the risk/benefit balancing question, this is a theme we have heard from a number of witnesses and written submissions. It was taken up by a House of Commons Committee, and one of the responses from the Government was to say: “Ordinarily this would seem a sensible approach. However in the EU context it could result in a disproportionate requirement to assess the potential socioeconomic benefits of novel crops.” This is talking about crops. “This would add a further layer of complexity, burden and subjectivity to the regulatory process.” In other words, if you have to start enumerating the benefits you are stuck in the regulatory hell for longer.

**Professor Austin Burt:** I would not go to a Government in sub-Saharan Africa with this idea of a genetically modified mosquito and not talk about malaria. That does not make sense.

**Viscount Ridley:** Is this a slightly defeatist response from a government department?

**Professor Austin Burt:** I cannot talk about the crop situation.

**Professor Luke Alphey:** It has been suggested that the developers should say what the full socio-economic impact would be, which would be like asking developers of mobile phones to have predicted micro transactions and so on, which I think is ridiculous, frankly. I can see

Professor Luke Alphey, The Pirbright Institute, Professor Paul Eggleston, Keele University, and Professor Austin Burt, Imperial College London – Oral evidence (QQ 48-55)

some things in the direction you are talking about that would be undesirable but, as Austin says, if you are developing mosquitoes to try to prevent malaria or dengue or crop pests or whatever, how could you not talk about the benefits? If you are not talking about the benefits and the reasons why you are doing it, how will you persuade anybody it is worth doing? At that level it does not make any sense.

**Q54 Baroness Morgan of Huyton:** Can I take you back to commercialisation for a minute? It is particularly appropriate to have Professor Alphey here because we have heard repeatedly, and certainly to my surprise, that your company was literally the only one in a UK context that has been involved in developing any of this technology at a commercial level. What we want to know, and we have heard some of this from previous witnesses, is whether the UK is supportive enough of the development at a commercial level of these technologies, particularly from the early stage to the next stage of development, where there seems to be a particular problem. Also—this is particularly directed to you, Professor Alphey—to what extent was the sale of the company driven by the business environment here, or was it the only natural partner?

**Professor Luke Alphey:** I should have said in my introduction that I am speaking in a personal capacity. I do not represent Oxitec or anyone else.

**Baroness Morgan of Huyton:** You are absolutely not, which is why it is handy to have you here because you understand the history, which is helpful to us.

**Professor Luke Alphey:** Oxitec is the only such company in the world, not just in the UK, so to that extent if the only such company in the world started in the UK, then there must be something good here.

**Baroness Morgan of Huyton:** The science might be good though, might it not?

**Professor Luke Alphey:** Precisely. I think the key benefit is the science base and the expertise in these general areas. Though perhaps not in this particular inquiry, I am sure this Committee is thinking about science funding going forward. What makes the UK attractive from this point of view is the strength of the science base, and I would say the BBSRC was the key to this, although other agencies were involved.

The key disadvantage is the lack of a local market. Business 101 would say start with a local market and expand from there, but we do not have a local market for GM insects. If we had set up Oxitec saying that we were going to sell GM insects in Europe, never mind in Britain, we would not have had investment—to the point that we would not have asked, I would not have asked, I would not have tried. One does not know how many other businesses have not started because of that. I do not see how one could know. The fact is it is impossible to sell this technology in Europe at the moment. Field trials, perhaps, but there seems to me no possibility of getting commercial registration in a reasonable time, or even having any idea how much time or money it would take. That is probably the biggest negative factor.

There are some things along the way. Although it is very small scale, the support of Innovate UK—the TSB as it used to be—for small companies is very valuable, and R&D tax credits are very helpful. For those relatively early stages, there is a good economic environment, albeit perhaps a little at risk at the moment. I feel I may not have answered every part of your question.

Professor Luke Alphey, The Pirbright Institute, Professor Paul Eggleston, Keele University, and Professor Austin Burt, Imperial College London – Oral evidence (QQ 48-55)

**Baroness Morgan of Huyton:** What needs to change? I suppose this is for Professor Burt as well, in a sense, because you were clear that yours had to be not for profit.

**Professor Austin Burt:** At the moment our core funding is from FNIH in the States—so it is overseas—which is part of a Gates Foundation programme. It is a complicated project that goes all the way from protein engineering and molecular entomology to field ecology and community engagement, specialists in risk analysis and things such as that. It is complex and not many funding sources are able to take on the challenge of funding something with so many moving parts. They have been very good to us over the years.

**Professor Paul Eggleston:** For any kind of commercialisation, there has to be a financial model that works for the business. Luke can correct me but Oxitec's business model, essentially, is that they can get rid of these mosquitoes for the same or less than the cost of insecticides. If you are talking about endemic diseases in poor countries, there is no financial model, and why would a company get involved in developing these insects when they have got no market to sell them to? The situation in Europe might change, let us say with climate change; if some of the arboviruses we see in southern Europe start to spread dramatically, that could create at least a governmental market. Or let us say Bluetongue becomes an even bigger problem across Europe; again, Governments might then want to find the money to try to commercialise tools to combat those diseases. In Europe, it is hard to see where the business model currently would come for most of this, unless it is agricultural pests.

**Professor Luke Alphey:** It is not that there is a lack of credible targets or targets that would benefit from this technology in Europe. We do not have a lot of vector-borne disease that we worry about, although there is some in political Europe. However, for agricultural pests, yes, absolutely, there are many relevant targets, but it would not be economic to work through the regulatory processes at the moment. That was clear when I was looking for investment for Oxitec right at the beginning to start up the company. When we talked to European-based investors, they felt that the risks associated with developing and commercialising this technology were rather high and, correspondingly, were disinclined to invest.

**Baroness Morgan of Huyton:** Primarily because of the regulatory environment.

**Professor Luke Alphey:** Yes, even though we were not talking about selling the insects in Europe. It was the atmosphere, the environment in which they lived, not so much the market we were talking about, whereas I think the first US-based investor we talked to invested. It was not that we were making a different pitch to the two. It is the view of GM in Europe which has this chilling effect on the investor community as well, because they think, "You will never be able to do that", or, "It will take too long or be too expensive".

**Lord Maxton:** You mentioned cotton and that was almost the first of the insects released. That must have been commercial. If you can find an answer that stops an insect destroying a cotton crop and the cotton crop develops, that is a commercial argument, is it not?

**Professor Luke Alphey:** Yes, I agree. That trial was done in collaboration with the US Department of Agriculture. In the US, some of these big insect control programmes are run by the government effectively on an infrastructure basis. They would see that as infrastructure investment dealing with this, particularly if it is an invasive pest.

**Lord Maxton:** It was done by them and not by a private company, in other words.

**Professor Luke Alphey:** Correct—a collaboration between the USDA and Oxitec.

Professor Luke Alphey, The Pirbright Institute, Professor Paul Eggleston, Keele University, and Professor Austin Burt, Imperial College London – Oral evidence (QQ 48-55)

**Q55 Lord Cameron of Dillington:** I am a farmer and you mentioned various possibilities of applications in the agricultural world. I am interested also in the natural environment. Professor Burt mentioned that it is unlikely that we will see a rollout of the antimalaria GM insects until 2030, so I am asking you to take a big leap forward here. What other applications can you see in agriculture? We have a pollinator problem at the moment. Could insects be increased or maybe even vaccination of wild animals? Tuberculosis in badgers springs to mind. Equally, if you are talking about lots of long-term benefits, maybe there are disbenefits. What possibility is there that countries could use insects as weapons and release them? What are the possibilities here long term?

**Professor Luke Alphey:** There are many potential applications that might become available over different timescales. *Drosophila suzukii*—the spotted-wing drosophila mentioned in a previous session—is a recent invasive pest into the UK which attacks soft fruit. These sorts of things would be potentially amenable to the technology that Oxitec is developing. The technical strain could be available in the very short term. We discussed the regulatory issues but from a technical perspective a strain could be available in short order.

You mentioned pollinators—so on rather longer timescales, and we have not really talked about beneficial insects. We have all talked about trying to do bad things to bad insects, but, potentially, you could think about doing good things to good insects. On insecticide resistance, a simple idea is to protect pollinators against agricultural uses. For example, neonicotinoids in bees is quite a big issue in Europe at the moment. What if we could make the bees more resistant to those or other classes of chemical that they might contact? If we could protect them against particular chemistry, could we use that chemistry against the varroa mite, for example? That is another area you might think of.

There are some bumble bees that are very good pollinators, but there are restrictions on using non-native bumble bees because of the threat to native bumble bees. What if you could engineer some sort of reproductive isolation, the sterility type things we have talked about for other purposes, into a pollinator, so then you could use a non-native pollinator in a new area, knowing that it would not be able to establish? Invasive species are a huge problem for conservation and biodiversity in any number of different places and some of those are insects, so what about controlling those? Those might be the same technologies as we are talking about here, but for a conservation biology target rather than a human health target—so, a pretty wide range.

**Lord Cameron of Dillington:** The downsides, weapons, is that a possibility?

**Professor Luke Alphey:** That is pretty hard to see.

**Professor Austin Burt:** I am not clever enough to think of one.

**Professor Luke Alphey:** In anything other than the most invasive gene drive systems, deployment would be a very visible and continuous thing, where it is pretty hard to imagine it being done in any way. It would be much easier to move a wild, non-native insect around than it would be to use a modified insect in some way to intervene against a wild population, I think.

**Professor Paul Eggleston:** It is worth bearing in mind that any of those applications is some way off because the tools and technology for these other insects are nothing like as well developed as they are for mosquitoes.

Professor Luke Alphey, The Pirbright Institute, Professor Paul Eggleston, Keele University, and Professor Austin Burt, Imperial College London – Oral evidence (QQ 48-55)

**Viscount Ridley:** That feeds in nicely to what I was going to ask. Can you see this technology being used in invertebrates other than insects to control invasive species, particularly signal crayfish or killer shrimps, which are problems in this country? They are arthropods.

**Professor Paul Eggleston:** Transformation of prawns and shrimps is feasible. I can remember from years ago someone telling me how easy it was to make a transgenic prawn. I have not done it myself but in principle, yes, that could be done in terms of the signal crayfish.

**Viscount Ridley:** What about grey squirrels?

**The Chairman:** I think that is an interest you have not yet declared.

**Professor Paul Eggleston:** I am sure you could make a genetically modified squirrels using the mouse technologies that are quite well developed.

**Professor Luke Alphey:** There certainly is interest. When I mention conservation biology, of course invasive insects are a problem, but rodents on island populations cause devastation, and there are people certainly interested in controlling rodents. Currently that is done with toxic baits and the like, but there is certainly an interest in the application of genetic technologies in those areas as well, which would be analogous, although obviously the molecular detail might be a little different.

**Lord Fox:** Would RIDL not work?

**Professor Luke Alphey:** It would certainly be population suppression; we will have to see about the exact mechanism, but it would likely be some form of sterility, or sex-ratio distortion.

**The Chairman:** We have come to the end of the questions we wish to put to you. Thank you very much for the full and helpful way you have answered them. There will be an opportunity to correct the transcript. On behalf of the Committee, thank you once more for helping us this morning.

## **BioIndustry Association (BIA) – Written evidence (GMI0026)**

### **Summary**

- The UK is a global leader in science and research. In line with its Industrial Strategy the Government has made significant investment in synthetic biology, a field that has diverse applications including healthcare and agriculture, and great potential economic and societal benefits.
- Oxford university spin-out company Oxitec Ltd has developed and commercialised innovative insect control solutions, and has recently been acquired by US-based company Intrexon Corporation. Oxitec will not only retain its UK R&D presence and skilled staff, but expects to make further investments in both people and facilities in the UK in the coming months.
- The business deal highlights excellent science and research that is being undertaken in the UK, and will send a positive signal: a) to other companies, encouraging them to invest and grow in the UK and potentially to list on the public markets; and b) to the investment community, stimulating additional interest in UK biotechnology from specialist and cross-over investors.
- Therefore, while it is still ‘early days’ for the UK’s synthetic biology industry, it is important that the Government continues its sustained strategic support (for life sciences and the Chancellor’s Eight Great Technologies) to enable emerging companies to grow, and help the UK to maintain its leading position. To give researchers and investors the confidence to develop and invest in emerging technologies in the UK, the importance of an evidence-based policy and regulatory climate must not be underestimated.

### **BIA response**

1. As the UK trade association for innovative bioscience enterprises, the BioIndustry Association (BIA)’s members include emerging and more established bioscience companies, pharmaceutical companies, academic research and philanthropic organisations, as well as service providers to the UK bioscience sector.
2. BIA runs specialist industry groups in two of the ‘Eight Great Technology’ areas identified by the Chancellor George Osborne, namely synthetic biology and regenerative medicine. Notably, one of BIA’s member companies, Oxitec Ltd, is directly involved in research and development (R&D) and commercialisation in the field of genetically modified (GM) insects.
3. BIA therefore welcomes the Committee’s inquiry into Genetically Modified Insects. We understand that Oxitec have submitted a detailed response to this inquiry, and BIA’s comments will focus on the broader life science and biotechnology business environment in the UK.

*The UK's supportive environment delivers innovative biotechnology*

4. As set out in BIA's submission to HM Treasury ahead of the 2015 Comprehensive Spending Review<sup>14</sup>, the UK is a global leader in science research, with a wealth of metrics to evidence our current strong position. Furthermore, our globally competitive tax environment helps to make the UK an attractive location for life science business investment.
5. The Government's industrial strategy - including the Strategy for UK Life Sciences and the Chancellor's focus on Eight Great Technologies including synthetic biology - has been welcome. This support, which has already helped to create a solid UK foundation in this promising area, includes: strong leadership through the Synthetic Biology Leadership Council (SBLC) and the Synthetic Biology Roadmap for the UK (published in 2012 and currently being updated); government investment so far totalling over £60 million; research centres and centres for doctoral training around the UK including the SynbiCITE Innovation and Knowledge Centre; the Knowledge Transfer Network special interest group; and overseas trade missions supported by UK Trade & Investment.
6. Described as "the design and engineering of biologically based parts, novel devices and systems as well as the redesign of existing, natural biological systems<sup>15</sup>", 'synthetic biology' is a term that defines a broad range of R&D with diverse applications including healthcare, agriculture, fine chemical production and more. Continued long-term commitment from the Government will enable UK researchers and companies to maximise the economic and societal benefits the field presents.
7. In June 2015 BIA published a report, Celebrating UK Bioscience<sup>16</sup>, which set out several case studies of UK bioscience that are delivering benefits to humanity. One of these was the example of Oxitec Ltd, a company spun out of research at Oxford University in 2002, whose work developing insect control solutions has applications in both healthcare (tackling disease vectors) and agriculture (tackling pest-related crop damage). Using advanced genetics and molecular biology, Oxitec has developed a new and innovative solution to controlling insect populations through the production of 'sterile', self-limiting insects whose offspring do not survive. Unlike conventional approaches to insect control using insecticides that can affect the broader ecosystem, Oxitec programs are directed at a single species.
8. The community and funding bodies involved in UK synthetic biology place particular emphasis on responsible research and innovation (RRI)<sup>17</sup> to address ethical, legal, societal and environmental considerations. However, some technologies and applications risk being politicised in response to perceived public concerns. To give

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<sup>14</sup> BIA (2015) *Submission to HMT for Spending Review 2015* <http://www.bioindustry.org/document-library/bia-submission-hmt-2015-csr/>

<sup>15</sup> *Synthetic Biology Roadmap for the UK* (2012)

<https://connect.innovateuk.org/documents/2826135/3815409/Synthetic+Biology+Roadmap+-+Report.pdf>

<sup>16</sup> BIA (2015) *Celebrating UK Bioscience* <http://www.bioindustry.org/document-library/celebrating-uk-bioscience/>

<sup>17</sup> SynbiCITE, Responsible research and innovation <http://synbicite.com/content-panels/responsible-innovation/>

researchers and investors the confidence to develop and invest in emerging technologies in the UK, and to fully benefit from the supportive frameworks and investments that the Government has already put in place, the importance of open dialogue and an evidence-based policy and regulatory climate must not be underestimated.

9. In August 2015, Oxitec was acquired by US-based company Intrexon Corporation. According to the press release, Intrexon intends to integrate its synthetic biology platform to advance Oxitec's existing initiatives to protect communities from diseases like dengue fever as well as against agricultural pests that impact food supply worldwide.
10. For Oxitec and their venture capital investors, the deal is an exciting one. Oxitec will not only retain its UK R&D presence and skilled staff but expects to make further investments in both people and facilities in the UK in the coming months. The deal also highlights the type of excellent science that is being undertaken and the highly innovative emerging companies and technologies that pose an investable prospect for potential buyers and investors in the UK and elsewhere.

*Government investment, and supporting companies to scale up*

11. Valuable provision is made for synthetic biology start-up companies, for example via the Rainbow Seed Fund<sup>18</sup> and incubator space at centres like SynbiCITE<sup>19</sup>. However, beyond start-up stage, considerably greater finance is required for companies to scale-up their activities.
12. Companies usually raise capital investment in progressive rounds or 'series'. One issue that is often cited by companies as a major difference between the UK and US life science business environments is that there is simply more investment capital available in the US.
13. Successful business deals like Oxitec's will send a positive signal: a) to other companies, encouraging them to invest and grow in the UK and potentially to list on the public markets; and b) to the investment community, stimulating additional interest in UK biotechnology from specialist and cross-over investors.
14. Therefore, while it is still 'early days' for the UK's synthetic biology industry (and likewise, for healthcare biotechnology companies, which are just recently experiencing an uptick in investor activity), in time a thriving business and investor community can develop in UK bioscience. There are signs of positive business activity currently ongoing within the UK synthetic biology industry.
15. The Oxitec deal illustrates that there is a supportive foundation for future UK R&D in synthetic biology; in just the last few years the UK's infrastructure and networks for synthetic biology have grown considerably. Now, to build upon and maximise

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<sup>18</sup> Rainbow Seed Fund <http://midven.co.uk/funds/rainbow-seed-fund/>

<sup>19</sup> SynbiCITE <http://synbicite.com/>



opportunity from the investments the Government has already made, it is important that this Great Technology continues to be the focus of sustained strategic support to enable emerging companies to grow and thrive.

We therefore call on the Government to continue its long-term support for UK science

16. BIA's submission to HM Treasury ahead of the 2015 Comprehensive Spending Review sets out:
  - a. The fact that – due to the interconnected nature of the life sciences ecosystem – publicly funded research underpins and is vital to the later translation and commercialisation of products that deliver economical and societal benefits
  - b. To maintain the UK's global competitiveness, continued long-term government support for science, research and innovation is essential
  - c. The norm in some of the UK's competitor nations is for state funding to support the R&D pathway beyond basic R&D and closer to a point at which projects are less risky and more investable to private investors
  - d. The Government's Biomedical Catalyst scheme (one of several Catalyst schemes including the Industrial Biotechnology Catalyst) is an excellent example of the power of public funding to de-risk early stage development and leverage additional private finance.
  
17. Our Spending Review evidence focuses on the Biomedical Catalyst but in the synthetic biology field the Industrial Biotechnology Catalyst has been relevant and beneficial to many projects. This kind of non-dilutive funding is extremely valuable to companies not just in terms of the initial finance boost but also in delivering wider benefits (such as job creation) and stimulating additional private investment, as set out in a recent BIA report<sup>20</sup>.

*September 2015*

### **About the BIA**

Established in 1989, the BioIndustry Association (BIA) is the UK trade association for innovative bioscience enterprises. BIA members include emerging and more established bioscience companies, pharmaceutical companies, academic research and philanthropic organisations, and service providers to the UK bioscience sector. The BIA also runs specialist industry groups in two of the 'Eight Great Technology' areas identified by the Chancellor George Osborne, namely synthetic biology and regenerative medicine.

Our members are responsible for over ninety per cent of biotechnology-derived medicines currently in clinical development in the UK and are at the forefront of innovative scientific developments targeting areas of unmet medical need. This innovation leads to better outcomes for patients, to the development of the knowledge-based economy and to economic growth. Many of our members are small, pre-revenue companies operating at the translation interface between academia and commercialisation.

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<sup>20</sup> BIA (2015) *The Biomedical Catalyst: Making the case to continue* <http://www.bioindustry.org/document-library/the-biomedical-catalyst-making-the-case-to-continue/>

## British Ecological Society (BES) – Written evidence (GMI0024)

*‘A world inspired, informed and influenced by ecology’*

The British Ecological Society (BES) is the UK’s academic learned society for ecological science and the oldest institution of its kind in the world, established in 1913. The BES has nearly 5,000 members, representing the full scope of ecological research and practice and breadth of ecological careers, from undergraduate students to established professionals. The Society welcomes the opportunity to respond to the Committee’s inquiry on Genetically Modified (GM) Insects and asks it to consider the ecological impacts of the release of GM insects, particularly for gene drive methodologies. There are early models and simulations on the ecological impacts of some GM technologies that make insightful discoveries; further research is needed on these impacts, on a case by case basis.

### Introduction

1. The most advanced applied research on genetically modified (GM) insects is being undertaken with the aim to control insect vectors of human diseases such as mosquitos in the spread of malaria and dengue, and to control populations of crop pests, including the diamondback moth, olive fruit fly, and Mediterranean fruit fly. There is potential for GM insects to be used to control insect-borne diseases in livestock including bluetongue and Schmallenberg virus<sup>21</sup>, and in wildlife conservation, such as the control of avian malaria (*Plasmodium relictum*) which continues to threaten multiple native species in Hawaii after the introduction of mosquitos in the early 19<sup>th</sup> century<sup>22</sup>.
2. The potential benefits that GM insect control could bring are obvious. This is especially significant in the case of malaria, where parasites are becoming resistant to drug treatments and mosquitos are becoming resistant to pesticides<sup>23</sup>, and for dengue where no licensed vaccine or dedicated therapy exists, and prevention and control solely depends on effective vector control measures<sup>24</sup>.
3. GM insect control presents numerous benefits when compared with the use of broad spectrum insecticides; it does not rely on the release of toxic chemicals into the environment, and works well against targets that are difficult to find, and /or difficult to reach by conventional practices<sup>25</sup>. These insects are unlikely to yield direct off-target effects however there may be some indirect impacts on wild populations and communities.

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<sup>21</sup> GM Insects and Disease Control. (2014) POSTnotes POST-PN-483.

<sup>22</sup> The Long Now Foundation, Work Group 1 -Paradise Regained. Eradication of Invasive Mosquitoes and Disease <http://longnow.org/revive/case-studies/#workgroup1> [Accessed 19.08.15]

<sup>23</sup> Hemingway J, Ranson H. (2000) Insecticide resistance in insect vectors of human disease. Annual Review of Entomology, 45:371-391

<sup>24</sup> World Health Organisation. Dengue and Severe Dengue Factsheet: [www.who.int/mediacentre/factsheets/fs117/en/](http://www.who.int/mediacentre/factsheets/fs117/en/) [Accessed 18.08.15]

<sup>25</sup> Alphey L, Nimmo D, O’Connell S, & Alphey N. (2008). Insect population suppression using engineered insects. In Transgenesis and the management of vector-borne disease (pp. 93-103). Springer New York.

## GM Insect Technologies

### *Gene Drive*

4. Gene drive systems promote the spread of genetic elements through populations by assuring that they are inherited more often than Mendelian segregation<sup>26</sup> would predict. Gene drive techniques insert a desired genetic modification into an organism along with DNA that increases the rate at which the change is passed to the next generation. This method has the potential to rapidly modify an entire population, depending on generation times<sup>27</sup>.

5. With the recently developed 'CRISPR', a gene-editing technique that allows researchers to make precise changes to DNA, gene drive has become a realistic tool with tremendous potential to address insect vectors of disease. Bier & Gantz (2015) showed that a mutagenic chain reaction which is based on the CRISPR could be used to spread a mutant gene onto both chromosomes in a pair, thereby passing on this genetic modification to nearly all of their offspring. In theory at least, the application of gene drive could mean the spread of a malaria resistant gene throughout an entire breeding population of mosquitos in one season<sup>28</sup>.

6. Bier and Gantz joined a host of other scientists in a letter to Science calling for multiple strategies to ensure the safety of gene drive experiments, since the accidental release of gene drive insects for the last could have unpredictable ecological consequences<sup>29</sup>. Some of these consequences are discussed later in the response.

### *Homing Endonuclease Genes*

7. A gene drive system using Homing Endonuclease Genes (HEG) is aimed at population suppression. HEGs are naturally occurring 'selfish genes' or 'parasitic genes'; these are genes that exploit the host cell functions in order to copy themselves into a particular sequence of DNA, again at a higher rate than would be expected in Mendelian segregation. HEGs can be engineered to cut a sequence in the DNA in the middle of an essential gene, therefore disrupting its function. For example, this could be for a gene that is essential for disease transmission but not essential for the host<sup>30 31</sup>.

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<sup>6</sup> Genes in sexually reproducing organisms normally have, on average, a 50% chance of being inherited. Single-gene functions are usually inherited in one of several patterns depending on the location of the gene and whether one or two normal copies of the gene are needed for the disease phenotype to manifest.

<sup>27</sup> Oye K *et al.* (2014) Regulating gene drives. *Science*: 345 (6197), 626-628.

<sup>28</sup> Bier E, Gantz V (2015) The mutagenic chain reaction: A method for converting heterozygous to homozygous mutations. *Science* 348 (6233) 442-444.

<sup>29</sup> Akbari O S. *et al.* (2015). Safeguarding gene drive experiments in the laboratory. *Science* 349 (6251), 927-929.

<sup>30</sup> Burt A (2003) Site-specific selfish genes as tools for the control and genetic engineering of natural populations *Proceedings of the Royal Society B* 270, 921-928.

<sup>31</sup> Deredec A, Burt A, Godfray H.C.J. (2008) The Population Genetics of Using Homing Endonuclease Genes in Vector and Pest Management. *Genetics* 179(4):2013-2026.

8. The rapid transmission dynamics of a HEG have been shown to work in caged mosquito populations<sup>32</sup>, and further, the HEG technique has been used to cut the paternal X chromosome in the malaria vector (*Anopheles gambiae*), preventing it from being transmitted to the next generation. This technique resulted in fully fertile mosquito strains that produced more than 95% male offspring<sup>33</sup>.

#### *Sterile Insect Technique (SIT)*

9. The Sterile Insect Technique (SIT) is not classified as genetic modification, but its application and precursor to GM induced sterility merits inclusion here. SIT is a self-limiting, population suppression system whereby radiation-sterilised male insects are released to mate with their wild counterparts, thereby reducing the reproductive potential of the target population.

10. Application of SIT within an area-wide integrated pest management programme (AW-IPM) successfully eradicated New World screwworm (*Cochliomyia hominivorax*) from the USA and Mexico<sup>34</sup>, and was successfully used to eradicate the parasite in Libya just four years after it became established in the late 1980s<sup>35</sup>. SIT is also used widely in Florida and California to control populations of Mediterranean fruit fly (*Ceratitis capitata*), and has been used for the control of the pink bollworm moth (*Pectinophora gossypiella*) and the codling moth (*Cydia pomonella*).

11. The application of SIT has been largely restricted to agricultural pests, although it has been used as a component of AW-IPM to create tsetse-free areas within Zanzibar<sup>36</sup>. SIT requires sterilization of a large number of insects, which can greatly impact on their fitness, making them less competitive with wild insects once released. This, along with the costs associated with SIT (i.e. expensive radiation sources and costly security), has limited its application in mosquitos, where few trials have achieved eradication of diseases like malaria and dengue in the target area, or long term control<sup>37</sup>.

#### *Release of insects carrying a dominant lethal (RIDL)*

12. The RIDL technique, developed by British biotech company Oxitec is a genetic enhancement of the SIT, whereby transgenic technology is used to insert a lethal gene into

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<sup>32</sup> Windbichler *et al.* (2011) A synthetic homing endonuclease-based gene drive system in the human malaria mosquito. *Nature* 473,212–215

<sup>33</sup> Galizi R, Doyle LA, Menichelli M, *et al.* (2014) A synthetic sex ratio distortion system for the control of the human malaria mosquito, *Nature Communications* 5: 2041-1723

<sup>34</sup> Van der Vloedt A, Klassen W. The development and application of the sterile insect technique (SIT) for New World screwworm eradication. Food and Agriculture Organisation of the United Nations: <http://www.fao.org/3/a-u4220t/u4220T0j.htm> [Accessed 27.08.15]

<sup>35</sup> Lindquist D, Abusowa M, Hall M (1992), The New World screwworm fly in Libya: a review of its introduction and eradication. *Medical and Veterinary Entomology*, 6: 2–8.

<sup>36</sup> Vreysen J (2006) Prospects for area-wide integrated control of tsetse flies (Diptera:Glossinidae) and trypanosomiasis in sub-Saharan Africa. *Rev Soc Entomol Argent* 65:1–21.

<sup>37</sup> Scolari F, Siciliano P, Gabrieli P, Gomulski LM, Bonomi A, Gasperi G, Malacrida AR (2011) Safe and fit genetically modified insects for pest control: from lab to field applications. *Genetica* 139(1):41-52.

the insects. This gene produces a non-toxic, lethal protein (tTAV) that allows larval development, but prevents the offspring of RIDL insects surviving into adulthood<sup>38</sup>.

13. RIDL has several benefits over SIT; it has a heritable visible genetic marker so that sterile and wild insects can be distinguished. There is no risk of accidental escapes of fertile, mass-reared pests as there would be using SIT. There is also a female-specific variant of RIDL (fsRIDL) that produces male-only cohorts of the insects on a large scale<sup>39</sup>.

14. Field trials using RIDL male mosquitoes (*Aedes aegypti*) have been undertaken in the Cayman Islands, with the aim of controlling dengue infections. This resulted in a suppression of the wild population by 80% relative to nearby untreated areas<sup>40 41</sup>. There is also evidence of this technology reducing the local *Ae. aegypti* population by 81% and 95% in field trials in Brazil<sup>42</sup>.

15. The United States Department of Agriculture Environmental Impact Statement on the use of genetically engineered fruit fly and pink bollworm in plant pest control programs concluded that the sterile insect technique using RIDL, was the 'preferred alternative' to radiation-based SIT, and state that 'the greatest potential impacts occur with the no action alternative, in that potential pest risks are not static and continue to increase with expanding trade and travel'<sup>43</sup>.

### Ecological impacts of GM Insects

16. The ecological impacts of GM insects (both direct and indirect) will vary according to the methods used, and the reproductive behaviour, habitat, life cycle and ecology of the insect and the geography of the target population. Therefore the ecological consequences of the release of GM insects should be ascertained on a case by case basis. The ecological considerations of gene drive, a self-sustaining GM technology, are distinct from the self-limiting release of sterile males; in SIT and RIDL, impacts will largely depend on the number of insects released. With gene drive, one release could be sufficient to change an entire population. In both cases, the change in population is likely to have further indirect impacts on inter and intra-specific competition within the community. An understanding of the ecological consequences of gene drive technologies should therefore be made an urgent priority if we are to gainfully utilise its potential.

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<sup>38</sup> Oxitec Ltd <http://www.oxitec.com/>

<sup>39</sup> Slade G, Morrison N. (2014) Developing GM insects for sustainable pest control in agriculture and human health. *BMC Proceedings*. 2014;8(Suppl 4):O43.

<sup>40</sup> Harris A, Nimmo D, *et al.* & Alphey, L. (2011). Field performance of engineered male mosquitoes. *Nature biotechnology*, 29(11), 1034-1037.

<sup>41</sup> Harris A, Nimmo D, *et al.* & Alphey, L. (2012). Successful suppression of a field mosquito population by sustained release of engineered male mosquitoes. *Nature biotechnology* 30 (9), 828-830.

<sup>42</sup> Carvalho DO, McKemey AR, Garziera L, *et al.* (2015) Suppression of a Field Population of *Aedes aegypti* in Brazil by Sustained Release of Transgenic Male Mosquitoes. Olson KE, ed. *PLoS Neglected Tropical Diseases* 9 (7):e0003864.

<sup>43</sup> Use of Genetically Engineered Fruit Fly and Pink Bollworm in APHIS Plant Pest Control Programs United States Department of Agriculture Marketing and Regulatory Programs Animal and Plant Health Inspection Service Final Environmental Impact Statement—October 2008  
[https://www.aphis.usda.gov/plant\\_health/ea/downloads/eis-gen-pbw-ff.pdf](https://www.aphis.usda.gov/plant_health/ea/downloads/eis-gen-pbw-ff.pdf) [Accessed 05.09.15]

### *Number of insects released*

17. Suppression technologies such as SIT and RIDL require flooding local populations with transformants. For RIDL, it has been modelled that a constant release may require between 1.5 and 2.2 times more insects to achieve local elimination<sup>44</sup>. This mass release of insect populations into a target location is likely to have ecological implications, some of which are discussed below.

### *Incomplete SIT/ RIDL releases*

18. The radiation methods used to sterilise males in SIT can result in a small proportion of fertile males; release of these incompletely sterilized males does not reduce the population as efficiently. In the case of mosquitos, the release of males does not increase bite rate (only female mosquitos bite), but a larger release of transformant insects is needed to collapse the population<sup>24</sup>.

19. The incomplete penetration of the lethal gene in RIDL is also feasible. However in this case, it would still mean that a proportion of the transgenic offspring that survive to adulthood would retain the transgene – therefore enhancing the overall suppressive effect of RIDL<sup>45</sup>.

### *Interspecific competition*

20. The interplay of interspecific and intraspecific competition dictates the coexistence of species and plays a major role in the structure of ecological communities. Bonsall *et al.* (2010) modelled the effects of SIT and RIDL control strategies on coexistence and exclusion in two vectors (e.g. two species of mosquito)<sup>24</sup>. This linear study showed that conventional and transgenic control techniques can affect the local existence or exclusion of vector species, and can allow the coexistence of species that would not otherwise necessarily occur; that is although we would expect a competitor to move in to the empty ecological niche after the end of a successful control programme, this study showed that the competitor may be able to *before* the existing occupant was removed. This may have important consequences for the persistence of disease, depending on if the competitor is a competent vector, or is much less competent than the species that is the focus for control. Again, this should be investigated on a case by case basis. For instance, malaria is transmitted by several species of mosquito, whereas *Aedes aegypti* is the principal dengue vector in most of the world (*Aedes albopictus* is a vector in some regions). GM transformants may need to be developed and released for several species in the locality.

21. The outcome of interspecific competition depends on the larval habitats and development times of wild and transformant vectors, which will vary according to season and location. Therefore there is a need to understand the effects of individual demographic

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<sup>44</sup> Bonsall, M., Yakob, L., Alpey, N., Alpey, L. (2010) Transgenic control of vectors: the effects of interspecific interactions. *Israel Journal of Ecology & Evolution*, Vol 560 353-370.

<sup>45</sup> Yakob L, Alpey L, Bonsall M (2008) *Aedes aegypti* control: the concomitant role of competition, space and transgenic technologies. *Journal of Applied Ecology* 45:1258-1265.

characteristics – survival, fecundity and development- to predict community interactions and vector control. Further research is needed on these types of ecological interactions.

### *Transient dynamics*

22. Bonsall *et al.* also discuss ‘Allee effects’ introduced by SIT and RIDL control strategies; *Allee effects* are a phenomenon whereby there is a decline in individual fitness when population densities are low, resulting in a further decline in abundance<sup>24</sup>. While in the case of SIT and RIDL, this can lead to local extinction of the focal control species; it also introduces stable and unstable coexistence points among competing vectors. Bonsall *et al.* call for an awareness of these types of transient dynamics when monitoring the emerging results of control programmes.

### *Migration*

23. Yakob *et al.* (2008) model the potential risk of inadvertent population increase through release of SIT and RIDL for the control of *Aedes aegypti*; the vector for dengue<sup>25</sup>. They explain that survival from the larval to the adult stages of the mosquito is severely restricted by resources, therefore a reduced density of pre-adult stages may actually result in an increase in the adult population. This effect may be seen in SIT control, since it acts by lowering the number of offspring (larvae) in the next generation. This effect would be unlikely where there are isolated areas with high proportions of sterile males, but would become a problem where sterile males migrate from the target area to neighbouring areas.

24. Yakob *et al.*'s theoretical study showed that there was indeed an *increase* in wild vectors throughout all non-target areas into which the sterile males had migrated. The magnitude of this increase declined with distance from the release site. This result was not evident in simulations based on the use of RIDL, which acts after the density dependent processes. With RIDL, all neighbouring wild vectors re-stabilise at lower populations compared to the pre-control level. They also stabilise at this lower level more quickly than with SIT<sup>25</sup>.

### *The food chain*

25. The local eradication of insects may have an impact on organisms at higher trophic levels that rely on them as a food source; however there is little evidence available on which to establish exactly what these impacts would be for transformant insects. One study that monitored the environmental impact of a 90% reduction in mosquitoes in Germany (through non GM technologies) showed that while there has been a reduction in mosquitoes ‘to a tolerable level’, the ‘ecosystem as a whole has not been damaged’. Other insects continued to develop in the absence of large mosquito populations, providing a ‘food resource for birds, amphibians and bats’<sup>46</sup>.

26. Eradicating mosquitos in the Arctic may impact on the diets of migrating birds (although few show up in bird stomach samples), and on the migratory routes of caribou.

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<sup>46</sup> Becker N (1997) Microbial control of mosquitoes: management of the Upper Rhine mosquito population as a model programme. *Parasitology Today* 13 (12): 485-487.

Elsewhere, the absence of mosquito larvae in water pools may impact on the diets of fish and other animals, and mosquitoes also act as a pollinator for thousands of plant species (although few which humans depend on as a food source). Expert opinion differs, but there is some consensus view that these ‘services’ would be filled, in the majority of cases, by other organisms that would inhabit the empty ecological niche<sup>47</sup>.

27. Investigation of the wider impacts of the long term SIT control of the Mediterranean fruit fly (*Ceratitidis capitata*) in Florida and California may also help to shed some light on these types of interactions within the food chain.

28. Under this theme it is pertinent to note that the ecological impacts of insecticides (the current most widespread insect control mechanism) and the subsequent detrimental accumulation of toxins throughout the food chain are well documented<sup>48 49</sup>.

#### *Disease free wildlife*

29. Nagel & Peveling (2005) summarise the impact of the eradication of screwworm on white-tailed deer in the United States; overall, both domestic and wild animals, including some endangered deer species benefited enormously, however the surge in deer numbers in turn caused an increase in the deer parasitising Gulf Coast tick, which then went on to infect cattle. The release of predator species from disease will also have an impact on prey species. These kinds of interactions again will differ according to ecosystems<sup>50</sup>.

#### *Resistance*

30. There is potential for an evolutionary response to GM technology, such that resistance develops to the modified gene. This can be monitored effectively, and is seen in other control methods including insecticides. A more hazardous risk is the evolution of more virulent strains of the pathogen following GM control<sup>51</sup>. There is very little research published on this issue, but examples can be found; for instance Medlock *et al.* (2009) model the evolutionary impact of different GM mosquito strategies on dengue virulence in both humans and mosquitoes<sup>52</sup>. Their model suggests that control strategies which raise mosquito mortality pose less of a risk of causing increased virulence to humans than strategies that block the transmission of the disease, or reduce mosquito biting. More research is needed to test such models.

### **Research funding**

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<sup>47</sup> Fang J. (2010) Ecology: A world without mosquitoes. *Nature News*, 466(7305), 432-434.

<sup>48</sup> Brown, Anthony William Aldridge. *Ecology of pesticides*. John Wiley & Sons 1978. Sánchez-Bayo, Francisco. *Ecological Impacts of Insecticides*. INTECH Open Access Publisher, 2012.

<sup>49</sup> *Ecological Impacts of Insecticides*. INTECH Open Access Publisher, 2012.

<sup>50</sup> Nagel P, Peveling R. Ch 5. Ecological Consequences of Eradication in Dyck, V. Arnold, Jorge Hendrichs, and Alan S. Robinson. *Sterile insect technique*. IAEA, 2005.

<sup>51</sup> Alphey L. (2014) Genetic control of mosquitoes. *Annual Review of Entomology* 59, 205-224.

<sup>52</sup> Medlock J *et al.* (2009) The impact of transgenic mosquitoes on dengue virulence to humans and mosquitoes. *The American Naturalist* 174.4: 565.



31. While there appears to be some funding available for the technical development of these technologies within the lab (i.e. through BBSRC, Wellcome Trust and the Bill & Melinda Gates Foundation), securing funding for field trials is extremely difficult. Comprehensive applied projects may require funding for several deliverables, including a lab component, a modelling component and a field component, interacting with each other to address knowledge gaps. This requires sufficient interdisciplinary funding and a range of expertise, including a good understanding of the ecology of vector populations.

32. Traditional funders require the delivery of a project within a defined timescale, which cannot be guaranteed due to uncertainties in the regulatory system of this technology. Conversely, regulators are unable to provide permits for research which is not yet funded. As such, field trials to date have been exclusively funded by risk capital to a private sector entity. EU funding could play a part here, but in practice the negative perceptions of GMOs in some European countries makes this funding extremely difficult to secure.

33. This problematic funding landscape is amplified for non-commercial GM insect projects, including conservation applications such as the control of avian malaria, which is unlikely to provide attractive financial returns to a commercial developer. This issue is also applicable for any target with relatively small potential market; the species-specific nature of GM insect technologies means that there are many more examples of beneficial applications with small markets than large ones.

### **Regulatory Framework**

34. In the EU, applications to release GM insects are assessed under Directive 2001/18/EC<sup>53</sup> and are bolstered somewhat by the European Food Safety Authority (EFSA) guidance on the risk assessment of GM animals<sup>54</sup>. There are international guidelines for the release of (non GM) insects which should also be considered when regulating the mass release of GM insects<sup>55</sup>.

35. The current regulatory framework has numerous limitations in its application for GM insects. There are a number of risks that have a greater prevalence in GM crops than in GM insects; gene flow for instance is less of a risk in insects due to their breeding specificity. However other issues, such as 'receiving environments' and dispersal of GM organisms presents a more complex picture for GM insects.

36. A report by the Advisory Committee on Releases to the Environment (ACRE) on GM Insects<sup>56</sup> explores some of these issues and calls for a more holistic approach than is currently provided by the Directive which includes a consideration of the risks of alternative

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<sup>53</sup> Deliberate release of genetically modified organisms (GMOs) <http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=URISERV:l28130> [Accessed 05.08.15]

<sup>54</sup> EFSA Panel on Genetically Modified Organisms (2013) Guidance on the environmental risk assessment of genetically modified animals. EFSA Journal 2013;11(5):3200, 190

<sup>55</sup> International Standards for Phytosanitary Measures No 3 (2005) Guidelines for the export, shipment, import and release of biological control agents and other beneficial organisms.

<sup>56</sup> Advisory Committee on Releases to the Environment (ACRE) Report on the ACRE information gathering workshop on GM insects (2010) London: Advisory Committee on Releases to the Environment, DEFRA.

control methods (such as insecticides) and the risks of inaction (continued and increasing disease prevalence as insects develop resistance).

37. As stated above, the ecological risks and hazards associated with the release of GM insects is 'product' specific; i.e. the GM technology, species, lifecycle, locality, and time of year, will all impact on the ecological consequences of its release. A broad-brush approach to regulation is therefore not appropriate in this context. Assessments should be made on a case by case basis, taking into account both the benefits and the risks of the release.

### **Management regimes**

38. The application of GM insects should be undertaken within an integrated pest management system, closely monitored with supplementary management practices. Lessons can be learnt from the good and bad management practices of herbicide resistant GM crops<sup>57 58</sup>. For human disease vectors, the implications of control mechanisms (both GM and non GM) on human herd immunity, and the possible effects on human health when insecticide application is terminated after GM insect release should be carefully monitored.

*23 September 2015*

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<sup>57</sup> Frisvold G & Reeves J (2010) Resistance management and sustainable use of agricultural biotechnology. *Journal of Agrobiotechnology Management and Economics* 13: 343-359.

<sup>58</sup> Tabashnik B, Gassmann A, Crowder D, Carriere Y. (2008) Insect resistance to Bt crops: evidence versus theory. *Nature Biotechnology* 26: 199-202.

British Ecological Society (BES), Dr Sarah Hartley, University of Nottingham, and Sciencewise  
– Oral evidence (QQ 16-25)

**British Ecological Society (BES), Dr Sarah Hartley, University of Nottingham,  
and Sciencewise – Oral evidence (QQ 16-25)**

[Transcript to be found under Sciencewise](#)

## **Buglife, The Invertebrate Conservation Trust – Written evidence (GMI0011)**

1. The development of Genetically Modified (GM) insects opens up considerable opportunities to reduce our reliance on insecticides in food production and pest control. As with any new technology it is important that the risks associated with its use are adequately assessed and that proper and precautionary risk assessments and management should be applied to each new GM organism.
2. By targeting individual species GM technology could be a realistic alternative to the use of pesticides to minimise harm to non-target and indeed beneficial species. This could be an important tool in the implementation of Integrated Pest Management programmes in agriculture. In addition, GM insects could be used in situations where traditional control methods are ineffective or impractical, such as in difficult terrain or where socio-economic factors limit the efficacy of pest control mechanisms.
3. However this raises a significant issue with the deployment of GM insects. To constitute a pest the target species is likely to be distributed widely and occur in significant numbers. The resulting GM control organism will need to be similarly pervasive, resulting in large scale releases being required.
4. The effect of these released insects would be difficult to monitor and the control exercise would be difficult, if not impossible to reverse. In addition, any incidental damage to the environment could occur over a large area.
5. It is therefore important that thorough risk assessments are undertaken as part of any application to release GM insects. Risk assessments should consider the full range of impacts on the environment, economic activity and human health. The complexity of ecosystems means that there may be unintended effects following the deployment of GM insects. Particular attention should be paid to the effect of removing a species from the ecosystem and the possibility that more invasive species may fill the empty niche. Similarly, the impact on food availability for other species is an important consideration. For example, biting midges (Ceratopogonidae) comprise a large proportion of the diet of Pipistrelle bats. An application of GM technologies to reduce midge numbers to prevent the spread of Schmallenberg and/or Blue-tongue virus could have a devastating effect on populations of insectivorous mammals and birds.
6. **Proposals should be assessed on a case by case basis**  
In assessing the likely effects of a modified insect on other species and the environment each approach has to be considered specifically. Some modifications may appear to pose substantial environmental risks, while others promise environmental benefits such as reductions in insecticide use. Just because one modification is environmentally safe, it can't be concluded that the next is safe.
7. **Rigorous testing should be undertaken for all proposals**

All proposals will require rigorous testing to ascertain as best as possible whether any unintended consequences may arise from the release of the organism.

8. Each risk assessment should be supported by bespoke science, including scientific trials in the laboratory and the field that are rigorous and statistically robust. Every trial, looking at efficacy or impacts, should be registered prior to commencement and there should be a publically accessible website showing all the registered trials and their results.
9. Areas to pay particular attention to include:
  - impacts on other species within the genus of the target species - it is important that thorough testing is undertaken to ensure that the modified insect does not attack or otherwise affect species closely related to the target species, for example other species in the same genus;
  - horizontal transfer or drift of genes between the modified insects and other species in the genus;
  - potential impacts upon predator/prey relationships - where the GM insect is predatory and is given an advantage over other predators this could lead to an unbalanced predator/prey relationship and subsequently result in the modified insect preying on a wider range of species, potentially leading to losses in the populations of non-target species;
  - incidental effects resulting from alterations to pheromones – genetic modifications to herbivorous insects so that they release more chemical signals such as pheromones could be used to attract predators to preferentially prey upon these insects. Whilst this may seem an innocuous and useful use of GM technology, there are a number of considerations that would need to be taken in to account. For example, evolutionary processes could lead to changes to the behaviour of the target insects making them less likely to be found and predated, rendering the modification useless. Conversely, the population of predators may increase significantly in the area where the modified insect is present. This could lead to a shortage of food for the predators causing them to prey upon other species, potentially reducing their numbers until their population was no longer sustainable. Such effects would have to be considered across the area affected by the dispersal of the GM organism and the pheromone, not just in the target area.
10. **Thorough risk assessments must be undertaken**  
The risks associated with the release of GM insects include environmental, economic and social impacts. Thorough risk assessments must be undertaken to inform the final decision on the release proposal.
11. **The precautionary principle must be adopted**  
Where scientific evidence is inconclusive but it is thought that an impact is likely to occur, and there is insufficient evidence that the risk can be avoided, then the precautionary principle must be applied and permission to release the insects refused.
12. **The impact of released organisms must be monitored**

Following release of modified organisms a monitoring programme monitoring should be instigated to check what impacts the modified organisms are having on the target species and any other environmental, economic or social impacts. Risk assessments should be reviewed and updated taking in to account the results of the monitoring.

13. **All releases should comply with the Cartagena Protocol on Biosafety**

The Cartagena Protocol on Biosafety seeks to protect biodiversity from the risks posed by genetically modified organisms. It applies to the movement, transit, handling and use of GM organisms between countries and ensures that receiving countries are provided with the necessary information to make informed decisions before agreeing to the import of modified organisms.

*17 September 2015*

**Buglife, The Invertebrate Conservation Trust and Nuffield Council on Bioethics – Oral evidence (QQ 56-64)**

*Evidence Session No. 6*

*Heard in Public*

*Questions 56 - 64*

TUESDAY 27 OCTOBER 2015

Members present

Earl of Selborne (Chairman)  
Lord Cameron of Dillington  
Lord Fox  
Lord Hennessy of Nympsfield  
Lord Kakkar  
Lord Krebs (co-opted)  
Baroness Manningham-Buller  
Lord Maxton  
Duke of Montrose  
Baroness Morgan of Huyton  
Baroness Neville-Jones  
Lord Patel (co-opted)  
Lord Peston  
Viscount Ridley

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Lord Taverne

**Examination of Witnesses**

**Mr Matt Shardlow**, Chief Executive, Buglife—The Invertebrate Conservation Trust, and **Professor Jonathan Montgomery**, Chair, Nuffield Council on Bioethics.

**Q56 The Chairman:** Could I welcome Professor Montgomery and Mr Shardlow. We are being broadcast on the web camera. Would you like to introduce yourselves? If you would like to make an introductory statement, please feel free to do so.

**Professor Jonathan Montgomery:** I am Jonathan Montgomery, I am here as Chair of the Nuffield Council on Bioethics. By background I am an academic lawyer and I am Professor of Healthcare Law at University College London.

I should say just a couple of things about the basis on which I am giving evidence. I am sure many of you will know that the Nuffield Council on Bioethics is a non-government organisation; it broadly has functions which are similar to national ethics committees in other countries. I should acknowledge that we are funded by the Nuffield Foundation, the

Wellcome Trust and the Medical Research Council, but under an arrangement that ensures that our agenda and opinions are fully independent. It is a five-year rolling funding programme. The council itself has about 20 members from a range of academic disciplines, clinical expertise, media and industry, but we draw a larger number of people into our deliberations, including a group of affiliates, and calls for evidence. We sometimes produce formal reports where we work through working parties. We do not have such a report on genetically modified insects but we have addressed some overlapping issues in work on genetically modified crops, the ethics of research in developing countries and, most recently, we have produced a report on the assessment of emerging biotechnologies, in 2012. I will be drawing on the strands of recommendations and evidence from that when I answer questions.

We have two pieces of work we are doing at the moment which overlap a little. One is on the use of the idea of naturalness in public debates. Our report on that will be coming out at the end of November; I will draw on a few elements and we will, obviously, pass the report to the Committee when it is finalised. We also have a programme of work on gene editing. We did look at whether or not a particular piece of work focused on genetically modified insects was appropriate, but we identified a broader set of questions around the use of gene editing. We set up a core group which will look at some of the ethical challenges and frame some of the questions, and it is about to embark on a call for public evidence. We anticipate that will produce a draft platform report in the middle of next year and we will then look at a number of case studies, one of which may be on genetically modified insects—if you have not solved all the problems by then.

**The Chairman:** We will not have solved the problems, I can assure you. Thank you for that. Your report on gene editing will come out after our report; nevertheless, I am sure, as we are possibly likely to revisit the subject, that that will be the time to look at that. Mr Shardlow?

**Mr Matt Shardlow:** I am Matt Shardlow from Buglife, the Invertebrate Conservation Trust. We are the charity based in the UK—but we operate further afield as well—which looks after the invertebrates and the conservation of invertebrates: that is, insects plus all the other little things without backbones. Our aim is to prevent the extinction of species and to maintain sustainable populations of invertebrates in the countryside. We take a strongly scientific approach to how we go about our work; it is very evidence based, whatever we are doing, but we get involved with sometimes controversial issues where the evidence is not there, and obviously we use our charitable objectives and our ethical stance to try to guide our way through that. Hopefully, that will be relevant today beyond perhaps the simple scientific evidence that I am sure you have all been poring over and has been presented by some of your previous witnesses.

We approach GMs as we approach any other potential technology: as potentially very beneficial but also with risks, and those risks have to be managed. You have repeatedly heard people talk about case by case, and we take a similar case-by-case approach to the need for attention to the risks associated with new technologies and traits. There has been discussion about whether it is traits or organisms, and there are potentially some shortcuts around traits once those become well established, but you still have to look across risks every single time you go about releasing a new organism into the environment. While we see opportunities we also see risks, similar to a lot of work we have done in agriculture around pesticides, which I think is quite comparable. Here you have something that is



released into the environment that has potential benefits and potential disbenefits, and we have learnt a lot from seeing how that has operated over the last few years, particularly how you look at benefits and how you might ethically weigh benefits against potential risks, damage and harm. That might come into some of my evidence as well.

**The Chairman:** Thank you very much. I am going to ask Lord Peston if he would like to start.

**Q57 Lord Peston:** My task is to get us going on ethical and safety questions and to introduce a general set of questions and discussion of those matters. To put it into context, I believe ethical questions can be meaningfully discussed in the abstract and in specific cases, whereas when I was an undergraduate the logical positivists held sway and we were all told that all ethical questions are meaningless. That is certainly not my view. In due course I want to see how you approach that. The safety question, I take it, is the risk question: our attitude to risk. Again, I think one can have meaningful discussion on what is a correct attitude to risk, especially when it comes to government decision making and financing. That is the background.

I would like to ask you to outline to us, first, what are the main ethical questions that you feel both do and ought to—to produce a logical paradox—dominate this field? Secondly, would you take us on—but let us get through the ethical, first—to the attitude to risks bit, and again tell us what is your view on the correct approach to that? All this I regard as background to the way this Committee will eventually come to its own conclusions. Is that a good start for you? Who wants to go first? Professor Montgomery? Professors always go first.

**Professor Jonathan Montgomery:** Fair enough, even if we are not all, these days, logical positivists! At Nuffield we are nervous about focusing on the ethics of technologies, as opposed to the context in which those technologies are being considered and used. We would be, I think, encouraging you not to think that you can answer the question: are genetically modified insects ethical? What we can do is look at the range of factors that need to be taken into account in that context. First of all, we would recognise a number of contextual factors which were described in the previous session as the reason why people do it, but they are ethical goods that are at stake in decisions you might make about the use of genetically modified insects: issues around health, not just human health but also animal health; issues around food security and bio-security. They are all things that are properly described as ethical goods, as is research and promoting our understanding of the world around us. We should not ask questions about the idea of safety without also understanding where those goods fit into the decision-making process.

The second thing we would want to say is that a focus on risk encourages you to look only at a subset of the disbenefits and the anxieties, particularly the rather technological versions of risk assessments that some of the regulatory techniques encourage us to go through. Our report on emerging biotechnologies argues that these suffer partly from being very narrow in focus and partly from encouraging people to calculate things that are actually incalculable, which I think has already been touched on. They give a spurious certainty to the answer to the risk question. That needs to be linked to what we mean by safety, and we should be particularly concerned about the difference between those people who are directly affected by risk, their assessment of what counts as sufficiently safe or not sufficiently safe to make a decision to use technologies, and the broader questions about collective goods. I am sure we

will come back to that in terms of the proper role of public opinion. Essentially, the question on safety is about whether or not it is worth taking the identified risks to secure the goods that are there, and we should spend some time thinking about who should really take those decisions, particularly where the decision to be directly affected may not be taken in the same place as the decision to develop the science.

I have two final observations. One is that our report on emerging biotechnologies drew attention to the importance of reflecting on the extent to which decisions we take to use or not use particular technologies tend to drive us down pathways which have consequences for crowding out other possible research agendas. We therefore need to have a debate quite early on about these technologies versus other promising ways to look forward.

The final observation is on the debate about the proper language and approach to take in relation to uncertainty and caution. The Nuffield Council is not particularly keen on the phrase “the precautionary principle”; it is very keen on proceeding with caution and making sure that we take steps in ways we can monitor and understand better, and also to bear in mind that some ways of taking those steps are less risky and offer more hope for benefit than others. It makes sense to choose the ones that seem wiser and less risky, but we do not think it makes sense to pull a shutter down on things, following the argument that you should never take a step for fear it might work.

**The Chairman:** Mr Shardlow, do you want to add anything?

**Mr Matt Shardlow:** At a simple level in terms of our objectives as an environmental charity, we see the risks as a nested set of risks. There are ethical risks and considerations around—let us not forget this; we might pass on quickly—the fact that you are doing things to individual animals as well. For insects we may pass that over quickly—it is not as if we are genetically modifying a human being—but we should also ethically bear in mind we are doing something to an organism when we are doing this work, and that is an ethical issue which should not be completely glossed over. Stepping out from that, there are potential effects on the target species you are doing your work on and that might include, for instance, extinction. I would say that extinction is a wrong, in the way that killing a human being is a wrong. It might be something that sometimes you do, but you need to justify why you take that otherwise immoral action.

Nested beyond that, you have the potential effects on the wider environment, which you might put into three broad categories: the effects on other species through gene transfer; effects on the eco-system and the web through predator and prey relationships, and effects on the eco-system’s usefulness and its beauty to us as human beings; the final one would be harm to people. That is how I would see the risk environment you are looking at around the specific potential things you need to consider, and obviously you can get much more detailed on that.

I would bring in another level of ethics here as well. You have heard a lot about the science, and the science is very important, and you have also heard people say that the European system for regulating GMO release is not working. When you quiz them further they have generally said: “The science bit is working okay but it is the political bit that is not working”. We would be foolish to ignore that. The ethics is not happening necessarily at the science level; it is not necessarily happening at the risk assessment level, where, it seems to me, most are broadly happy that the risk assessments are being done in a sensible way, but the ethics is happening between the public and their politicians and is kicking in at a later stage.

Some of that is not about trust necessarily just in the technology; it is about trust in the companies, the politicians and the scientists.

We need also to consider whether we are putting enough space between those different sectors, or whether to the public this just appears as an avalanche of positive scientists and industry people with a mixture of vested interests which they do not really understand but, “They are probably up to something”. That is a really important part of this ethical discussion and probably one of the main reasons why GMOs in Europe are struggling to get released, even if they get through the ethical risk assessment.

**Lord Peston:** Can you clarify a couple of aspects of that? First of all, I had never heard of the precautionary principle until we started taking evidence, but it seems to be dear to the hearts of lawyers. I have wasted a lot of time on this—I think it is rubbish, but that is by the way and we do not need to go down that line—but what bothers me is the ethical side. Why do we not adopt a Rawlsian approach? In other words, why not say that, ethically, human life rates above the environment, and therefore the correct ethical position is that trade-off is not the meaningful approach; the approach is, “Have we done all we can to save life?”, as in the poor malarial countries in the world? Then, subject to that, the environment is also important. Would either of you agree with that Rawlsian ethical position, or do you want to adopt the trade-off approach?

**Mr Matt Shardlow:** I can take the precautionary part and you can have a think about the second half of the question, Jonathan—I have left the difficult part to him. The difficulty with the precautionary principle is we love the precautionary principle as we define it, but it seems to me that everyone defines it differently. There is a whole bunch of people who hate the precautionary principle who seem to have a completely different definition of it from the one that I recognise. I recognise the precautionary principle as one based around risk, but based around taking action before you have absolutely conclusive knowledge; that you do not have to push the evidence to the absolute Nth degree of final certainty; that you do something about climate change before 100% of scientists say it is happening; you do something about a pesticide damaging bee populations before every single paper is absolutely in agreement. Once you have all the stages in place, the theory is there, the scientific evidence is here, here and here, and if there is not enough evidence to counter that, you do not allow a continued discussion around whether action is necessary; you get in and you take the action at that point. Some people seem to interpret it as, the moment you have some suspicion that something might not be working or if you have a vague fear that something might happen, you do not do it. That fundamentally is not what the precautionary principle was ever intended to be. I love the precautionary principle, but I seem to have a different definition from other people.

**Professor Jonathan Montgomery:** I was going to say something similar about the precautionary principle. I would add that there are many versions of it, so you will need to be clear if you are going to refer to it and describe the versions you think are worth talking about. We would take the view that another vice of the precautionary principle is it feels as though you only do it as a snapshot—it is a stop/go question—whereas actually, as I described earlier, there are many reasons to remain cautious even if you get the green light and go forward. Therefore, it is an attitude more than a decision vehicle. I am not quite sure I would draw out of John Rawls’s work the particular issues that you pick up about the comparative value of human life and other aspects. We would probably share the view that there is an intertwining of environmental and human benefits.

In our understanding of the challenges of public ethics in these sorts of decision-making processes, we would certainly draw out some things from John Rawls: we believe that they should be governed by principles of equity, solidarity and sustainability. Our version of solidarity is recognising the importance of looking to the least advantaged in decision making, which is clearly one that draws from John Rawls's own work. That is important, because our assessment of fairness in the use of technologies tends to break the question of who is developing and exploiting the technologies from the question of who is to benefit from where it would be deployed. That has both positive and negative challenges for technologies developed in Europe and used in developing countries; both the benefits and the disadvantages are going to be felt by people who are probably different from the decision makers. We might come back to that, I suspect, in questions. We also recognise that if you take a perspective on these decisions which recognises the long timescales, you do need to think about questions of sustainability, which includes the fragility of the ecosystems and thinking differently about those choices made that will be reversible, or will allow for a diverse ecosystem, from those which would make things very narrow and, therefore, more vulnerable to shocks.

**Mr Matt Shardlow:** Can I just add to that, which I agree with, often you are not left with the simple decisions you set out; you are often left with a set of decisions such as, do something now to disbenefit a small number of people because it will potentially benefit a vast number of people in the future. A lot of environmental protection is that sort of ethical decision.

**Q58 Lord Hennessy of Nympsfield:** I was interested, Mr Shardlow, when you were describing the parody view of those who have a down on industrial science; they think there are covert and dark forces at work with commercial interests trumping the science, and all the rest of it. Do you not think there is a danger, as there turned out to be in the GM crops debate, of parody views of each side of the protagonists making the running? For example, you could be parodied—not that I would ever think of it—as the trade union for the bug: “My brother the bug”; the invertebrates’ trade union. I would not suggest that for one minute. When you were describing the “red in tooth and claw” commercial instincts, and views of that, there is this terrible danger. Do you think it would be a great pity, as I do, if the parody world of the GM crop mutated into the world we are talking about now?

**Mr Matt Shardlow:** Yes, I agree with you absolutely. I am warning against it rather than encouraging it, I think. I am also saying, let us also have regard for the fact that is going on and is becoming a dominant factor. Look at the number of countries who in recent weeks have declared they are not going to release GM crops into their land: Scotland, France and Russia; an avalanche of countries now saying, “We are not having GM releases at all.” That is coming from an ethical point of view which is not based on scientific risk per se. We have to recognise that and we have to work our way through that.

I would say part of that is about making sure there is sufficient transparency. We have recommended in our submission having a register of trials so people can see what is going on with the science before it is done. This is very important because when this is done, for example, in pharmaceutical industries, you find a massive change in how the science is reported and understood. For instance, a paper published this year showed that before 2000, when in the States you didn't have to register large clinical trials, 57% of the clinical trials on heart disease showed positive effects, and after 2000 when they had to register them the percentage of positive clinical trials reported went down to 8%. Fifty-seven per

cent dropped to 8% as the proportion of positive results being reported. There is a whole series of reasons for that and I am not saying it is because they were deliberately cherry-picking only the ones that fitted their results—although many would say that—but also the fact that journals only publish things that look interesting. Somehow trying to get around some of the cloudiness and obscurity in the relationship between government, industry and science and trying to make them more transparent and spaced apart could be part of the way of getting away from a debate that is about polarising “them over here” and “them over there”.

**Professor Jonathan Montgomery:** I should inform the Committee that, in addition to the Nuffield Council, I also chair the Health Research Authority which oversees health and social care research for the English NHS and manages their research ethics committees, so we have very much an interest in the question of research transparency and the registration of trials and results. Although progress has been made, the fact remains we know a lot less of the knowledge base of science than we should do because it remains unreported and secret. Nuffield would also support, as part of the opening up of debates, processes to make sure that the science is as transparent as possible.

I would make two observations about the crossover with other debates. In relation to the GM crops question, as we are reviewing the report on the use of naturalness we have not particularly picked up a lot of direct discussion about GM insects, but it is clearly still the case that people are anxious about genetically modified crops. Our main understanding of the evidence so far—and, as I say, this is only a draft report at present—is that what seems most clear is that people talk across each other. The language of naturalness and unnaturalness is understood in different ways by scientists and the public. Therefore, used unreflectively, we have been unable to create a proper discussion of what is at stake because people use the phrases differently and we have not managed to bring them together. It is a clear challenge to do that going forward.

The other crossover is in relation to concerns around commercialisation and industrial interests. Certainly in the context of health and especially pharmaceutical research, the UK public displays considerable suspicion of research it thinks is motivated by industrial interests. The Health Research Authority’s public engagement shows that very clearly. That will also play out in the public discussions in this context, which will need to be pulled out into the open and discussed carefully.

**Q59 Lord Taverne:** Coming back to the precautionary principle, would you agree with the recommendation of the Royal Society that, in light of the confusion about the precautionary principle and the way it is often abused and used for antiscientific purposes to abolish or prevent any new technology being supported which somebody does not like, the term should not be used in scientific discussions? Is that not wise advice?

**Professor Jonathan Montgomery:** I think it is wise not just in scientific discussions but more generally. For the reasons we have talked about, it is misunderstood, but we should not lose the concerns that lie behind it: that there are important questions about thinking reflectively as opposed to rushing ahead without thinking. Nuffield does not use the phrase “precautionary principle” except to explain that it does not use it, but it still wants to hold on to the idea of proceeding with caution and in a measured way.

**The Chairman:** We will treat it with great caution.

**Viscount Ridley:** Would Mr Shardlow agree with me that by far the biggest manmade cause of extinctions of species is invasive species, particularly the introduction of rats to islands and things like that? I am not necessarily talking about insects but I am sure it probably is similar in insects. This technology is potentially, as we have heard in the previous session, a way of addressing that. The benefits from a conservation point of view of this technology could easily outweigh the disadvantages.

**Mr Matt Shardlow:** It is certainly an important factor. Habitat destruction and intensification of the intervening bits, and the fragmentation of land associated with climate change pushing up the southern margins of species distribution while the northern margins are frozen, in my mind, would be a bigger conservation issue.

**Viscount Ridley:** Historical records show that most extinctions we know about have happened on islands, where the problem has been manmade introductions of invasive species.

**Mr Matt Shardlow:** Certainly on islands you are right, as is your point about invasive species and the potential here, and we would welcome that being researched. You come back to requiring a sufficiently sized public purse to do that, because it is not necessarily going to be economically viable to try to eradicate something like the white-clawed crayfish. You need a programme of activity, and at the moment the programme around eradication of invasive species is not adequate to support the necessary level of scientific research investment. In principle, I would agree and we would like to see that area of work developed. Looking at how genetic modification could be used to introduce a sterile gene into white-clawed crayfish in the UK would be very useful.

**Viscount Ridley:** Just to correct you on that, the white-clawed is the native one. The signal crayfish—

**Mr Matt Shardlow:** I am sorry; yes, of course. I was thinking of a different crayfish that I am aware of.

**Q60 Baroness Neville-Jones:** This is a very rich debate. I wonder if I could perhaps drill down slightly into one of the aspects which has come up tangentially. As I understand it, we both agree you cannot validly answer ethical questions if you simply look at these various technologies in isolation from the context in which they are going to be used. Nevertheless, people are going to ask questions about, particularly, the ethical aspects of population suppression versus, for instance, replacement. Do you think the ethical and safety concerns vary and, if so, in what respects? One of the rather striking things is that the population replacement strategy, particularly if gene drive technology is used, is very difficult to reverse, so you create a new, ongoing situation which you are not likely to be able to change at all easily. That seems, in many respects, not to raise the same degree of ecological concern and worry as population suppression strategies. Do you have any comment on that and your general view on the whole question of the ethics that apply to these two different techniques?

**Professor Jonathan Montgomery:** I suspect Mr Shardlow will be better placed to do the specific answers. The framework we have developed suggests it may not be possible simply to answer that the same way in every circumstance, so we would clearly want to weigh out the ecological effect of the two strategies, which will depend on the ecosystem in which they are placed. It will depend a little on the relative effectiveness identified, so that if you have a

very important public health problem and the relative effectiveness of one is different from the other, that would seem to count in favour of it and might outweigh a certain amount of ecological negative impact. Equally, if the efficacy is broadly similar our “proceed with caution” approach would suggest that something reversible, or which had fewer expected knock-on effects, would be the more cautious rather than the reckless approach. Our framework would give some tools to address that, but it would be very hard to do that without knowing the very specific circumstances.

**Baroness Neville-Jones:** Does it differ in any real essential, compared with conventional strategies—insecticides—or is it a variant of the same thing?

**Mr Matt Shardlow:** The main difference is around the first category, where you are effectively trying to get rid of something so you are introducing a process—whether that is through eradication or an actual genetic modification of that organism—and introducing something which is going to die out and disappear. That is a different level of risk category from introducing something where you might attach, for instance, a gene drive or you might hope it has some beneficial effect which will spread throughout the population. That is very different from anything we have done up to this point. We do not do that with genetically modified crops; our crops generally are highly altered already and dependent on us—they are domesticated plants, effectively. We are talking about the replacement of traits in wild populations to introduce something that is going to get out and go broader, which brings in other ethical considerations. For instance, if we have a system at the moment where the regulation allows countries to opt out of having certain genetically modified plants released into their territory, they cannot opt out of their neighbour introducing mosquitoes and them blowing over the border. There are a bunch of ethical considerations around introducing stuff into the countryside.

Coming back to Lord Ridley’s point about the signal crayfish, we heard earlier about perhaps introducing a gene into bees that makes them immune to neonicotinoid pesticides. There does come a point where one starts to feel, “Maybe we should be avoiding some of these problems in the first place”. That is the important thing, and we are not doing enough around that. It feels a bit odd to be making bees immune from a chemical we are still applying in the countryside and exposing them to.

If I may, I would like to quote from the Pope’s recent Encyclical on Care For Our Common Home, which is relevant to this ethical debate. He said, “Often a vicious circle results, as human intervention to resolve a problem further aggravates the situation. For example, many birds and insects which disappear due to synthetic agrottoxins are helpful for agriculture: their disappearance will have to be compensated for by yet other techniques which may well prove harmful.” There is a slight “old woman swallowed the spider to eat the fly” situation we might get into here, whereby we are creating problems, not fixing those problems, and having to come up with a further technical fix which may have further technical problems. We need to bear that in mind not only because that starts to bring in risks which are potentially harder to control if they become widespread throughout populations, but because of the public reaction to our trying to introduce genes into populations of wild animals which we are hoping will continue to be wild animals into the future.

**Professor Jonathan Montgomery:** We would be anxious about thinking that population suppression and population replacement using gene modification techniques are somehow

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ethically in a very different category from population suppression through herbicides and insecticides.

**Baroness Neville-Jones:** That was one of my questions.

**Professor Jonathan Montgomery:** The same ethical issues are going to apply to other techniques that end up displacing, replacing or suppressing populations. Our view would be that if you are going to suppress a population and you can do it in a more selective, targeted way, that may involve fewer risks to the ecosystem than others, and that we should consider this as not being somehow a special question around gene modification but a question around the appropriate response to its suppression.

**Baroness Neville-Jones:** Essentially, the answer is, it does not really differ.

**Professor Jonathan Montgomery:** It is the same set of ethical questions. It will not universally produce the same answer.

**Q61 Baroness Manningham-Buller:** I wanted to ask about public understanding in this area. Mr Shardlow, you have talked about this perception of the government, or whoever, as “up to something” and the number of countries that have put all genetically modified stuff in the same “prohibit” bin. Do we actually have data on what the public understands on this subject? Lord Ridley is going to come on to how we can improve understanding. Both of you have touched on this, but any further comments would be welcome.

**Professor Jonathan Montgomery:** I can only say I do not think we have any direct information on this because we have not set up a project targeting this. We have some indirect indication from our discussions around the naturalness project, which has not identified any particular concerns in the context of insects.

**Baroness Manningham-Buller:** As far as you can tell, the public differentiate between crops and insects.

**Professor Jonathan Montgomery:** As far as we can tell they have not really thought much about the potential for a difference, but we have not set out to discover that. Importantly, we are not saying we have any evidence that they are not concerned.

**Baroness Manningham-Buller:** This is anecdotal, not substantial.

**Professor Jonathan Montgomery:** We have not asked that question directly. If it was very, very obvious it might have leapt out at us, and it has not, but it does not tell us what we would find if we did.

**Mr Matt Shardlow:** Just to echo that, it seems to be an issue of very little public awareness and debate. It is different, particularly, when we get into the realm of wanting things to continue to thrive in wild populations in the future. That is a different debate from the one we have been having about controlled release into agricultural fields.

**The Chairman:** You said earlier that you think the debate should be conducted around the context rather than the technologies. Would you not agree that, in practice, there has indeed been a debate about the context because it includes the wider GM organisms, not just insects?

**Professor Jonathan Montgomery:** That still feels like a debate driven by, “Do you like this technology or not?” defining it as GM. A contextual debate around different ways of addressing health problems caused by malaria, looking at a range of different technologies,



would be Nuffield's proposition because it enables you to ask whether there are good reasons for going down this particular technological route as opposed to other possible routes, and explain what motivates people to explore those reasons.

**Q62 Viscount Ridley:** Some of what I was going to say has been overtaken by events. It is really a question of who should lead a public debate, how should one set it up and—the point you have touched on—should it be about GM insects or about how we solve infectious diseases and weigh the different technologies? In that context, in response to Mr Shardlow's comments about the Pope and the old lady who swallowed a fly, given that we know that GM crops have in many cases hugely reduced pesticide use, when are we going to see a conservation organisation champion genetic modification rather than say, "We are not against it" or "We are against it"? When are they going to say, "Actually, this is a very good conservation tool that could be used to reduce the amount of harm we are doing in the countryside with pesticides and chemicals"? That is in the context of public debate. The public debate will work much better if next time round, Greenpeace is on one side and Friends of the Earth on the other, rather than them all being on one side of the debate.

**Mr Matt Shardlow:** I can only speak for my charity, Buglife; I cannot speak for those other organisations. You would have to bring that up with them. Buglife do take an open-minded and scientific approach to this issue; we do not have an absolute, dyed-in-the-wool, "This is right/this is wrong" approach. We do look at the evidence, we do look at the factors and we have said some positive and hopeful things about insecticide reduction with GMs. That is certainly an ideal to aspire and aim for, and we are supportive of people's efforts to try to do that. I am not sure all the evidence is in, and most organisations are quite careful because we do not want to end up promoting something that turns out to be a real problem.

In the last three weeks, in the Punjab, on GM cotton, £420 million has been wiped off the value of cotton by whiteflies. Whiteflies survive the Bt toxin in a way that many of the other pests, the bollworm and other things, do not. Here you have a situation which appears to be a huge problem—from the press reports you obviously cannot get a full analysis of what is going on in the Punjab: there is massive loss of profit from the yield, and 17 farmers have so far reportedly committed suicide in the Punjab. It is a problem with the GM crop, in that it is occurring in the GM crop; farmers are reporting spiders and beetles running around eating the whitefly in the non-GM crop, but in the GM crop they are not, and there is possibly a link to a different pesticide.

**Viscount Ridley:** Is this a well-evidenced story?

**Mr Matt Shardlow:** It is in the Indian papers at the moment. The regional agricultural director has been arrested for buying the wrong pesticide, which is apparently not strong enough. Those sorts of stories coming out in the press—talking about 17 farmers committing suicide and £420 million off the value of the GM cotton crop—are obviously going to make NGOs with an environmental concern very cautious about signing off on these technologies at this point.

**Lord Fox:** It is also going to give anti-GM campaigners an awful lot of anecdotal to peddle, none of which may actually be true.

**Mr Matt Shardlow:** You will notice I am trying to paint the picture of a lack of clarity about what has gone on there—lots of different reports, all slightly different. It is not as if there is

an obvious answer where one can say, “That is the answer”. That is the problem. There is something happening.

**Viscount Ridley:** There is well-evidenced data about the decline in the use of pesticides in Bt cotton in the subcontinent and the increasing yields. There may have been one problem in one part of the range in one year that you are telling me has been in the Indian newspapers; I am talking about stuff that is in properly evidenced scientific reports. There again, why can we not say that the benefits of this technology are so great that conservation organisations want to be championing it?

**Professor Jonathan Montgomery:** Could I pick up on a couple of aspects of that to get back to the question about what is the best way of framing the debate? One of our recommendations from the emerging biotechnology report is that it is important to understand what people believe is at stake because of the distrust in who speaks accurately about scientific facts. You end up, if you are not careful, trading peer reviewed versus non-peer reviewed science, anecdote against anecdote. To try to develop what we call a robust form of public reasoning, it seems important to try to find ground where people argue about the same things at the same time, as opposed to past each other. We would certainly think it appropriate to avoid the incentives on researchers to over-hype the possible benefits of their work. In many of our reports, including our recent research culture one, we have identified a range of ways in which journalistic pressures and funding pressures encourage people to claim things they really cannot with any certainty predict in order to get into over-claiming about potential benefits. That is as much a vice as the anecdote on campaigning organisations on the other side. We need to somehow insulate that into a bit of territory where it can be picked through.

However, more important, I think, is understanding what those sorts of arguments are symptomatic of in terms of values. We were particularly concerned in the emerging biotechnology report about the difficulties in getting voice for people who might be the likely beneficiaries of the technologies, which is something I picked up earlier. In our work we recently published on children in clinical research, we made use of some community engagement programmes funded by the Wellcome Trust to get an understanding of how communities in Africa would reflect on the involvement of children in research. It is very difficult to use those community engagement processes that are seen to be closely linked with the technologies, but it is a way of understanding what the benefits and the potential of these things might look like from the point of view of communities where they are most likely to be used early on. We have to get that perspective into the framework.

It is very difficult to get through the suspicion that this is being driven by people who want to use the technologies, and our advice is that that is one of the reasons why it is important to frame the debates in terms of a social challenge—what are we going to do about malaria?—to stop you saying the answer needs to be a technological answer. The answer might not be; it might be a technological answer; it might be an old technology better used or it might be a social intervention. However, if you are asking about the value of GM technologies in responding to those challenges, people have a sense of what they are comparing it with and they can have a debate.

We would be very keen to encourage you to think about not the instrumental—the ethical, legal and social implications of this technology—but the tools we might have to address these challenges, whether these new technologies improve on what we have, or whether we

need them. You are much more likely to have common ground for debate if you frame it in those ways than if you ask something about a technology whose usage we cannot easily predict and, therefore, you are opening up the possibilities of all sorts of science fiction, both positive and negative.

**Q63 Lord Krebs:** In case I have not done it before I want to declare an interest as the deputy chair of the Nuffield Foundation, which is one of the funders of the Nuffield Council. My question, which was going to come a bit later but it does lead directly from the discussion which Lord Ridley's question started, is about how we nail the facts as opposed to the rumours connected with GM technology. We had the discussion about the Punjabi cotton farmers. Do either of you think there is a role here for independent expert groups? In the regulatory environment there are groups like ACRE, which is a statutory body, and there are other groups like the Royal Society which publish independent reports and have no vested interest and simply look objectively at the available evidence. Do you think that is a way of holding to account the different sides who are making claim and counterclaim?

**Professor Jonathan Montgomery:** I would certainly support that approach. Nuffield sets out in its working practices to be inclusive in respect of the voices contributing to the bioethical debates and it tries to make sure that no one feels unheard, but it commits to testing those arguments against consistency, coherence and against the best available evidence. It wants to say: we should know what everybody thinks, but we should accept that public reasoning has some ground rules and that building an argument on something that is inaccurate is not good public reasoning.

**Lord Krebs:** On that question of inclusiveness, do you think that if, let us say, the chief scientist from Greenpeace were on ACRE, he should declare an interest just as a chief scientist from Monsanto should?

**Professor Jonathan Montgomery:** If it were our working party, we would deliberately recruit people we know are going to disagree because we think we will get a better debate, and we would make it explicit.

**Lord Krebs:** My question is: should he declare an interest?

**Professor Jonathan Montgomery:** I would expect it to be either formally declared or made apparent in the membership statements.

**Lord Krebs:** Thank you.

**Lord Patel:** Before I ask my question, which is about regulation, Professor Montgomery, do you think the Nuffield Council, in the light of this inquiry, should do an ethical review of GM insects, taking on board what you have suggested should happen in discussion around the benefits of eradicating disease?

**Professor Jonathan Montgomery:** As I touched on earlier, we have set up a programme approach to gene editing prompted by the CRISPR technologies. In our long list we had the possibility of a topic on GM insects. Our approach is, we think there are some significant common features to questions about gene editing, and we want to identify and draw those out, first, as a platform report, and then we anticipate there will be a series of case studies. We almost certainly will find ourselves looking at human genome editing as one of those case studies, but our early assessment is that that is rather further off than something like GM insects and issues in crops. Certainly, one of the case studies will be in this area because

it is already on our long list, and we would expect to take that decision towards the middle of the year, when we have our platform report in place.

Obviously, one of the factors is, who else is doing work in the area? We would not expect Nuffield to duplicate work that is already done by others; we would only pick up a project if we identified that we could make a timely and distinctive contribution. We are also very pleased to work in partnerships, so if there were to be a big public exploration of attitudes around this we would certainly be keen to see what we could bring to that in our way of doing bioethics in partnership. You saw Sir Roland Jackson in an earlier session and he is also a member of the Council. We are often looking for ways in which we can better inform our debates but, also, take what we have learnt into wider debates.

**Q64 Lord Patel:** Moving on to the regulatory environment—we have touched on this in conversations about previous questions—do you think the current regulatory environment, both in the EU and in the UK, is fit for purpose for GM insect technology?

**Mr Matt Shardlow:** Broadly it is, in terms of the risk assessment process. The risk assessment process seems to be working for the crops and I do not see any reason why it should not work for the insects as well. The problems, as we have highlighted before, come at different stages from that regulatory process. I made points earlier around increasing transparency in the scientific evidence, increasing the registration and pre-registration of trials, making sure that the information out there is transparent and that we see studies which have not worked as well as studies which have worked. Other than comments around the quality of that science and making sure that it is properly and statistically robust, one of the problems we have seen in pesticide regulation, which is in some ways comparable, is studies done by the industry which turn out not to be statistically robust and they are quoted as showing no evidence. If you do not have the statistical power to show the evidence, you are not going to find a conclusion. Getting good science as the basis of this is absolutely essential. To come back to your previous point, it sounds very much as if the Nuffield Foundation is doing an excellent job leading some of this debate.

**Professor Jonathan Montgomery:** It is the Nuffield Council; the Foundation is slightly different.

**Mr Matt Shardlow:** I am sorry; the Nuffield Council.

**Lord Patel:** The Foundation is the money.

**Mr Matt Shardlow:** Our universities have a 600-year history of having fantastic debates and moving issues forward within the academic community. This one is slightly harder because there is a sense of lack of trust in the academic community over this. How we break that out and make it a more public conversation is, I think, quite a difficult question.

**Lord Patel:** We have heard in evidence that people, with good scientific bases and good evidence scientifically, apply to EU regulators and because it has the label “GM” it goes in a “pending” box for ever.

**Mr Matt Shardlow:** My understanding is that that is because of the politics of different countries not wanting to have GM and to block it going through.

**Lord Patel:** So the current regulatory framework does not work.

**Mr Matt Shardlow:** If you look at the conclusions of scientific committees within countries, they often tend to parallel the political stance within those countries. In the UK we have had politicians for the last 15 years who have been pretty broadly supportive of genetically modified crops, and we have scientists who are pretty broadly supportive of genetically modified crops. That situation is not reflected in most EU countries; that is why it is blocked and gets stuck.

**Lord Krebs:** What about EFSA? EFSA is the EU's risk assessment body. What is its view? Does it coincide with the British view or these other views?

**Mr Matt Shardlow:** My understanding is it largely presents scientific analysis of the data to the EC, which then cannot get a qualified majority through the voting system. If you cannot get a qualified majority through the voting system and you have countries which are digging their heels in, then it gets stuck at that level. That is a political level which is to do with the broader ethical concerns in other countries, and people do have different perceptions of the truth and different perceptions of the risk. Those clearly vary from one country to another—how they are dealing with that and how they are politically expressing that. I am not sure how you easily fix that through a regulatory process or a single piece of legalisation. Obviously, the effort to allow countries to opt out of GMs has been an attempt to defuse the tension at that level so that countries can feel they have more control over their territory and genetically modified crop use, with the hope that that will have a reciprocal relaxation at a higher level within the process that will allow more crops to go through if there is a sufficient number of countries who really want that crop to go through. As that has only gone through this year, we will have to see if that works. In my mind that is almost a level above the regulatory process; that is more to do with the overall political wishes of the countries involved. To view that as a success or a failure depends entirely on which of those countries you are sitting in.

**The Chairman:** Lord Maxton, then Lord Ridley and we will probably then come to a conclusion.

**Lord Maxton:** I am going to be slightly difficult here, in the sense that human genetic modification, which was mentioned briefly by Professor Montgomery, is the thing that causes most of the problems. There are large organisations throughout the world, particularly in Europe, which are opposed to genetic modification of human beings. They then transfer that down to genetic modification in crops and then down further to insects. Am I right in making that assumption?

**Mr Matt Shardlow:** Instinctively, there probably is a link. I do not have any data; I am not sure if Jonathan has.

**Professor Jonathan Montgomery:** It is very hard to tell. The technology that makes people think about human gene modification actually becoming possible has only emerged in the public conscience quite recently, but the idea in terms of science fiction has been around for a very long time. Which is really driving this? I am not sure. It may actually be more to do with attitudes to technology, manipulation of nature, a sense of what is normal and natural, and it may be the same thing that is driving both concerns. That, of course, is why we have kicked off our project to try and dig into that more deeply.

**Lord Maxton:** Human genetic modification is not just a recent thing. You quoted the Pope: that whole religion is opposed to genetic modification simply using certain genes from

certain sources. Are you telling me that has nothing to do with the way in which people react to genetic modification?

**Mr Matt Shardlow:** No, I do not think we are saying that. We might be saying there may be more to it. One example—which shows the complications—is people having a fear that if they eat genetically modified food that is going to somehow genetically modify them. That might be their fear, hence to them it all looks like a big bundle of things to be very afraid of, that they do not trust. I am going to regret quoting the Pope, but in some ways they feel there might be someone playing God. That, again, to a lot of people feels morally wrong: that someone is playing God by creating life. There is more to it than simply human beings. There is a level of grade: just as we value human life differently from how we value the life of our pet dog, and how we value the life of a bird and the life of a bug in a field, there is a gradient in ethics in how we look at those different things. But I do not think it is just about humans.

**Viscount Ridley:** As a final point, I wanted to get on the record that last Friday's *The Indian Express* had a headline reading: "Proliferation of unregulated hybrids not Bt is to blame for pest damage to cotton this year."

**Mr Matt Shardlow:** As I said, it is a morass of confusion, but it is the sort of thing that adds to the fear of organisations coming out and saying anything positive.

**The Chairman:** We all recognise—and I say this to Lord Ridley, as a columnist—that we do not always believe everything in the papers! That is very unfair, but he is quite right to draw attention to anecdotal evidence as opposed to peer-reviewed evidence, and that was his point.

Professor Montgomery, we would be very interested in hearing when your report on naturalness comes out later this year. Whether it will be in time to contribute to our deliberations I cannot quite be certain, but we will certainly be very pleased to keep in touch with that. Thank you both for your contribution to our discussions today; we have moved quite some way—from GM insects into wider ethical issues—but I think we have benefited from that. Thank you very much.

## **Buglife, The Invertebrate Conservation Trust – Supplementary written evidence (GMI0031)**

### ***Benefits to society***

A genetically modified invertebrate should only be approved for release into the environment after the benefits have been scrutinised and considered in the context of the identified and assessed risks.

It is already the case in pesticide regulation that a use should only be approved if it is sufficiently efficacious. Article 4 of Regulation No 1107/2009 ‘concerning the placing of plant protection products on the market’ states:

“A plant protection product, consequent on application consistent with good plant protection practice and having regard to realistic conditions of use, shall meet the following requirements:

- (a) it shall be sufficiently effective;
- (b) ...”

This is expanded in Annex II which states that “An active substance ... shall only be approved where it has been established for one or more representative uses that the plant protection product, consequent on application consistent with good plant protection practice and having regard to realistic conditions of use is sufficiently effective.”

It is therefore anomalous that Directive 2001/18/EC ‘on the deliberate release into the environment of genetically modified organisms’ does not contain any explicit assessment or consideration of efficacy or benefits.

It is ethically important that the regulators of pesticides and GMOs consider how effective and beneficial a GM modification is likely to be and after release keep this under routine review.

Taking any risk with the health of the environment is difficult to justify morally if the only benefit is to the financial position of the GMO manufacturer.

The market is a poor judge of efficacy as there are a great many examples of products selling very well, but not achieving their stated aims, harming the public good or even providing disbenefits to the purchaser. The mounting evidence that neonicotinoid pesticides have become the predominant global insecticide, without providing consistent yield benefits is one example where the current regulation appears to have failed. Outside the EU there are even worse examples, such as with rice where scientists have shown that planthopper outbreaks are primarily caused by excessive insecticide use and result in the loss of 2 million tons of rice in an average year. Rice farmers are the main victims of a poorly regulated pesticide market in which insecticides are sold as if they were fast-moving consumer goods (Heong et al. 2013).

Scientists are naturally optimistic and enthusiastic about their innovations and companies are well practiced in convincing investors of their investability. However, the decision maker in protecting the best interests of the public must pass a strongly sceptical eye over the claims for benefits made by the applicants.

When the decision maker considers that the benefits may not outweigh the risks he/she should be able to take this into consideration and where appropriate ask for more evidence of efficacy.

Public perception of benefit from GM crops is frail. The 2014 poll of British public attitudes to science found that 36% felt that the benefits outweighed the risks, while 28% felt the risks outweighed the benefits (Castell et al. 2014).

Scientists are trusted on the basis of their intentions. 77% of the British public think the independence of scientists is often put at risk by the interests of funders, and 66% specifically feel that scientists are too dependent on business and industry for funding. 90% trust university scientists compared with just 60% who trust scientists working for private companies (Castell et al. 2014).

Given the widespread public distrust of the motivations of large agrochemical companies and associated scientists and politicians, nothing would be more damaging to the appropriate development and implementation of GM technology than the approval of GM products that the public perceives as confirming their worst fears.

Perhaps there would be a greater trust in GM if there was a clear scientist led movement to develop altruistic applications from GM technology that would fix environmental and societal problems without a central focus on the commercialisation of organisms. Unfortunately investment in science, and particularly natural environment science, has been declining since 2009 and Defra programmes that might benefit from GM technology, such as invasive species control, are stricken by a paucity of resources.

Ensuring that GM releases provide a genuine positive benefit to society is essential for the public and for the development of GM business and should be explicitly required by the legislation.

### ***Pesticide use and GM crops***

The public perception of benefits from approved GM crops, while not directly relevant to the risks and benefits posed by GM insects, is relevant to the acceptability of the technology.

There is good evidence that GM crops expressing Bt toxin genes have resulted in a reduction in insecticide use (Benbrook 2012, Brookes and Barfoot 2013, Cattaneo 2006, Coupe and Capel 2015). Although caution is advised as many studies suffer from considerable selection and cultivation biases (Stone 2012). There are outstanding concerns about the potential



impacts of Bt toxin containing pollen on beneficial insects with herbivorous larvae (Holst et al. 2013).

GM crops that are herbicide (usually glyphosate) resistant are often associated with increases in herbicide use (for instance Benbrook 2012) and this can result in elevated biodiversity damage. Indeed there are growing concerns about the environmental risks posed by glyphosate, including sub-lethal effects on bee navigation (Balbeuna et al. 2015).

In India, increases in cotton yield since the introduction of the GM technology largely occurred before its widespread adoption, undermining claims that Bt Cotton has provided large yield benefits (Stone 2012). Now this season's failure of the Bt cotton crop, the causes of which remain unclear (Raghavan *Times of India* 2015), means that confidence in Bt products amongst farmers has had a significant set-back (Nair and Bhardwaj *Reuters* 2015).

### ***Risk of gene transfer***

The key EU directive - *2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms* – sets out the risks to consider for GMOs other than higher plants.

The first two listed are:

- “1. Likelihood of the GMO to become persistent and invasive in natural habitats under the conditions of the proposed release(s).
2. Any selective advantage or disadvantage conferred to the GMO and the likelihood of this becoming realised under the conditions of the proposed release(s).”

For genetically modified insects produced with the aim to replace populations rather than suppress them these first two risks are established. It is the aim of the release for the GMO, or its new genetic trait, to become persistent in natural habitats, and this would usually be achieved through a selective advantage.

The next risk to consider is:

- “3. Potential for gene transfer to other species under conditions of the proposed release of the GMO and any selective advantage or disadvantage conferred to those species.”

Here recent evidence indicates that the horizontal transfer of genes to other species, including unrelated species, may be commoner than previously suspected, and can confer unexpected and selective advantages.

Brachionid wasps provide a useful example. These are numerous and diverse little parasitic wasps. They lay eggs in other invertebrates (often caterpillars) that then develop inside the host and hatch out to pupate and transform into wasps, a familiar example are the little yellow cocoons that cluster around many unfortunate Large white butterfly caterpillars. Brachionid wasps all have the genome of a virus, known as a Bracovirus, incorporated into

their DNA, this virus type has not been found existing separately from the wasp so is perhaps better considered to be part of the wasp than an independent organism. The wasp injects the Bracovirus genome into the host insect at the same time that it lays its egg/s. When the larvae hatch the host produces Bracoviruses that suppress the host's immune system, allowing the wasp larvae to thrive. The incorporation of the virus into the wasp DNA is thought to have happened c.100 million years ago.

This year a startling discovery has been made, it is now apparent that this virus DNA has also been incorporated into the DNA of a number of the butterfly and moth host species. In the case of the Monarch butterfly this happened about 5 million years ago and the DNA has persisted since then. It appears that this horizontal transfer provides the host butterfly or moth with a selective advantage by improving its resistance to a different threat - baculoviruses (Gasmi et al. 2015).

In another recent study authors found horizontal gene transfer to be common across 40 animal species and identified 33 gene sequences in the human genome that they believe have been horizontally acquired from other organisms. They conclude that the "expression of multiple horizontally acquired genes is a hallmark of both vertebrate and invertebrate genomes" (Crisp et al. 2015).

While we are a long way from understanding how often horizontal gene transfer occurs or what proportion of events create a persistent genetic change, the evidence indicates that this does happen with some frequency and can change the course of evolution. The potential for such transfer must be seriously considered in assessing any release application.

Clearly in instances where it may not be possible to put the cat back in the bag it is even more important that decision makers firstly consider the possible impacts from horizontal gene transfer and secondly are convinced that the benefit will be realised.

### **Is the Precautionary Principle "often abused and used for antiscientific purposes to abolish or prevent any new technology"?**

The European Environment Agency (EEA) has produced a thorough analysis of the application of the Precautionary Principle 'Late lessons from early warnings: science, precaution, innovation' (2013). The report is substantive and constitutes a serious volume worthy of exploration.

The EEA report includes an analysis of 88 issues identified in the literature as 'false positives' – cases where false alarms were raised about risk to health or the environment and these resulted in unwarranted regulatory action. In most cases it was found that the risk had subsequently been confirmed, the 'jury was still out', or the alarm had not resulted in regulation. Only four cases were confirmed to be genuine false positives, and of these three occurred exclusively in the USA (Hansen and Tickner 2013). In the EU and UK only alarms about the irradiation of food resulted in regulation which may now be viewed as overbearing.

There are several definitions of the precautionary principle and elements of it are found in many places. In relation to GMOs the Cartagena Protocol on Biosafety refers to Principle 15 of the Rio Declaration (1992) which states that “Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation.” The Protocol itself states that "Lack of scientific certainty due to insufficient relevant scientific information . . . shall not prevent the Party of import, in order to avoid or minimize such potential adverse effects, from taking a decision...."

There have been no cases where a safe new technology has been prevented by the Precautionary Principle. While the principle is often invoked as the enemy of science and innovation, it is nothing of the sort; it is simply a sensible approach to avoiding harm occurring while regulators dither, or hide behind uncertainty, to avoid taking difficult political or economic decisions.

*8 November 2015*

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Professor Austin Burt, Imperial College London, Professor Luke Alphey, The Pirbright Institute, and Professor Paul Eggleston, Keele University – Oral evidence (QQ 48-55)

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[Transcript to be found under Professor Luke Alphey, The Pirbright Institute](#)

Professor Tim Dafforn, Department for Business, Innovation and Skills (BIS), Innovate UK, and Biotechnology and Biological Sciences Research Council (BBSRC)—Research Council UK – Oral evidence (QQ 1-15)

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[Transcript to be found under Biotechnology and Biological Sciences Research Council \(BBSRC\)—Research Council UK](#)

Dr Amaro de Castro Lira Neto, State Institute for Agronomy (IPA), Dr Marcia Almeida de Melo, Federal University of Campina Grande and Dr Professor Paulo Paes de Andrade, Federal University of Pernambuco – Written evidence (GMI0006)

**Dr Amaro de Castro Lira Neto, State Institute for Agronomy (IPA), Dr Marcia Almeida de Melo, Federal University of Campina Grande and Dr Professor Paulo Paes de Andrade, Federal University of Pernambuco – Written evidence (GMI0006)**

[Written evidence to be found under Dr Professor Paulo Paes de Andrade](#)

Professor Paul Eggleston, Keele University, Professor Austin Burt, Imperial College London, and Professor Luke Alpey, The Pirbright Institute – Oral evidence (QQ 48-55)

**Professor Paul Eggleston, Keele University, Professor Austin Burt, Imperial College London, and Professor Luke Alpey, The Pirbright Institute – Oral evidence (QQ 48-55)**

[Transcript to be found under Professor Luke Alpey, The Pirbright Institute](#)



## European Commission – Oral evidence (QQ 87-99)

*Evidence Session No. 9*

*Heard in Public*

*Questions 87 - 99*

TUESDAY 10 NOVEMBER 2015

Members present

Earl of Selborne (Chairman)  
Lord Fox  
Lord Hennessy of Nympsfield  
Lord Hunt of Chesterton  
Lord Krebs (co-opted)  
Baroness Manningham-Buller  
Lord Maxton  
Duke of Montrose  
Baroness Morgan of Huyton  
Lord Patel (co-opted)  
Lord Peston  
Lord Vallance of Tummel

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### Examination of Witness

**Dr Ladislav Miko**, Deputy Director-General of DG SANTE, European Commission

**Q87 The Chairman:** Good morning, Dr Miko. Thank you very much, to you and your colleague, for joining us today on this link. I should just explain that this is being broadcast on our broadband network, so I am going to ask you to introduce yourself, for the record. If you would like to make any opening statement to us, do please feel free to do so.

**Dr Ladislav Miko:** Good morning. My name is Ladislav Miko. I have worked as a deputy director-general in the DG for health and food safety of the European Commission since 2011. One of my responsibilities is also in the area of biotech and genetic modifications. I would like to thank you for giving both me and the European Commission the opportunity to participate in this inquiry on GM insects. I understand that this issue has already led to interesting discussions in the Committee, and I am pleased to provide you today with an insight into the regulatory approach on the GM animals issue at our level in the EU.

I would like to start by stressing that the Commission is in favour of innovation, which is a core driver towards growth, jobs and competitiveness in Europe. Obviously, the innovation has to be in tune with the broad values of society and match the demands of the European citizens. This is why the European authorisation system for biotech products is based on sound science and strict case-by-case risk assessment. I would like to highlight that, as of

today, there is no pending application for GM animals in the European Union. However, in order to be prepared for expected and possible future applications in this field, in 2007 the Commission requested that the European Food Safety Authority develop guidelines for the safety assessment of genetically modified animals for food and feed and release into the environment. EFSA published in 2012 and 2013 two guidance documents: one on the environmental risk assessment of genetically modified animals and the other on the risk assessment of food and feed from genetically modified food animals and on animal health and welfare aspects. Should an application for genetically modified animals be submitted into the European Union for field trials for placing on the market, the existing European Union legislation on GMOs and the EFSA guidance documents would be appropriate. GMO labelling requirements would apply to any GM animal and its derived products in line with the GMO legislation.

I would like to underline that the Commission closely follows the development of genetically modified animals. We are aware of citizens' concerns that might be raised in the future, as described in a recent research project funded by the Commission. I am looking forward to the discussion we will have this morning, and I hope that I will be able to help you probe some of the areas raised in the previous sessions, and establish a clearer picture for the scientific community, regulators as well as the public, as it will be needed.

**The Chairman:** Thank you, Dr Miko, that is very helpful. Would your colleague like to introduce herself?

**Dr Ladislav Miko:** I can introduce her. She is Dorothee André, who is the head of Biotechnology Unit. You cannot see another colleague from the same unit, who is here if I need any assistance in terms of documents or papers.

**Q88 The Chairman:** Welcome to our meeting from a distance. Thank you very much. Let me start the questioning. We note that the deliberate release of GMOs directive is, effectively, the regulation which determines the release of any GMO, whether crop or insect. In practice, do you think it is fit for purpose for GM insect technologies, recognising that when the directive was drafted insect technologies probably were not as well understood as they might be now? Do you think that the regulatory environment could be improved in respect of insects?

**Dr Ladislav Miko:** Yes. In short, I would say, I think the existing legal framework is sufficient and fit for purpose. Until now we have never had any applications, so we do not have practical experience; but, as we have theoretically tested the system, it should be working and applicable also for the case of GM insects.

**The Chairman:** In the light of that, do you think that there would be a willingness by member states to reform the regime in respect of GM insects?

**Dr Ladislav Miko:** I am not sure that I understand the question. I believe that the existing framework will not need to be reformed. Basically, we can proceed within the existing legal framework in the case of GM insects. I do not see any obstacle or problem with the process, so basically it will start flowing as it is regulated now. As much as we can assess, there is no need to change anything in the legal framework.

**The Chairman:** No, I understand.

**Dr Ladislav Miko:** If you are asking about the positions of member states towards this issue, that is very difficult to predict from my point of view. I can only refer to existing experience with crops. As you know, the system which is set up is based on the scientific assessment by our scientific body, which is EFSA, based on the application, and then proceeding—which includes the positions of member states and their vote. Obviously, the European Commission is obliged to follow this procedure. We have had very different views of individual member states to genetic modifications in general. For me, it is very difficult to prejudge what would be the situation with GM insects. If the patterns that we have witnessed in the crops are followed, we can expect that some member states will support, some will not, and some will abstain. In the final result, what we have had in the crops as a general rule, basically from the beginning, is that the respective committee will reach no opinion on any of the genetic modifications. The legislation covers that situation. It requires another try, and so forth, through the appeal committee. Following the appeal committee, if there is still no result, the Commission will be obliged to decide on the issue, which is the case. That is how we basically approve the GM.

**The Chairman:** One of the issues is that when the directive was originally drafted, some of the concepts we have on the horizon now, on gene drive and gene editing, were probably not as well developed. We therefore wonder whether the directive needs to take account of advances in the technology. From your response, I understand you think the directive is still fit for purpose for GM insects.

**Dr Ladislav Miko:** I have lost the picture—I can hear you but I cannot see you. I hope you can see me.

**The Chairman:** Yes, we can see you.

**Dr Ladislav Miko:** We believe the development of new techniques is not influencing, at least for now, what we have been looking at as far as the existing regulations being able to address these issues. The question will potentially be whether this or that technique will fall under the scope of this regulation. That needs to be carefully assessed but, per se, the regulation can work and deliver.

**Q89 Baroness Morgan of Huyton:** Dr Miko, we have had a fair amount of evidence that has effectively said that the current regulation is fit for purpose in theory, but not in reality in the way that it works. In a sense, the regulation functions at the scientific level, but as soon as it leaves the science committees, it is overruled and changed by politicians, and consequently very little is moving forward in the EU with, obviously, potentially detrimental effects both economically and scientifically within the EU. I wonder whether you would like to comment on that perception. We have had a range of people giving us that impression. When you say “fit for purpose”, they sort of agree but then it does not function.

**Dr Ladislav Miko:** As I said, the problem is not in the legal framework. The problem is in how it is implemented, as you indicated; but on the other hand, there are procedural steps that we have to follow. Obviously, we have to reflect the scientific opinion, and this is what we have as the basis for the proposed decision, but then we are obliged to follow the voting of the member states and they have a right to represent their views. The reality is that in the history of this legislation we have never had a clear opinion either for or against any proposal. So, every time we have ended up with what is called a “no opinion” situation where the Commission has to decide. Then it follows the process and sometimes, because of

the difficulties in the past in the political discussion, when they came to the level of a Commission decision, some decisions took a longer period. But since we started with the last Commission, President Juncker's Commission, the issues have been reviewed from our side, and we came up with solutions which we believed would help. One of the blocking elements in the political discourse was the issue of cultivation and we came up with a proposal on opting out for those countries which have other legitimate reasons for opting out of cultivation. Despite a very complex and lengthy discussion on this proposal, at the end we can say, after adoption, it really works. You may know that out of 28 member states, 19 actually used this legislation, including some parts of the UK, which indicates that for those who are willing to correctly follow on a scientific basis the approved safe products for cultivation, they can do so. We were also considering and proposing the same approach for food and feed uses. Nevertheless, this is the proposal which is now in discussion, and we have a rather negative attitude in Parliament and we will see what the final position will be in the Council to this proposal. This is a little strange for us because we genuinely thought, as with cultivation, this could ease the procedure. I cannot say now about the result because the discussion in Council is not yet concluded.

**Q90 Lord Fox:** Thank you for coming today, Dr Miko. You mentioned food and feed being in difficulty in terms of the opt-out. Insects are clearly not in food or feed, as I would regard them. Do you think they are potential candidates for this opt-out process? Do you think that would have a positive effect in moving towards some sort of implementation in disease control?

**Dr Ladislav Miko:** Yes. I repeat that, as the Commission, we do not have any experience, so what I can give you is my personal assessment of the situation. For us, I think that the sensitivity of the GM process has a clear link to the food or the feed. When we speak about the particular case of insects—if we do not speak about insects as a source of food or feed, but about their other uses—I expect that we would have fewer problems in the procedure, but we do not need to change or modify the existing legislative framework. I think we can go through, and I would not expect as many problems as we had with the food or feed-related applications.

**Lord Fox:** In your introduction you used the word “animals” throughout, and you seem to have bundled everything into one classification of creature. Is there some merit for unbundling that? Where you have insects, which are clearly not part of the food and feed play or objective, is it beneficial to pull them out and have a separate classification rather than as animals—as insects?

**Dr Ladislav Miko:** Sorry, I am not sure if I understood your question.

**Lord Fox:** You seem to have bundled everything that was not plants into animals. So you spoke of animals as a single classification rather than perhaps breaking that up into different uses and different objectives.

**Dr Ladislav Miko:** Not really; sorry if I was not clear. We are analysing all non-plant issues, and what we can expect in the near future, and looking at how to deal with the potential applications which come from the non-plant side. Basically, it is looking at fish, insects and potentially other animals that could be genetically modified. According to these tests, we are convinced that the existing procedures and framework could work. We do not need to adapt any specifically for the animals. We wanted to be prepared in case we concluded there was a

need to change something, we needed to have some time to do so, but the conclusion was that we do not need to change the legal framework.

**Lord Fox:** To be clear, if the insects are not regarded as food or feed, then there is more chance of the opt-out working in their favour?

**Dr Ladislav Miko:** I would not say the opt-out, I would say the smooth application process. We do not need to opt out. Theoretically, when there is an application for insects not intended for food, I expect we will get the application filed with all the necessary information following the guidelines from EFSA. We will ask EFSA to assess all the existing risks, we will get EFSA's opinion, go to the committee and vote on the approval process. I do not see, in any element of that, any particular problem or obstacle. My judgment—of course, because we do not have the experience—is that this process would be smoother and faster than the other processes because there is no link to food, which creates the sensitivities in some member states' positions.

**Duke of Montrose:** Dr Miko, on this question about the need for an application, does this need to be made at a national level, or are you asking for researchers or companies to submit applications?

**Dr Ladislav Miko:** It depends what you are speaking about. If we are in the phase of the scientific trials, then the application should be submitted to the national authority in the country where the trials are going to happen. If you are speaking about the approval of the genetic modification for use in the European Union, then the application should be submitted to the European Union and assessed by EFSA.

**Q91 Lord Hunt of Chesterton:** There are a number of different models for the regulation of GMOs internationally. Canada regulates the products rather than the process, and therefore uses a different word. The G word, or the GMO word, makes life difficult, as you have explained. In fact, the House of Commons suggested using some other words, particularly for GMO insects. Do you have a view on that? Perhaps I may follow that up with another question. What research is the Commission sponsoring to clarify these issues? Research, presumably funded by you, will have some European acceptance. Is that in fact an important part of your strategy? The EU has its own laboratory at Ispra. Is it involved in helping to establish the best way forward for regulation?

**Dr Ladislav Miko:** Yes. First, on the potential different types of approach to regulation, we do not think that changing the model from the European one would deliver a better result. We believe that the existing one is appropriate. We could discuss trait-based regulation, for example, as a model, or the model in Canada and other countries which includes the socio-economic benefits as part of the assessment. Personally, I would expect that it will not change the pattern, because it is linked to the GM as such. Secondly, we will only extend a potential amount of the products which need to go into the approval process because we check now—I am being very simplistic—only if the GM application is as safe as its non-GM counterpart. When we vote for the trait-based regulation we will have to assess any result of the breeding which brings a new trait—be it GM or not—so it will extend rather than limit the approval process, and we do not believe this will be helpful for the process.

Regarding the research in the Commission, I have to say that we have very limited capacity ourselves to do the research. Obviously we have our Joint Research Centre, which also looks at the GM issues, but it is rather more about the needs of regulation. For example, methods

of assessment or methods of detection of GMs help us to select the ones which could be broadly used in the European context in a harmonised way. They do not do the GM research per se. We finance the GM research within the rather large amounts of moneys that are distributed to the European researchers via DG Research and Innovation. I am aware that there are some projects which allow for researching genetic modifications, but this is support to science in general. It is usually not a concrete question to be answered, but rather support for the new trends in genetic modification to support the innovation process. I do not have with me an overview of the projects, but if you would be interested in that, I would recommend either to go to DG Research colleagues or, alternatively, we can provide you with a written overview of the projects relevant to GM in the last five years.

**Q92 The Chairman:** That would be useful. Thank you. Could I follow up your reference to the Joint Research Centre? We understand that the JRC's Institute for Prospective Technological Studies in Seville hosts the European GMO Socio-Economics Bureau. Has this group considered GM insect technologies?

**Dr Ladislav Miko:** I do not think that we had a particular assessment of any GM insects in socio-economic terms because basically it was always about the crops.

**The Chairman:** What is the role of the European GMO Socio-Economics Bureau? How does it connect with the regulatory process, whether for crops or insects, or any other GM? What are its functions or benefits within the regulatory framework?

**Dr Ladislav Miko:** If we are speaking directly about the approval procedure as such, there is no direct work by this bureau, but we have plenty of discussions with member states related to the potential benefits as, let us say, a counterweight to the potential risks. For that, we need to establish a capacity which will be able to analyse and provide us with quantified potential positive effects. In this sense, the bureau is delivering the information which is then used in our role as the risk manager, so when we then decide, and substantiate our decision, on the application before the final approval, we can use the results of their work. I would say that the bureau is not directly responsible for a better or worse result of the approval, but it is rather our tool to provide arguments on the positive socio-economic effects in particular decisions.

**The Chairman:** One of the issues that has come up time and time again, as we have taken both written and oral evidence, is the need for an exchange of technical and scientific information regarding the socio-economic implications of GMOs, whether insects, crops, or anything else. We would be very interested to know whether you feel that this bureau could play an enhanced role. We know very little about it ourselves.

**Dr Ladislav Miko:** It is quite difficult for me to judge, to be honest. In my view, all the experience we have shows that the position of member states which are not supporting the GMs will not be dramatically changed by any socio-economic analysis. I may be wrong, but this is my opinion. It is rather useful for us because we need to communicate broadly with the public, and with the scientific community, and we need to provide information because, as I said, every decision in the end is a decision by the Commission, because there is no opinion. We need to show the reasons for that because the issue of the socio-economic impact is often raised in the vote as one of the reasons why member states abstain and do not provide an opinion, and we feel obliged to have this information in our communications. So, for that reason, it is helpful. I do not believe that making it an obligatory part of the

procedure or the decision-making will dramatically change the patterns of the vote, because I do not think this is the major reason for it. I think that the data on the benefits are more or less highlighted quite well in the applications. The companies which come with applications try to show why they do it. We try to extend it and, with the help of the bureau, to analyse it in the European context, so we are able to answer some of the questions, but I do not believe the approval procedure would benefit if we add the socio-economic analysis as an additional step. It is rather the argumentaire for the final decision where we can use this information.

**The Chairman:** That is helpful. Lord Fox, do you want to follow up or have you covered the point?

**Lord Fox:** No, I think I have covered it. Thank you very much.

**Q93 Lord Patel:** Dr Miko, I would like to explore with you the level of awareness in both the Government and the public of GM insect technology. What do you think shapes that view? Are the attitudes of the Governments of different EU countries being shaped by the attitude to GM crops? What do you think is the level of awareness of the different EU member states?

**Dr Ladislav Miko:** First, I think you are right that the main debate, and the main source of the positions of the member states to GMs, is linked to food and feed, or the food chain, if you wish. I think this is the reason why the crops are treated as they are. Personally, I do not think there is a broad awareness about the non-food/feed insect GM technology within Europe. I think most of the public have no clue that something like that exists. If we are to get any application we will have to invest, and I assume the companies developing these methodologies will also have to invest, in communication of this tool. I am reluctantly more optimistic—I do not want to wait because it is difficult to predict with that technology—because we have very clearly seen that the other GMs which are not related to food do not have particular problems going through the system. If we are speaking about the medicines based on GM technology, for example, they go through quickly. There is support. We do not have any problems with that. If it is not food, there is a broad acceptance. If it is well presented and communicated—and here we are speaking, and are very well informed, about the plant protection use of GM insects—I would be rather optimistic about the result.

**Lord Patel:** Is there not a risk—and you had a good example with GM medicines where GM medicine applications are controlled and regulated by the Medicines Regulatory Authority—that in this case any applications related to GM insects will go to the GM authority, which mainly concerns itself with the crops, and they would not understand the distinction, especially as there is, as you say, no awareness of the benefits of GM insect technology?

**Dr Ladislav Miko:** I disagree slightly. Of course, there are different authorities deciding, and the problem is not in the authority but in the substance. When the issue is linked to food and feed, the member states and the public remain sensitive. Even if you consider distinguishing between pure food and feed uses and cultivation, there is a much more dramatic negative reaction when it is about cultivation, which means releasing GMs into the environment, compared with their use. GM feed in particular is so broadly used in Europe that, even if we have no opinion by the member states in the process, the usage of GM feed is accepted. Maybe there are one or two countries which do not use it broadly, but all the others use GM feed for their animals. As you can see, there is acceptance if there is a clear and beneficial

use. If we are able to communicate, together with the applicants and the scientists, that this is a tool for caring for plant health and is nothing to do with the food chain per se, the result should be easier to achieve.

**Lord Patel:** Do you think that your evidence today and our inquiry are going to help raise awareness about GM-insect technologies?

**Dr Ladislav Miko:** There is already quite a lot of information that we could use, but there is a question about the extent to which it is advisable to start this communication campaign before we have practical examples of applications. As I said at the beginning, this is very much a case-by-case issue, so we need to know the details of the application in order to communicate properly. What I see as a big risk is if we, let us say, communicate something in general and then the application is divergent in certain details from what we communicated before, it is highly sensitive and will be used against this communication. I think it is better to communicate on a concrete case, where we know all the details, and then we can cover all the questions related to this particular case.

**Q94 Lord Peston:** Some of us regard the antipathy to GM crops as entirely irrational and not based on any evidence whatsoever. Is there any danger that this irrationality will spill over into the question of GM-modified insects, so that a life-saving strategy—admittedly long term—will be denied to those who need it most, namely those in the poorest countries in the world? Do you see this as a danger, or are you confident that it will not happen?

**Dr Ladislav Miko:** To be very direct, I cannot exclude that because we have witnessed all kinds of abuse coming from Europe. I cannot say a priori that nobody will hijack GM insects within this discussion, but the probability for that is much lower than the issues related to food and feed.

I also want to say that, yes, on one side it is clearly without scientific assessment, so we can say it is completely irrational, but we also have to admit that the legislation recognises what are called “other legitimate factors”, so we should admit that there are issues other than science which should be taken into account, because this is required by the legal framework. We cannot blankly deny it if someone is raising these issues. We have to assess carefully each of them and address them. Obviously, if you have reasons like culture, tradition or religion, et cetera, these are areas which are very difficult to assess by scientific methods. As the legislation recognises that such reasons could exist, we cannot avoid discussing these issues.

**Q95 Baroness Manningham-Buller:** Dr Miko, thank you for helping us on these issues. Perhaps I may recap some of the things you said. I think you said that you thought there would be less of a problem in this area than in the crop area, and that if the benefits were clear, you have some optimism. But you then went on to say that it was up to the companies which might wish to use this technology to communicate that. At the same time, you felt you could only communicate if you had a specific application to deal with. In our recommendations, which we are going to discuss later, we want to think about how we can resolve these slightly conflicting problems. Could the European Academies’ Science Advisory Council be of value in beginning to facilitate these conversations with member states to improve public understanding of the benefits of this technology? What do you think about that?



**Dr Ladislav Miko:** Obviously, we believe that this is one of the ways. It is nevertheless another issue which we have tried. We have already organised several events—workshops, conferences—of broad or narrow audiences with the member states, relevant industries and relevant NGOs, to discuss these issues. I have to say that it has had some effect, but it is a very lengthy process, very burdensome and also capacity consuming. Nevertheless, in my view, the opt-out as regards cultivation would not have been finally accepted and adopted without that process, where we pushed people around the table and we brought all the evidence together. We had a discussion and we were trying to answer all the questions related to that—on the one side, scientific, and on the other, procedural. After that, I would say that there was a better feeling by the participating bodies that things can move forward. In my view, it makes sense to invest in discussion, awareness-raising and communication. It should be very well structured—and this will look a little controversial from what I said before—and when you have a discussion, it is better to have a discussion about the general elements which are questioned rather than a concrete application, because in a concrete application you have pre-set positions of the players and they usually have very little space to debate. When you discuss the issue per se, there is more willingness and acceptance of the arguments.

When we come to a new area, for example GM insects for plant health, we need to explain what it is in general, and that could be done also in the way you describe, but we need to use a concrete proposal as an example to answer more detailed questions if they come. Yes, in principle, it is beneficial, but we only have a certain capacity to do it.

Last years, at the request of our Commissioner, who was very keen to go for the discussions, we organised three events. To organise three events, from our point of view, is an overload, and we were overworked and at the limits of what we could do. That is why I say it is also for member states, industry and business operators to contribute to that.

**Baroness Manningham-Buller:** Can I make one observation, Dr Miko, and ask you one final question? I think you have touched on my observation. There is an argument that you prepare people to think about these issues before there is a specific application, so that there is plenty of time to think through the principles. You seem to be saying that you cannot have these debates very easily without a specific application. Is that really what you are saying?

**Dr Ladislav Miko:** Sorry, the point is what we want to communicate. It is relatively easy to communicate the general principles. We could have a GM application that is not food or feed related, which falls, nevertheless, within the framework of our legislation, and we can communicate why it is good, and whether or not there are potential risks. We can do that. If we do not know enough about a concrete application, we will not be able to have the discussion, or to answer concrete questions.

My judgment is that it will not be helpful because in such a discussion people will say, “In general it’s fine but the devil is in the detail. So unless we know exactly what you are proposing, we cannot actually tell you our view”. In that sense, we need to have a concrete application in order to be more detailed in the answers. If a campaign is needed to introduce the technology per se, that could be done in general, but I do not think that it will be helpful if it is us who starts with that. I think we need to be able to answer the questions and that is not possible without an application.

**Baroness Manningham-Buller:** You said that in the last years you have had some of these debates and meetings, which had been quite resource intensive, so you saw some value in them without having a specific application. Do you plan to have any more next year?

**Dr Ladislav Miko:** These discussions were only about crops and the problems which were repeatedly raised where we had divergent rules, so it was about how the risk assessment is done, how it is communicated and how the risk management is done. We had a very clear scope for the discussion and experience from the concrete cases, so we could answer the questions from experience.

**Q96 Lord Hunt of Chesterton:** I want to ask you a question about Europe and the rest of the world, because of the frustration felt by some groups that there is no research involving GMOs in other countries, for example in Brazil. What is the policy of the European Union? The EU is a major international player in diplomacy. In some senses, will you be encouraging the application of EU research in other parts of the world where there is not this problem of regulation? In particular, how is the EU working on this with the main United Nations agencies—the Food and Agriculture Organization and the World Health Organization—because I believe they respect very much the EU’s work. Finally, it seems to me that if we can get international projects working, then that may be one of the ways of educating or explaining to European politicians and groups the value of this approach.

**Dr Ladislav Miko:** First of all, we generally follow the line of supporting any pro-export activities. This is not excluding anything, including potential GM products produced in Europe. The difficulty is that we can export our science, but we can hardly export our produce, because there is no GM produce in Europe, except in the area of medicines. In general terms, my answer would be yes.

We also have very close contact and collaboration with international agencies and bodies. The discussion usually comes back to the situation in the European Union and how we can speed up our procedures, rather than about the limits of our export of science results or technologies outside. I do not see any problem. It was not raised as a problem and I do not think there is a difficulty there.

If you ask about the active promotion of concrete science results, we do not have a mechanism to do so. At the moment, when it comes to the application, and if it is part of the export—and obviously I can only speak for the food and feed area—we are prepared to do whatever we can for the promotion of European products.

I have one comment on countries such as Brazil, China, India and others. One of the elements of why GM is so broadly accepted is the dramatic change which has happened in the last two decades through the introduction of GM technology there. It was one of the tools which contributed dramatically to solving poverty issues, securing food for the poor people in these countries, and also providing job opportunities. It is connected with a very well-perceived, immediate, positive effect by many people. Therefore, the general atmosphere in the acceptance of GM is much broader because the people have witnessed themselves the positive effects.

One element of the European reality, and I am speaking about food and feed now because it is one food chain, is that people do not see the need—and now I am speaking in general—because they do not have the feeling that we have a problem with the production of the very broad variety of different foods, et cetera.

One of the ideas we have been developing in the last few years is to find the arguments which will show those European citizens who are, let us say, doubtful or do not want GM, the concrete benefits that they could bring to them. Generally speaking, you can imagine people going to the supermarket and having two products which are declared by the regulatory systems as the same. One is GM and one is non-GM. What is the reason for anyone to pay for the GM product if they hear from parts of society, “Who knows what the problem is? We don’t believe there’s a system”—blah, blah, blah—and the authorities say, “Actually, it is the same”, so they say, “Okay, if it’s the same, I’ll take the one I know. I don’t have a reason to go for the GM”. I think this effect—which I have not described very well but I hope you understand what I mean—is here, and there is not a push from society for these technologies, which could indeed save many people in the developing world, could help many businesses, and jobs, et cetera. There is no question about that, but the perception in the European public is not like that in many places, although not everywhere.

**Q97 Lord Fox:** You have talked about the need for a concrete example in order to start the process of communicating. There is credible evidence, from what we have received from other speakers here, that the scientific community is put off from going through the process of the member states giving no opinion, the Commission then punting it back, and it going round in circles, so you are almost in a catch-22 situation. What message do you think the current process sends to researchers in this area? Also, it has not been clear in anything you have said, and that is because we have not asked, whether you value this research? Is this something that you think we should lead on? How is the regulatory process helping the objective of delivering leadership?

**Dr Ladislav Miko:** Absolutely not, sorry. I was concentrating on explaining our regulatory role. As I said at the very beginning, we are very supportive of anything which can contribute to innovation efforts in the European periphery, and GM is clearly the road to that. Yes we do value, obviously, the new applications. If you ask me, I am a biologist and an entomologist by education, and I found this application to be a very smart and very good solution, which has very close to zero risks. If I may assess it—and I am not the one who has to assess it—it is very low risk and has very good benefits. It is a very smart and very good approach, which I really think should be supported. It will have another side effect because we will need to use fewer chemicals to address the same problems, et cetera. There is no question that this is a very positive idea.

You mentioned that sometimes we are in a kind of catch-22. It is difficult for me to judge because we have not had, I repeat, a single application for GM insects in our system. I do not think it will be the case here. I think it will be fairly simply processed and adopted once we get it, with of course the required information which is given in the guidance from the EFSA. You referred to the process in Spain with the trial. This is very difficult for me to comment on because I do not know the details. I know that there was a demand for additional scientific information and the company decided to gather this information throughout one or two seasons, so it was a reasonable load and timeline. There was additional information provided and then the conditions, which had been set up by the national body—and I do not know the details of why—were so difficult for the company that, instead of getting an inconclusive or negative opinion, they would rather withdraw. This is my information, but I do not know the details about that. So, it is difficult for me to comment.

**Q98 Duke of Montrose:** Dr Miko, your recommendations appear to be that you want specific applications either from companies or countries on particular issues. There is a whole European issue, and I do not know whether Europe has a body that looks into this whole question of the vectors of diseases, a great many of which are insects. We have had some fairly disastrous examples of diseases being carried across Europe. Will Europe be looking at overall research and control on that aspect?

**Dr Ladislav Miko:** Yes. This is broadening the scope of the discussion, but, yes, we should address it. In my view, we are now in the process of addressing the crisis preparedness of the European Union in relation to potential harmful organisms coming into both the animal and plant health areas, and here we are not speaking only about food. Indeed, we are now concluding that the risks, especially in plant protection, are growing, and we can expect more and more dramatic impacts, which are also linked to climate change, globalisation of trade, more goods being moved, et cetera. In that sense, we started already with an information campaign that we need to increase our ability to deal with a potential crisis in that area. It is not specific to GM, but indeed you are right, the GM solution could be presented and promoted here as one of the elegant solutions for cases where insects are vectors. That is true and we can include it in this discussion. We are just at the start of this campaign, of this work, so there is no problem including this example as one of the modern tools on how to address the problem.

**Q99 The Chairman:** Could I put a last question to you? I think we have recognised that the burden of insect-borne diseases falls particularly on low and middle-income countries. That is the nature of dengue fever, malaria and much else. In answer to Baroness Manningham-Buller, you explained how you had the capacity to structure dialogues with participating bodies. Would this include the potential beneficiaries of these lower and middle-income countries? After all, it seems that there is a disparity. Much of the excellent research in this field comes from North America and Europe, and the beneficiaries will be in other countries, so there is a need to have continuity between research workers and potential beneficiaries, if there are to be any. Do you think, were you to be able to structure a dialogue, you will be able to involve such potential beneficiaries? Could I also ask, just to be quite clear—and I may have missed the point—when you set up these dialogues and the discussions, who owns the discussion in Europe? Which body are we talking about?

**Dr Ladislav Miko:** May I start from the end? The discussions were organised by the Commission at the initiative of our Commissioner. We invited all interested parties to these discussions: businesses, member states' administrations, member states' bodies and civic society, represented by NGOs or different organisations. We usually also have the international bodies present, by the way.

This brings me to the first part of your question. It is very difficult to structure this dialogue individually with all potential partners. We collaborate quite closely with international organisations such as the OECD, FAO or specialised expert bodies, such as the OIE or the Codex Alimentarius, where we are trying to present and promote solutions which have been found or born in Europe.

Within the activities at this international level, we communicate and propagate European solutions. I am not aware—which does not mean it does not happen—of particular meetings addressing the concrete beneficiaries in the different regions of the world. Apart from one thing, we have a system called Better Training for Safer Food—BTSF—where we invest quite

a significant amount of money in addressing the problems at source. We send in our experts and we teach, train and pass information to the regions of the world where there is a problem, either a problem for the locals or the problem of the food which is later exported to the European Union, because that was the reason we established that. This is a mechanism by which we can pass the information and communicate with the potential beneficiaries, and we are using it to the extent we are able to. There is quite a comprehensive budget for that and, as I said, our inspectors and experts from the EU level, but also from the national level, are part of these BTSF activities throughout the world. In different parts of the world we have quite a comprehensive amount of these efforts.

**The Chairman:** We said that we hoped to have you available to help us for an hour and we have taken an hour of your time. We are most grateful. We have run out of questions on this end. You have very kindly said that you will send us some further information on an overview of GM science, particularly the research over the last five years and, if you could send us that information, we would be enormously grateful for that. We will read the record in order to pick up any other points. You will get a copy of the transcript in case any minor corrections are required because our transcript is incorrect in any respect. On behalf of the Committee, thank you for being so forthcoming with us today. It has been most helpful to us.

**Dr Ladislav Miko:** Thank you very much. Obviously, we will provide you with the material as discussed. I hope I was able to help you and to elucidate some of the issues which are relevant to our work in the GM area. Thank you very much for the invitation.

**The Chairman:** Thank you.

## Bill and Melinda Gates Foundation – Written evidence (GMI0027)

*Evidence Submitted by Fil Randazzo, Ph.D., and Dan Strickman, Ph.D.*

- 1. Which human diseases, across the world, could be addressed through GM insect technology? Are there any human disease risks in Europe, particularly the UK, for which GM insects are under development?**

In theory, any of the vector-borne diseases principally transmitted by one or a few vector species could be addressed with this technology. Important examples include malaria in sub-Saharan Africa, visceral leishmaniasis in northeastern India, and the complex of viruses transmitted by *Aedes aegypti* (yellow fever, chikungunya, and dengue). The UK currently has very little risk of human vector-borne disease and no GM vector control program is contemplated for Britain. Historically, malaria was a problem in southeastern England and animal diseases like bluetongue virus are a current threat. With global warming, increased international trade, and increased international travel, new threats could emerge in the future.

- 2. What are the possible livestock and agricultural crop applications of GM insects across the world? Of current livestock disease risks and agricultural insect pests that could be addressed through GM Insects, which should be the highest priority for Europe?**

GM insects could be a good solution for livestock and non-indigenous crop pests. For example, the New World screwworm fly is a terrible pest of cattle, but it has been eradicated from North and Central America by the use of sterile males. An infestation in Libya in the 1980s was eliminated with the same technology. Current efforts are under way to refine that technology through the use of GM screwworms that produce only males when tetracycline is withdrawn from their diets. A similar strategy is being developed for various species of fruit flies that are important invasive pests (Mediterranean fruit fly, Mexican fruit fly, etc.). In Europe, the principal livestock pests are stable flies and horn flies, the latter species involved in spreading enterotoxigenic *E. coli* to cattle in systemic infections that create a food safety threat. These two species of flies reduce productivity of cattle even when no pathogen is involved. A sterile male or gene drive approach to control in Europe would lower costs of production. Ceratopogonid flies (biting midges) transmit bluetongue and Schmallenberg viruses to livestock in Europe; however, these flies are so numerous and periodic that it is hard to imagine using either sterile male or gene drive mechanisms against them. There are many crop pests in Europe, but some of the principal invasive ones are the Colorado potato beetle, the western corn rootworm, the tarnished plant bug, and the Olive fruit fly.

**3. Are there likely to be opportunities provided by GM insects that cannot be provided by other approaches, such as biological control methods? How could GM insect approaches be complementary to existing Integrated Pest Management (IPM) programmes?**

Biological control is likely to work well against non-indigenous crop pests, though regulatory hurdles in Europe currently make their application difficult. In some ways, a GM approach could be safer and more precise than other methods, particularly broad-spectrum insecticides. With improvements in technology, development of GM approaches for invasive insects might be much faster than the 10-15 years typically required to develop and prove safety of biological control agents. Classical biological control, in which a natural enemy reproduces on its own and maintains control, has not been as successful against veterinary pests as it has against crop pests. For example, although biological control agents for flies are commonly sold for, and applied to, concentrated sites like chicken operations, they tend not to maintain themselves. GM approaches can be designed to overcome some of the limitations of biologic control. These include faster dispersal within populations and the capacity to sustain themselves over longer periods of time.

**4. How appropriate are current EU and UK GMOs regulatory frameworks in addressing the issues raised by GM Insects? Are there lessons to be learnt from the regulation of GM insects in other countries such as Brazil?**

European regulations on GM insects reflect the European public's general distrust of GMOs and are perhaps more restrictive than would be warranted based solely on risk profile. For example, GM sterile males from colonies that produce only males are unlikely to persist in any way, since they immediately cease reproduction. Such strategies are inherently safe and the real technical issues have to do with practicality and effectiveness. A more useful framework might be to regulate the technology on the basis of the proposed product, and the risk/benefit profile of that specific product, rather than focusing primarily on the GM aspects.

**5. Do the World Health Organization (WHO) guidelines on the release of GM mosquitoes provide the basis of an effective regulatory framework? How should issues regarding the emergence of resistance be considered?**

See 4. The WHO guidance describes best practices intended to foster quality and consistency in the processes for testing and regulating new genetic technologies, but was not meant to serve as the basis of a regulatory framework. The guidance reviews existing regulatory frameworks that are relevant to GM insects. Ideally, the regulatory framework for GM insects would look a lot like that for biological control agents. Resistance has not been observed to the sterile male technique; however, that is not to say it could never occur. The possibility of emerging resistance to GM insects is similar to that for other types of products, such as drugs and insecticides, and can be managed in similar ways. These would include quality control of released insects and monitoring of target populations, development of combination strategies such as application of GM insects in

combination with other vector/pest control methods, and continuing research to develop next generation products that could be made available if resistance is detected.

**6. Do the European Food Safety Authority (EFSA) guidelines on the environmental risk assessment of GM Insects for commercial use sufficiently address the different risks from population suppression and population replacement approaches? How should the ecological risks and human benefits that might arise from the application of gene drive techniques to population replacement approaches be assessed?**

The best framework would look at risk/benefit, rather than just risk, as is currently the framework in Europe. Risk is never zero, but many of the GM approaches have very low risk compared to a huge benefit.

**7. How is research into the development of GM insects currently funded? Are there opportunities to attract more private investment into this area?**

Research comprises only a minor portion of total funding for malaria. The G-Finder public search tool provides access to publicly available information on research funding for neglected diseases.<sup>59</sup> According to this source, approximately \$549 million was spent globally on malaria research by all sectors in 2013. Of this, slightly less than \$21 million supported research on biological products for vector control, the category containing GM mosquitoes.

Well over half the 2013 funding for biological products came from philanthropic sources and no private sector funding was identified for malaria. At this time, the commercialization potential for GM mosquitoes intended to control malaria transmission in disease endemic countries is uncertain and research on such products is being pursued as a public good. Public recognition by the Government of the potential health benefits of GM mosquitoes for malaria control nevertheless could provide an important boost for this research by attracting additional funding and enhancing public acceptance.

*October 2015*

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<sup>59</sup> <https://gfinder.policycures.org/PublicSearchTool/>



## **Government – The Department of Environment, Food and Rural Affairs (Defra) and the Department for Business, Innovation and Skills (BIS) – Written evidence (GMI0022)**

### **Introduction**

1. This is a joint submission by Defra and BIS as the two Government departments most directly involved with issues relating to the potential release of GM insects. Defra is the UK competent authority for the EU legislation that governs the release of GM organisms, including insects, into the environment. BIS' interest is as the department that leads in promoting UK excellence in, and economic growth from, science and technology, including its role as funder of the research councils and sponsor of the Sciencewise programme. The devolved administrations in Wales, Scotland and Northern Ireland are responsible for policy in relation to the possible release of GM insects in their own territory. This response to the call for written evidence focuses on the Committee's questions on the regulation and risk assessment of GM insects, and on research funding.

### ***How appropriate are current EU and UK GMO regulatory frameworks in addressing the issues raised by GM insects? Are there lessons to be learnt from the regulation of GM insects in other countries such as Brazil?***

2. As the Committee has noted the release of GM insects is regulated by means of EU Directive 2001/18/EC, which deals with the deliberate release into the environment of all genetically modified plants, animals or other organisms<sup>60</sup>. Complementary domestic legislation provides for the Directive to be implemented in the UK<sup>61</sup>, but does not add anything significant to the controls as agreed at EU level. The requirements of the Directive focus on ensuring that GMOs will only be authorised for release if they do not pose a risk to human health or the environment. The key stipulation therefore is for any proposed release of a GMO, whether for research or commercial marketing, to be subject to a robust risk assessment. The criteria and evidence requirements for this are set out in the Directive. In broad terms, applicants for GMO release approval have to provide a relevant dossier of risk assessment evidence which is then evaluated by independent scientists<sup>62</sup>. Decisions on whether to authorise the release of GMOs for any purpose other than placing on the market

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<sup>60</sup> There is also an EU Regulation (No 1946/2003) on the transboundary movement of GM organisms, providing for implementation of the Cartagena Protocol on Biosafety to the Convention on Biological Diversity. Broadly, this aims to ensure there is prior informed consent before a GMO is exported from one country to another, including in the case of GM insects. In addition, there is a separate EU and UK control regime for the contained use of GM organisms, for which the lead UK authority is the Health and Safety Executive. The key EU legislation for this is Directive 2009/41/EC.

<sup>61</sup> The Environmental Protection Act 1990, supplemented by the Genetically Modified Organisms (Deliberate Release) Regulations 2002 in relation to England, and equivalent statutory instruments in respect of Wales, Scotland and Northern Ireland.

<sup>62</sup> In the UK the Advisory Committee on Releases to the Environment advises Ministers on the environmental safety of GMOs, while the European Food Safety Authority oversees the GMO evaluation process at EU level.

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(e.g. research trials) are taken at national level<sup>63</sup>, while decisions on the marketing of GMOs as products are taken at EU level<sup>64</sup>.

3. To date no applications have been made to release GM insects in the UK for research purposes, and Defra is not aware of any prospective applications that might be submitted in the foreseeable future. Across the EU as a whole there has only been one recent application for a trial release of GM insects in Spain<sup>65</sup>, currently being considered by the Spanish authorities. No applications have been made or are expected in anything other than the longer term for approval to place a GM insect on the EU market.

4. The UK has not therefore had any practical experience with the operation of the GMO regime in relation to the release of GM insects. In principle, however, Defra considers that if applied pragmatically there is no reason why the EU rules as written should not enable sensible regulatory decisions to be made. Defra would therefore expect to be able to reach a sound, science-based decision should an application be made to conduct GM insect research trials in England. Although EU Directive 2001/18/EC was drawn up mainly with GM crops in mind, the general principles that it enshrines for the risk assessment and effective oversight of GMO releases are equally applicable for GM plants or animals, and the regime should have sufficient flexibility to be able to address any specific issues that may arise for a particular type or class of GMO on a case-by-case basis.

5. The experience in the EU to date on the commercial planting of GM crops indicates that political pressure from some Member States hampers the operation of the GMO regime. A significant number of Member States oppose the growing of GM crops and do not want EU regulatory decisions to be taken solely on the outcome of a science-based risk assessment, even though that is what the agreed Directive requires. It is not clear whether the Member States that oppose GM crop cultivation would also be against EU authorisations to release GM insects. Their outlook might depend on the particular characteristics of the GM insect in question (e.g. is it for human disease control or agricultural pest control, or would its release inherently be confined to only a part of the EU?). If several Member States were to adopt a policy of generally opposing the use of GM insects, then the problems that have been experienced reaching EU decisions on GM crops could also apply in the case of insects. The UK Government will continue to argue for the EU regime to operate as it should for all types of GMO, with a science-based risk assessment process that avoids unnecessary burdens on applicants, and a decision-making procedure that does not suffer from unjustified delays.

6. As noted, EU Directive 2001/18/EC requires regulatory decisions to be based on an assessment of potential safety risks. There is no provision for potential benefits to be taken into account as part of the formal decision-making process. There is an argument that benefits should be considered. However, it is unlikely that such a change could be agreed

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<sup>63</sup> By Defra in respect of a proposed release in England, and the Devolved Administrations for Wales, Scotland or Northern Ireland for a proposed release in their territory.

<sup>64</sup> The EU decision-making process usually involves the Member States voting on a proposal from the European Commission as to whether or not the GMO in question should be authorised, with the outcome determined on the basis of a qualified-majority voting system.

<sup>65</sup> GM olive flies developed by the UK company Oxitec Ltd as a potential means of reducing the population of this agricultural pest insect.

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and there would be difficulties in establishing such a test and ensuring it did not dilute the environmental assessment currently in place.

***Do the European Food Safety Authority (EFSA) guidelines on the environmental risk assessment of GM insects for commercial use sufficiently address the different risks from population suppression and population replacement approaches? How should the ecological risks and human benefits that might arise from the application of gene drive techniques to population replacement approaches be assessed?***

7. Ministers would receive independent scientific advice on the risk assessment of applications to release GM insects from the Advisory Committee on Release to the Environment. ACRE is also responding to the Committee's call for evidence to give its own views on the regulation and risk assessment of GM insects, including the EFSA and WHO guidelines.

***How is research into the development of GM insects currently funded? Are there opportunities to attract more private investment into this area?***

8. Over £55.7m<sup>66</sup> of public funding for research on GM insects has previously been provided by the Biotechnology and Biological Sciences Research Council (BBSRC), the Natural Environment Research Council (NERC), the former Technology Strategy Board (now Innovate UK) and the Medical Research Council, all of which are public bodies sponsored by BIS but operating with independence. The Haldane principle governs how this funding is allocated, with independent peer review and expert assessment determining which projects should be funded. Innovate UK and Research Councils UK (on behalf of BBSRC, NERC and MRC) will be responding separately to the committee's call for evidence.

***Given the possible health benefits of GM insects, should the Government be funding their commercialisation? Would this result in a conflict of interest with regard to the regulation of releases? If so, how might this be managed?***

9. As the relevant regulatory authority for England, Defra does not foresee any significant problem as regards a potential conflict of interest should it be decided in future to sponsor the use of GM insects. There is a distinct, legally-specified process for reaching decisions on the release of GMOs, which operates on its own terms without reference to any wider considerations. It is moreover an open and transparent process, with opportunities for the public to submit comments on any applications for approval.

***How can the gap between regulatory approaches and public concerns over GMOs be addressed? Is there a role for 'responsible innovation' approaches? What are the critical factors in effective public engagement from lab to final release?***

10. Government, through the Research Councils, is supportive of a responsible innovation approach to the development of new technologies. The submission being made to the Committee by RCUK will provide further detail on this point.

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<sup>66</sup> This figure was amended on 9 October. The original submission had given an incorrect figure.

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*September 2015*

Government – Mr George Eustice MP, Minister of State for Farming, Food and the Marine Environment, Defra, and Mr George Freeman MP, Parliamentary Under-Secretary of State for Life Sciences, BIS and DH – Oral evidence (QQ 75-86)

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*Evidence Session No. 8*

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*Questions 75 - 86*

TUESDAY 3 NOVEMBER 2015

Members present

Earl of Selborne (Chairman)  
Lord Cameron on Dillington  
Lord Fox  
Lord Hennessy of Nympsfield  
Lord Hunt of Chesterton  
Lord Kakkar  
Lord Krebs (co-opted)  
Lord Maxton  
Baroness Morgan of Huyton  
Baroness Neville-Jones  
Lord Patel (co-opted)  
Lord Peston  
Viscount Ridley  
Lord Vallance of Tummel

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**Examination of Witnesses**

**Mr George Eustice MP**, Minister of State for Farming, Food and the Marine Environment, Department of the Environment, Food and Rural Affairs (Defra), and **Mr George Freeman MP**, Parliamentary Under-Secretary of State for Life Sciences, Department for Business, Innovation and Skills (BIS) and the Department of Health (DH)

**Q75 The Chairman:** Welcome, Ministers. We are grateful to you for joining us this morning. We are nearly coming to the end of our inquiry into genetically modified insects and the potential for this new technology and the regulatory background to it. We are being broadcast by the web cameras, so I should warn you of that. Would you like to introduce yourselves for the record and, if you would like to make an introductory statement, please feel free to do so?

**Mr Freeman:** Thank you, Lord Selborne, and the Committee, for the invitation. I am George Freeman, Minister for Life Sciences at the Department for Business, Innovation and Skills and

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the Department of Health. As well as my core job, which is focusing on developing our UK infrastructure for medical innovation, the Prime Minister has asked me also to support the policy framework at the Department for Business, Innovation and Skills for the bioeconomy, for the appliance of bioscience and for industrial biotech more broadly with Jo Johnson, the Science Minister. We are actively looking at ways in which we can support the UK leadership in that rapidly growing global field of the appliance of bioscience particularly in food, medicine and energy, and in industrial biotechnology more generally. We have a range of programmes at BIS for supporting it, which no doubt we will touch on. As the BIS Minister responsible for the agri-tech strategy working with George, as Minister at Defra, I am leading the work at BIS on supporting the deep science for 21st-century agriculture to help British farmers produce more from less and to help Britain export that technology to help emerging markets.

I would just say on this issue—George will lead on the regulation, because that is a Defra function—that genomics and genetics are playing an increasingly transformational role in biomedicine but also in energy and agriculture. The UK is a global leader in the study of genetics and the study of how we can harness genetics for clinical as well as agricultural and other industrial benefits. Crucial to that is making sure that we support the raising of sufficient funds to support the science base and to build an ecosystem in which that science can support emerging companies and support emerging technologies with existing companies, and to make sure that we get the international framework right. We see a huge opportunity for the UK to attract inward investment into our science base and to export that science expertise to support technologies around the world.

The idea behind the agri-tech strategy is that as the world faces some pretty profound challenges to double food production on the same land area, BIS, working with Defra and DfID, has a key role to play in making sure that we are supporting those technologies for tomorrow.

George is going to lead on the regulatory aspects, because they are a Defra function. On the medical sector, the genetic modification of insects, particularly the drosophila fruit fly, has been essential in some ground-breaking medical research. Last week I visited the MRC institute at Hammersmith, where the study of the drosophila fruit fly intestine and genomic and metabolic science is leading insights into human metabolic science as well. In the medical sphere, a lot of this work is completely accepted and the genetics of insects for research is crucial, although I appreciate that today we are talking about a particular aspect of that, which Defra leads on the regulation of.

**The Chairman:** Thank you. Mr Eustice.

**Mr Eustice:** I am George Eustice. I am the Minister for Farming, Fisheries and the Marine Environment. Also, as part of that, I lead on agri-tech, particularly regulation on pesticides and GM crops. When it comes to the EU regime on GM regulation, we do not think there is anything particularly wrong with the regime as written, but there is certainly a great deal wrong with the way it is implemented, in that if all member states followed the evidence and had a risk-based approach, there are actually lots of checks and balances in the system, but there is no reason why an application, if it were proved to be safe, should not proceed to commercial cultivation in a relatively straightforward way and in a relatively short timeframe. In practice, we have seen, frankly, political deadlock over the last 10 years between member states and an inability to get qualified majority voting to block cultivation,

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or indeed to allow cultivation, and a feeling generally from the Commission that because this is such a divisive hot potato, there are usually lots of reasons to ask for more evidence and new reviews and for outdated information to be updated. So we tend to have applications that have been stuck in limboland in most cases for many, many years. We hope that the agreement reached last year on allowing national derogations for commercial cultivation might unblock that logjam and make other member states less inclined to try to block these cultivations so that we can allow member states that want to do the commercial cultivation of crops that are shown to be safe to do so.

Finally, because the specifics of your inquiry are GM insects, which I think is a really interesting area, I should say that sterile insect techniques have been around since the 1940s and the process of radiating insects and releasing them is not new, but what is new is using GM technology to achieve the same result. It is encouraging that companies such as Oxitec, which is a UK company, are world leaders in this field. In principle, from a regulatory point of view, we do not see any reason why the GM process that exists for crops in the EU should not equally be applied to GM insects, were any such applications to come forward, but at the moment there is no indication of anybody wanting to do even field trials on GM insects in the UK or in the EU.

**The Chairman:** No indeed, as we understand it.

**Q76 Lord Kakkar:** I think, if I have understood it correctly from those opening statements, that the Government are strongly enthusiastic about the development of GM insect technologies.

If I may move on from that first question, unless you disagree with that, do you think that independent scientific advice informs the UK Government position on these technologies, and if so how, and how you think independent scientific advice might better inform the European scenario that you have just described?

**Mr Eustice:** In the UK, if we have an application from a company that wants to do field trials of particular GM technology, Defra is the lead competent authority that assesses the application. We would then go to ACRE—the Advisory Committee on Releases to the Environment—which is an expert committee that has been established for many years now. They would carry out an assessment and actively peer review the science that a particular technology developer was bringing to the field and would make a recommendation to Ministers. As a general rule, we would follow that advice. In fact, I do not think there has been an instance yet where a Minister has gone against the advice of that expert committee.

When it comes to the European Union, if you want to commercialise a crop so that we have control nationally on trials and to get commercialisation on an EU level, a developer would, for the sake of argument, come to the UK and we would then lead on risk assessing the commercialisation. Again, we would take advice from ACRE, our expert committee on that, and if we were satisfied that it was safe for commercialisation we would inform the Commission and notify all other member states. If all other member states agreed with that assessment, it could proceed to commercialisation quite quickly. That process could happen probably within six months. What tends to happen is that member states that have more political objections to these technologies find reasons to question the science, to question the recommendation. Again, that is foreseen in the process, so when that happens the Commission asks the EFSA—the European Food Safety Authority—to carry out its own

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independent assessment. When that authority concludes, it then makes a recommendation to the Commission, and at that point the matter should go to a vote and either be carried or not under QMV. The difficulty is that whenever these have come back and gone to QMV, there is never a QMV to do either one thing or the other. What should happen at that stage is that the Commission can go ahead and authorise it if that is where the balance of evidence lies. I hope that it will be more inclined to do that now that we have allowed the national derogation.

**Lord Kakkar:** Minister, you will be aware of the report on our nation's footprint in terms of global health, and here I should declare my interest as an officer of the All-Party Parliamentary Group on Global Health. Do you think that the particular process just described is holding back our ability to take forward these technologies—I think from your answers that we have heard that the Government support GM insect technology—and that we should ensure that they can be applied more broadly throughout the world to help us make a contribution to tackling important global health problems?

**Mr Freeman:** I think, Lord Kakkar, that you put your finger on a really key issue that sits behind and across this particular subject. It is a well-timed question. On Monday I am going to meet Commissioner Moedas and speak at the European Bioeconomy Investment Summit to signal that as the world stands at the dawn of an extraordinarily exciting age of bioscience in the bioeconomy, there is the opportunity to harness genomics and informatics and these technologies, which have really been pioneered in medicine but have extraordinary applications across agriculture, energy, clean tech and industrial cropping for sustainable development. We are concerned that the European Union should not just actively invest in the science, which it is doing, but equally puts in place a regulatory framework that as well as building public trust and confidence in the regulatory protections actively supports investment into the European bioeconomy for the creation of jobs and prosperity. There are signs at the moment in medicine and in agriculture, and in some of the emerging areas where different technologies are creating new opportunities where food and medicine meet and some of the latest technologies, that the European Union is in danger of sending a signal through a zealous application of the precautionary principle that the assumption is no until everybody in the system is perfectly happy to say yes. That will send a bad signal, and we have already seen some disinvestment from Europe. There is a strategic question here of science advice.

I would just add that the UK leads. We have more scientific advice at the heart of Government in the UK than any other country. We not only have the Chief Scientific Adviser, but every department has a chief scientist. For decades, we have led in science and evidence-based policy-making, and we are keen to ensure that the European Union adopts that and puts science right at the heart of evidence-based policy for the 21st century.

**Q77 Viscount Ridley:** I hope I am not pre-empting a later question. We heard a pretty shocking statement from Oxitec that they would never in a million years dream of raising funds to do their work here in the UK, because it would be impossible to get regulatory approval. That is after their experience with olive fly in Spain. There are plenty of insect pests in this country that we would like to tackle, such as flea beetle or aphids. There is something wrong when we are able to lead in the development and commercialisation of this technology but there is not a hope of applying it here.



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**Mr Freeman:** You make a really important point, which echoes the one I made in response to Lord Kakkar, that there is a very big difference between the application and the licensing of technologies for use in the UK and the UK science base being able to develop solutions for global use. This is particularly heightened in the wider GM debate, where there are some extraordinary opportunities for GM crop advances, industrial biotech, drought-resistant crops, pest-resistant crops, and global and tropical agricultural use but which are being held back by a European regulatory framework that is about “protecting” European consumers. There is a real issue for the UK, if we are ambitious for our science base, to help global agriculture and global energy. GM technology is taking off across the world. The question is not whether we are going to stop it; the question is whether we are going to help contribute to leading it and getting the right regulatory framework in place.

**Mr Eustice:** I think there is another point to note when you are looking specifically at GM insects. I can understand the point of view of people who might be concerned about this that there is a difference between insects that are sterile, and therefore self-limiting because they die anyway and that is the end of the gene, and, say, gene drive technologies where you are introducing a gene into an insect population. What Oxitec is doing on mosquitoes in places like Brazil, for example, is the former. You could argue that that is a slightly more reassuring technology than releasing genes.

**Viscount Ridley:** That was what they wanted to do with the olive fly in Spain and they gave up. They said it was impossible.

**Mr Eustice:** I would hope that now we have this new approach and the ability to gain approval Europe-wide but for individual nation states to have the ability to opt out, there will be less of an incentive for those member states to muddy the water, throw spanners in the works and play for time. The jury is out. It is now two years since the maize strain 1507, where we worked very hard with Spain to get to the process of this deadlock where there was no QMV either way, but still we are waiting for the Commission to do what it now has the power to do, which is to actually authorise its use.

**Baroness Neville-Jones:** Is there a test case forthcoming? Presumably somebody needs to do something to cause the Commission to respond? Is it going to respond otherwise? I cannot see what it would respond to. Is this actually in the pipeline?

**Mr Eustice:** As I understand it, the ball is in the Commission’s court when it comes to the maize strain of 1507 in that in two years there has been no QMV to block it or authorise it. In such a deadlock situation, the power rests with the Commission.

**Baroness Neville-Jones:** So you are saying that there is an unfinished process?

**Mr Eustice:** That is right. It is unclear why the Commission has not yet exercised the power that it has, particularly given that we now have the national derogation in place. Initially it might have thought, “Let’s get the national derogation in place before we do it”. The danger with all these things is that if you leave it too long, people start to say, “Ah well, the evidence on which this is based is a bit out of date, so maybe we need to go back and start again”, and you end up in a sort of Never Never Land if you are not careful. I am not aware at the moment that we have had any applications to do field trials on insects. I know that in the US, for instance, there are trials under way for the diamondback moth, which is also a common pest of brassicas in the UK.

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**Mr Freeman:** As well as the pressure from applicants, the danger is that the appetite of applicants reduces if the regulatory framework is the wrong way. The other pressure is economic, and my message to the Commission on Monday will be that Oxitec is a very good example but that there is a far bigger one, BASF, the global German industrial major, which wants to shift from chemical agriculture leadership to biological crop protection in the 21st century and is announcing that it is leaving Germany and Europe with its agriculture division to go to the US. That is a very profound wake-up call. If Europe is serious about generating an innovation economy, and Commissioner Moedas has admirably set out that it is, my argument will be that you need a regulatory framework strategically that encourages commercial application as well as academic research.

**Baroness Neville-Jones:** So where does the German Government stand when something like that happens?

**Mr Freeman:** I think it is fair to say that it is a complex coalition of interests. George, as a Defra Minister, leads on more of those negotiations.

**The Chairman:** I think it is better if we ask you about the British Government rather than the German Government.

**Q78 Lord Peston:** My question follows Lord Ridley's question. I am very confused by your answer. If we carry out the thought experiment that our scientists have cracked the theory and the application side of GM insects, is there European involvement then as to whether we can proceed further? Is there any basis for Europe stopping us exporting all this technology to the countries that need it? I am very pro Europe, but I do not see any European interest, us having solved the problem, in our getting it applied.

**Mr Eustice:** I think you are right. I ought just to clarify that when it comes to our doing trial work and field trials, that is a national decision and we do not have to get the agreement of other European countries. If we decided that we then wanted to export that technology from a UK science base to Brazil, for instance, or to the Cayman Islands or Indonesia, or other countries that are open to this technology, there is nothing to stop us doing it; we just have to satisfy the regulatory regimes of those individual countries. Brazil, for instance, has quite a permissive approach to this and has embraced it. If we wanted to commercialise these techniques, GM insects for use in the European Union, we would have to go through that European authorisation process.

**Lord Peston:** Viewing it as an aid problem—namely that we want to help the countries of sub-Saharan Africa, which I hope we do, I hope you will confirm that we do—there is no European angle to this at all, is there?

**Mr Eustice:** No.

**Lord Peston:** It is only if we wanted to save lives in Europe that we might be told, “No way”.

**Mr Eustice:** That is right. In fact, a more likely application in Europe might for instance be to control midges to prevent the spread of animal diseases, such as bluetongue, or indeed to deal with certain insect pests, such as caterpillars from the diamondback moth.

**Mr Freeman:** To take research from the deep academic lab through to field applications, most companies will want to do that. Even if they are free to do that field research in the UK, if there is no UK or European likelihood of that technology being put to use in that

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agricultural system we are likely to become a place where you do the very advanced deep science but all the translational science and the product development is likely to go into a territory where the products are actually being used.

**Lord Peston:** In other words, sub-Saharan Africa.

**Mr Freeman:** Outside the UK.

**Q79 Lord Fox:** Turning slightly aside from regulation, which I am sure we will return to in a minute, Mr Freeman, on the subject of the BIS view of strictly the insect part of what we are talking about here, how commercial is this? We have heard differing views from witnesses as to whether this is even a commercial possibility or is this really, as Lord Peston inferred, about international development and international help?

**Mr Freeman:** As George has just highlighted, there are no applications at the moment for the use of that technology in the UK. As the previous question highlighted, there are enormous international opportunities in Brazil and other tropical economies. In the UK, through BBSRC and Innovate UK, we supported Oxitec specifically. Innovate UK is supporting a sustainable dengue prevention programme. There is DfID funding. Imperial College is working with Gates and the European Research Council. The Synthetic Biology Leadership Council is looking at how we can use and develop our leadership in these technologies. If you look at the pace of growth in agricultural technology—I have come this morning from the World Agri-Tech Investment Summit here in London—in 2013 the total figure raised globally was £0.5 billion; this year we are on track for £4 billion. This sector is rapidly developing, huge volumes of money are coming in, and it is a big opportunity for the UK science base.

**Lord Fox:** So BIS does view this as an important commercial opportunity?

**Mr Freeman:** Yes, globally. As I say, at the moment there are no applications for GM insects in UK agriculture, but globally we see a huge opportunity.

**Q80 Baroness Morgan of Huyton:** We have had evidence from Oxitec, and it is a bit depressing on one level that it was taken over by an American company, so our British flagship has been taken over. Is there anything else in particular that BIS should be doing, not so much to support the research, which is clearly strong—we have had clear evidence about that—but to support development and commercialisation more? We had something of a hint from Innovate UK that we should do more. What is your response to that? Clearly we are well placed to do this, but there is something missing in the system.

**Mr Freeman:** There are three responses. First, on the takeover, you have heard evidence from Oxitec. I think it would argue that it was not a hostile takeover but that it was in Oxitec's interests, that the American company is a technology partner and that will help Oxitec to globalise that technology. In these science and technology sectors, those global collaborations are viewed as a success.

**Baroness Morgan of Huyton:** It is just a bit sad when the one British flagship goes. I recognise that it is still employing people.

**Mr Freeman:** In relation to support for emerging companies—this is really what the agri-tech strategy is about—we have set out a 10-year vision of how we can harness our agricultural science and technology base, which is not inconsiderable at £0.5 billion a year. If you asked the industry, they would have reduced that figure by a very large sum. They were not aware

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of how much we were spending. Through the leadership council the sector has come together to help us identify long-term priorities. We have launched a catalyst fund for agricultural innovations: 100 projects funded, £50 million across the UK. Last week, the two of us opened the UK Centre for Agri-Informatics and Metrics of Sustainability, which is pulling together all the data on field cropping and agronomy and genomics to help drive insights into new technologies. I think we are supporting the landscape. Through the Synthetic Biology Leadership Council, which I chair, we are actively both funding and providing leadership of the sector. There is an international market that we are determined to go after.

On the regulatory discussion, which Defra leads, I am signalling on Monday more broadly that in the bioeconomy we need a benign framework. On GM, the painfully negotiated settlement, which does open up derogation and derogated powers, allows us to begin to catch up and make sure that we in the UK do not get left behind.

**Baroness Morgan of Huyton:** Have you any thoughts about how the range of possibilities that you are describing and the range of investments at the moment can be encouraged to scale up? We have seen in a lot of other tech areas that we are brilliant at the bottom, we are brilliant at the first stage, and then we are not so good at the next stage.

**Mr Freeman:** This goes back to the previous question about how important it is that we have licence and regulation for use in our own agriculture. That is also the issue in biomedicine, as Lord Kakkar is well aware: if the NHS is a slow adopter of innovation, we are a great place to do the research but not such a great place to commercialise. Unless we are also a good economy for using innovation, putting it to work and testing it in the field, we are in danger of being simply a good place to do research but the commercialisation will go elsewhere. That argument writ large confronts the European Union on an even bigger scale.

**Q81 Lord Kakkar:** The Minister has answered my question specifically, but just to be clear for the record of our report, it is an important potential disincentive to those who want to invest and develop these technologies that the ability to test them in the field and then apply them commercially is not facilitated through the European approach to regulation at the moment.

**Mr Freeman:** Absolutely right. The best example of that is the blight-resistant potato that has been bred. Your Committee will know that the average potato crop has between 10 to 15 sprays annually of fungicides—George will correct me if I am wrong—to prevent blight. The blight-resistant potato will not need those sprays. That is 15 expensive applications of chemical. That is a huge breakthrough, but BASF, which has been sponsoring the research in Norwich, has decided the likelihood of getting clearance in Europe is so slim that they have decided to focus elsewhere in the world. The derogations that we have negotiated will help, but BASF has already announced that it is moving. We are catching up. I think that speaks to the volume of the disinvestment that we need to deal with.

**Lord Hunt of Chesterton:** Can I just comment on that? There are other research councils; we have telescopes in Hawaii. There is nothing to stop research councils having projects in other countries around the world. At the moment probably all our biological agri is in the UK, but if there are difficulties, and speed is of the essence, presumably we could go to overseas institutes. Is that being considered?

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**Mr Freeman:** It is. That is partly why we built DfID into the agri-tech strategy: because it is fundamentally about those global markets. Historically, the UK, as you well know, has led the world in tropical agriculture. There is still an institute in Nairobi and there are institutes all around the world.

**Lord Hunt of Chesterton:** Do you have a budget to do this? How will the budget appear for this activity?

**Mr Freeman:** DfID has signalled active enthusiasm for exporting agri-tech technologies into developing countries around the world, and that is part of what the agri-tech strategy is about.

**The Chairman:** Mr Eustice, you wanted to come in?

**Mr Eustice:** I just wanted to re-emphasise what I said at the start. The issue is not so much the regulatory process as written in the European Union but the way it is implemented. All the EU has to do is not necessarily rewrite its process but just gain some credibility by sticking to the process that it has written down. That is when there is a huge lack of confidence in the industry, when they see that they are going to get stuck in the morass and nothing will happen. If the EU could get to the stage where it can demonstrate that it can move from the beginning of the authorisation process for commercialisation to the end in, say, a nine-month window, which ought to be eminently doable in uncontroversial cases, then you start to get back the confidence of industry.

**Lord Vallance of Tummel:** For BASF, which is a multinational that will have infrastructure around the world, not having a home market in Europe is something you can get over, but if you are a start-up in the UK, or another European Union company, not having a home market is a major problem.

**Mr Freeman:** Yes.

**Baroness Neville-Jones:** I wanted to come back to something you said, Mr Eustice, which is that the theory that European assessment is okay but it is the way it is conducted. We have heard other witnesses say that there is a problem with the methodology itself in that it does not really allow consideration of the benefit, it is all on the risk side, and that that queers the pitch in a sense. It clearly gives those who want to block something an added advantage if you can constantly create a climate of extreme risk aversion. Is there some merit in trying to get the process itself modified so that benefit, which after all has real economic implications, has more of a hearing?

**Mr Eustice:** I know I have heard that argument. If I am honest, I am less persuaded by it for a number of reasons. First of all, if what we were seeing was member states saying, “We don’t think this is safe”, or, “The risks are too great”, or EFSA carrying out analyses and saying, “This is a bit risky”, then you might say, “Well, maybe they’re not taking full account of the benefits”. The evidence is that even when they are saying, “This isn’t risky. We’re absolutely satisfied that this is safe”, member states are still saying, “Ah well, we don’t agree with that science”. The problem you have is not that on a precautionary approach to the evidence you risk coming up with a no answer too many times; the problem is that even when you have a precautionary approach and people are telling you there is no risk based on the science, politics and political obstacles get in the way. My argument would be if the problem is a political barrier and an overly cautious political culture, to say that we are just going to balance the risk against benefits does not do much to reassure that problem.

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**Baroness Neville-Jones:** You are really saying an improved procedure does not actually solve the real problem?

**Mr Eustice:** I do not think it does. It is just about sticking to the procedure that they have, and there are way too many delaying tactics.

**Q82 Lord Krebs:** My question follows on from the discussion of regulation. You will understand from what you have heard that we have been impressed by the amount of written and oral evidence that we have had that the current regulatory environment is not fit for purpose. Baroness Neville-Jones has just addressed the question of whether it is the regulation or the implementation. We have covered quite a lot of this. I just want to pick up on the particular aspect that both Ministers have referred to, which is the relatively recent derogation to enable member states to opt out if they wish to. I wondered if you would agree that this makes things even worse in some ways, because the opt-out does not have to follow any scientific evidence. As I understand it, member states can say, “Okay, here’s the evidence, the science says it’s all fine”—this is essentially what you just said, Mr Eustice—but for other reasons, such as, “We feel frightened of it”, or, “We don’t like the look of it”, or, “We want to grow organic crops next door, we will opt out”. Surely in terms of the overall perception of Europe as a place to do research and business related to genetically modified products, including GM insects, this sends the message that Europe is a confusing place, because some people are prepared to ignore science and go for emotion, and Europe says, “That’s fine, we’ll reject things on the basis of emotion, because we don’t think the science is good enough”. Do you not think it makes it worse rather than better?

**Mr Eustice:** I understand the point, the UK’s position being that we should have a science-based approach and to assess the risk. You are right on one level that having a derogation that enables member states to say, “We’re not having this anyway, notwithstanding the science”, does send that signal. We have been deadlocked and going round in circles on this for the best part of 20 years, getting nowhere fast. Europe is always a place of compromises and fudges and muddles, and sometimes it is the only way to break out of a deadlock and get progress. If the 10 or so member states that want to have the option of using these can do so under this compromise, that is a step forward. It may be that over time other countries will come on board.

I understand that Holland has signalled at the moment that they would like to exercise their national derogation to opt out, but interestingly it has have not ruled out cultivating. It just wants an additional national filter on each application as it comes. A lot of the other countries that are currently saying that they will opt out might just want an extra layer of national filter before they will give it the go. Maybe over time, suspicion of this technology will dissipate and we will start to see progress.

**Lord Krebs:** Is the maths at the moment, from what you have just said, that about a third of the member states would want to ahead with GM technology and nearly two-thirds would want to use the derogation clause?

**Mr Eustice:** Yes. It is a complicated picture because they have also allowed regions within member states to opt out. From the latest figures I saw—my officials will correct me—19 member states have so far signalled that they want to opt out and the remaining nine say they want to opt in. We have said that we want to opt in, but Scotland, Northern Ireland and Wales have each said they intend to have the ability to opt out. I think Flanders has also

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signalled that it wants to opt in, even though the rest of Belgium is opting out. It is a complex picture. Broadly, a third versus two-thirds is about right.

**Mr Freeman:** I think Lord Krebs made a really important point that what we are witnessing here is some very non-science-based political objections to proven science and technology leading to serious fractures of the single market. It is inelegant, and I think we are both saying that it is not the ideal position; we would much rather have a European single market and the principles of a European economy unleashed to drive European leadership in this. This is a way of protecting the UK's ability to do our bit for global agriculture, but it is not ideal. My message to the Commission on Monday will be that this is a very serious fault-line that is not good for Europe and not good for our reputation as a single market leading in these innovative areas.

**Lord Maxton:** With all due respect, there are political objections, but politicians only object if they are driven by other forces. What are those other forces that are driving some parts of Europe to reject the scientific base?

**Mr Freeman:** There is a range of them. It is complex. I looked at this before becoming a Minister when I wrote a report on EU regulation of the bioeconomy and bioscience. I would not claim to be an expert by any means. It was clear that one of the factors is that, because of the way the European decision-making and policy-making structure is set up, those who get early influence in the corridors can have a very disproportionate influence. Often the companies, particularly in new sectors, are not busy in the corridors of the legislature or the Commission and are often in receipt of things coming their way that they were not aware of.

Secondly, the economic crisis in Europe, which has triggered a very visible political backlash and the rise of a lot of anti-business, big business, big government, has an anti-big science element, so some of the coalitions that have been formed with some of the nationalist minor parties across Europe have a noticeable vein of anti-science and anti-big business that has been quite profoundly influential. There are also other historical, cultural and religious influences across Europe, which have been there since time immemorial. It speaks to the earlier questions the Committee asked about the importance of science-led evidence-based policy-making.

**Q83 Lord Patel:** My question follows on from Lord Krebs's question and is still related to regulation. Some of the evidence that we have heard suggested that the regulatory environment for GM insect technologies could be improved by including consideration of benefits and moving on to a trait-based system. Do you think that might be helpful, or will it further confuse?

**Mr Eustice:** I covered the benefits earlier in the answer to Baroness Neville-Jones.

**Lord Patel:** Yes, you did.

**Mr Eustice:** People sometimes cite this in the context of Canada, which has a regime that looks at traits. I think it is wrong to conclude from that that it is necessarily the right approach. It just means Canada is obviously a single independent nation state that can make these decisions on its own and has things much easier. My concern about traits is first of all that with any European process you always have to be conscious that by taking the lid off things and trying to play around with the wiring, you might end up with something worse. It

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is a terrible thing to say, but I am afraid there is a track record of trying to tamper with things in Europe that are not quite right, and they end up worse than ever.

**Lord Patel:** That sounds as though you go for a compromise.

**Mr Eustice:** The point I would make is that there is a reason why I think we should be a bit concerned about switching to a trait-based approach, and that is that the Commission is currently considering whether other novel breeding techniques, such as cisgenics and gene editing, should be covered by GM legislation. Our view is that they should not, because this is about moving genes within species; it is not about moving them between species. We would not want those to be treated as GM, otherwise you are going to hold back the development of a very exciting new area, modern gene techniques, that has its genesis, if you like, and is still rooted in conventional techniques. We have used irradiation and things like that to get gene mutation for many, many years. I think they are closer to conventional techniques than GM, and we want to try to protect that distinction. Once you start talking about trait-based approaches to this, I think there is a danger that you start to tip some of those other novel techniques too closely to the GM regulatory regime, which is the worst of all worlds, because then you have other exciting new technologies that we hope to protect from this and to maintain an understanding that they are not GM, and get muddled up in this unsatisfactory regime as well.

**Mr Freeman:** I would strongly echo that. There are companies in the UK in agricultural breeding that have set themselves out as not GM, they do not do GM technologies, but they are actively investing in traits and a whole range of non-GM technologies for accelerating naturally occurring traits. It would be a disaster if we lumped them into the GMO regulations, which are very specific and intended to cover a very particular intervention.

**Q84 Lord Cameron of Dillington:** George Eustice, you were saying that political influence overcomes the scientifically stated absence of risk, and therefore that benefits are not relevant. Taking up Lord Maxton's point, if benefits were very much part of the process, I think the politics could easily change, as they do for instance in health, where you get genetic modification of antibiotic clusters and the people's general reaction is, "Go for it. What are you waiting for?". It does not seem to be the same in agriculture. Perhaps if we highlighted some of the benefits—the GM potatoes that George Freeman mentioned are a very good example—we could make a difference.

**Mr Eustice:** I suppose this is about the point at which you argue the benefits. I take your point. If after EFSA has done its risk assessment and told everybody that even on the precautionary approach it is safe, and then it gets to the point at which there is a vote in Council on QMV, that is time to say, "It's safe and, do you know what, there are some really good benefits here that we should not turn our back on". I completely accept that that is the point.

**Lord Cameron of Dillington:** If the benefits were recognised as part of the earlier process, they would come to that, it seems to me, so the Austrians, who are probably the most fervently anti-GM, might see the benefits of not spraying potatoes.

**Mr Eustice:** I suppose my preference would be to be able to say, "It is absolutely safe and it has been independently assessed as so and, do you know what, there are benefits here".

**Lord Cameron of Dillington:** But you are just a politician.



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**Mr Eustice:** You are right. The science can be there, but effectively to compromise a risk assessment by trying to introduce a notion of benefits alongside it probably does not help to reassure people. That is not to say that you cannot emphasise the benefits once you have demonstrated it is safe. Does that make sense?

**Lord Fox:** Coming straight to that and emphasising the benefits, there is no public debate at the moment on insects. Should there be? Who should be helping to lead and steer that public debate?

**Mr Eustice:** We do not have any applications even for trials in the UK—this is a very early technology—so I am not sure that there is a case for a big national debate until there is something that we are willing or able to start bringing forward and consider commercialising. My understanding, talking to some of the other companies involved in GM, is that public opinion on GM has somewhat mellowed over the last 20 years. There is still a caution and an apprehension about this technology, but there is more openness to it than there was 20 years ago when the idea was first mooted. If you explain the benefits of it and reassure people about its safety, the consumers are more open to it than perhaps many presume.

**Lord Peston:** For the second time in your evidence session I am totally bewildered. I thought the Government's position on Europe was that we should be able to opt out of everything; we want a Europe where a country decides solely for itself what it wants to accept or not. What is the difference? Supposing we were told, "If you want to be in Europe you've got to be in the single currency", you might well scream the place down. What is the difference between that and a genetically modified potato?

**Mr Eustice:** It is precisely for that reason that we were comfortable with a national opt-out on the point of cultivation to get progress. We would prefer it if all other countries had an evidence-based approach as well, and that is what we have argued for, but where we draw the line—

**Lord Peston:** Sorry, just to interrupt you, it is not to do with an evidence-based approach. If you believe in a free market, and I speak as an economist, you believe in a free market. "The genetically modified potato exists, it has not been shown to be damaging, end of story", would be how Adam Smith would argue it.

**Mr Freeman:** If you go back and read the Prime Minister's seminal speech setting out our position on Europe, absolutely central to it was the urgency of Europe embracing a more entrepreneurial, more innovative economic model.

**Lord Peston:** We agree with all that.

**Mr Freeman:** I think this fits perfectly with trying to make sure that it focuses more on unleashing its economic potential for the benefit of its citizens and the globe, and less on this drive for ever-closer political union and ever greater regulation. We want a Europe that is ideally a single market of evidence-based support for the bioeconomy, but we want a Europe that is looking actively at how it can unleash its power globally in the bioeconomy.

**Lord Peston:** So you would reject all those economists who say that the single currency is the best way to get exactly the economy that you have just described?

**Mr Eustice:** Yes, I would reject that.

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**Lord Peston:** All the economists are wrong.

**Mr Eustice:** Yes, the economists who advocated British membership of the euro were all proved wrong in the event, and I say that as someone who was involved closely in that debate.

**The Chairman:** We are moving away from GM insects.

**Lord Peston:** My interest is in genetically modified potatoes. I find it amazing that you should be able to opt out of genetically modified potatoes.

**Q85 Lord Hunt of Chesterton:** I have a couple of questions to do with public dialogue. I think your position was something that we have heard before: that the situation is not necessarily ripe for having a large public debate on this issue, because there are a lot of technical issues. One of the issues of the public perception of this is the name. Indeed, the House of Commons Science and Technology Committee strongly suggested a change of name for this, rather than using “GM”. I have forgotten the word they used.

The other point you made was that some businesses regard public sensitivity towards GM as becoming easier. Presumably this is partly because in Europe most animal feed is now using GM animal feed imported from the United States. There is a huge level of GM. Is this something that you publicise or explain? What is the role of Brussels, since we have a lot of GM as part of the business?

One more small point. A lot of the euro debate is that this is big private enterprise making its decisions, but in fact the European Community has its own European laboratories, and for some people if you have government laboratories that is a way of ensuring safety as opposed to just academics and business. Do you feel that the role of these state laboratories and institutions should be raised in profile as a form of giving safety? Not everybody believes that, but a lot of people feel that if it is a state-run organisation there is a level of security and long-term safety. What is your view?

**Mr Freeman:** Perhaps I will start on the public dialogue about science issues, and then George and Defra can lead on the feed issue. Lord Cameron made the point earlier about the striking difference between the debate about genetics in the context of healthcare and the debate in the context of agriculture. I think healthcare has led the way and that we have a very good system whereby the Government receives high-level scientific advice from both the chief scientists from the office of the chief scientist and from ethical advisory councils.

On the genetics of embryo research, our system works well, the Government get a piece of advice that new science and technology is making things possible, and Parliament needs to debate these, we need a consensus and we need a steer from Government. You have seen a number of debates in the last few years in the House. There is something in that. On healthcare I do not hear a great public outrage that our system for regulating genetics in healthcare is inappropriate. In fact, most people would cite the UK as leading in it. I think there is a lesson for a wider application of genetics there.

On the wider question of debate, who could not be in favour of debate as long as it is well informed? The GM debate has been characteristically ill informed. That is partly a function of all sorts of complex issues. The House of Commons is rather less good than your Lordships' House at debating science. There are not many people in the Commons with experience of

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science. Food is much more emotional in some ways than medicine. There are differences. It is important that we try and rebalance the debate. I would just point out that when somebody like Mark Lynas, who was a major spokesperson for the anti-GM movement, switches not slightly but 180 degrees and says that the previous things he said were completely undefendable and wrong, that is a big wake-up call to all of us that this debate needs to be rebooted. The benefits point is crucial. When we explain to people that genetics in agriculture, whether it is insects or crops, has the potential to allow us to grow crops in areas where they are currently not able to grow—drought-resistant crops in the Horn of Africa, disease-resistant crops that do not need spraying in the same way that can reduce the cost and the environmental impact, that can help emerging economies—the debate changes profoundly. There is an interesting question about how we in the UK could use our science advisory infrastructure to help change that. I suspect that the worst people to lead the debate are the companies doing the research and the politicians doing the regulation. I think it needs to be led by food consumers, by environmentalists. Mark Lynas and people like him, who have been very close to the debate, have a very big role to play.

**Mr Eustice:** I think you make a very good point on GM feed. I know that some of you from this room attended an APPG meeting last week, which looked at the issue of the Commission's current GM feed proposal. It is fair to say that there is a huge amount of frustration in the Commission at the moment. Commissioner Andriukaitis, who leads on this, is pretty much laying down the gauntlet to member states and saying, "If you are going to keep voting against applications that we have for GM animal feed coming into the European market, then have your opt-out and do not use it". The reality is that all but one member state in the European Union are heavily reliant on GM soy coming into the European Union, and their livestock industries would be massively compromised if they were not able to use it. There is a lot of frustration in the Commission that it sometimes suits some member states to vote against these things, blame the Commission for forcing it on them and look as though they have done their best to their domestic audience, while actually being perhaps a bit hypocritical in that they are voting against something which they know in their hearts they would not take up if they were given the option. There is an argument going on about that at the moment, and we suspect that the GM feed proposal is not going anywhere fast because the European Parliament has expressed concerns about it and there is no support in the Council, so it is probably not going anywhere. I think the fact that it was brought forward—

**Lord Hunt of Chesterton:** When you say that it is not going anywhere, are you just going to carry on having GM feed in use?

**Mr Eustice:** Yes, GM feed will continue to be used and there will probably be no national derogation as things stand. Having had a lot of negative reaction both from the Council and the Parliament, it looks as though it will not go anywhere. I think that in some ways it was brought forward by the Commission perhaps for tactical reasons to try to get countries to face the reality that they are buying and heavily reliant on GM feed for their livestock industries.

**Mr Freeman:** I would just make the point that if we were going to have a public discourse about GM modified insects, we would need to be able to explain to people that there is a difference between population suppression and population replacement; that there are pros and cons of both. Where you have a vector like the mosquito—although people may think it

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provides absolutely no value to society at all, there is evidence that it does important pollination functions—you may not want to suppress the population but to follow a replacement model so that it is still an effective pollinator but not in a vector of disease. I think the debate would need to be informed by some clear science, and Parliament and the Office of Science and Technology have a role in making sure that public discourse is properly informed.

**Lord Hennessy of Nympsfield:** When it comes to public discourse—I speak as an old journalist—the scare story will always trump the benefits story. There is a great pool of existing neuralgia with the words “genetically modified”, as Lord Hunt was saying, as there is with “nuclear”. It only takes one scare story and the whole terms of the debate, the terms of trade as it were, informed or not, change. You live with that as politicians, but there it is, that is the reality. Listening to all this is fascinating, but I get a great sense of fragility about this question, because it only takes one run of particular stories and evidence-based rebuttal can never quite catch up. We are on a precipice—mixing my metaphors—on this, are we not?

**Mr Freeman:** If one was starting with a blank piece of paper and asking how we could maximise the UK’s potential to put our science and innovation to work for global good, you would not start from this point with deep public confusion and fear about those initials “GM”. Notwithstanding the fact that somebody like Mark Lynas says that the debate is completely skewed and needs to be revisited, we are in a bad place to start. That is just the fact of where we are. The more scientific advice and evidence and the more we can initiate debates in Parliament with a process that says, “Here is the issue. You do not need to debate the facts. This is the choice. This is what is going on at the moment. The public policy debate is should we do X or Y”, the more one can frame the problem, the solution and the benefits, the more politicians have a chance to have a better debate.

**The Chairman:** The final question from Lord Patel.

**Q86 Lord Patel:** My question is about exploring the state of the science. For instance, the United States’ National Academy of Sciences has set up a committee to look at the state of the science in technology such as gene drive, gene editing, using other gene-slicing technology. They hope that this will then inform them about what kind of regulatory framework they should build. Do you think we should do a similar exercise? If so, who should be responsible for doing it?

**Mr Eustice:** It is an interesting question. In the case of commercialisation, while we have a process that is driven at a European level we are always going to be coming back to the art of the possible and what can we agree with 27 other member states. That is always going to be the nature of it. As I said at the beginning, I do not think there is much wrong with the process that the EU has as written. It all comes down to the implementation, and that is the bit that we have to get right.

**Lord Patel:** We have talked a lot about the regulatory framework in Europe and who should inform it. The US National Academy of Sciences has taken a different route and said, “Let us set up a committee and carry out a study of where the science is going to go and therefore what the appropriate regulatory framework will be”.

**Mr Freeman:** In the UK we have a parallel system. The chief scientist, the office of the chief scientist, advises the Government periodically on issues that have been thrown up by the

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pace of science and technology and by developments in science and technology that might create opportunities for the UK. Indeed, I have spoken with him this week about this subject. Your inquiry has already triggered some of those conversations. Chief scientists in each department have a duty to signal opportunities in that department and the chief scientists grouped together signal to Government periodically when there are opportunities. In the Department for Business, Innovation and Skills we are actively looking at areas where there are opportunities for the UK in science. As I say, we have set up the Synthetic Biology Leadership Council to advise on this broad field. We have channels of advice making sure that we are aware of areas of opportunity. The issue really is how we make sure that Parliament is able to initiate debates that are properly focused on the public policy questions that are legitimately in front of us.

**Lord Patel:** So you are relying on the government advisers to advise you? Might it be better if an independent, external, professionally respected academy were to be advising the Government on where the science is and therefore the regulatory framework?

**Mr Freeman:** That is a very interesting idea. I would be delighted to follow it up with you and have a look at the American model and see whether there are lessons for us.

**The Chairman:** I think that on that note we should conclude the session. We have taken a lot of your time. You have drawn attention to the need to have an informed debate, and I hope that when our report is published it will indeed help that process, both in Parliament and out. Thank you very much indeed for having helped us so much this morning.

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[Transcript to be found under Government: Mr George Eustice MP, Defra](#)

## **Sarah Hartley BSc, PhD, University of Nottingham – Written evidence (GMI0023)**

### **Introduction**

1. This evidence is presented to the Select Committee to provide a perspective on the governance issues related to GM insects, including public engagement, in the UK, EU, Brazil and US. I welcome Dr. Ball and Dr. Bonsall's invitation to contribute.
2. I am a political scientist working at the interface between science and public policy and have researched and written about the governance of plant and animal biotechnology for the last 15 years. My PhD compared UK and Canadian policy responses to GMOs (completed in 2005). I began studying GM animals 10 years ago (in the EU, US and Canada) and focused on GM insects for the last 3 years (EU, UK, Brazil and US). I have an edited book on animal biotechnology governance and several academic articles related to the governance of GM insects. I am currently funded by the Leverhulme Trust.
3. My expertise in GM insect regulatory governance and 'Responsible Research and Innovation' (RRI) will be of direct relevance to this Committee. I have solid understanding of the various applications of GM insects for use in human disease control and agricultural applications, including the range of insects under development and the various applications to release GM insects in contained and open trials globally. I have expertise in risk assessment and management of GM insects in the UK, EU, US and Brazil and followed these developments closely since 2012. I have expertise on science-based public consultations and GMO governance internationally. In addition to my work on regulatory governance of GM insects, I am a recognised expert in RRI. I manage several RRI projects and have papers published and under review addressing RRI generally and applying the framework to GM insects.
4. Specifically, I possess knowledge of the following areas: **EFSA's *Guidance on the Environmental Risk Assessment of GM Animals*** – interviewed experts policy-makers and analysed EFSA's public consultation; **Governance of the GM mosquito in Brazil in the context of RRI** - researched development and regulation of the GM mosquito; **Governance of the GM diamondback moth in New York** - analysed the public consultation conducted in the regulatory approval process; **RRI** - conducted several research projects, interviewed experts and policy-makers and organised and attended numerous workshops internationally; **RRI and risk assessment** - hosting an international expert workshop in November 2015; **Regulatory governance of GM insects in the UK** - researched UK regulatory responses to GM insects (contained use and deliberate release).
5. This submission is made in a personal capacity. I have no interests to declare. I am at the disposal of the committee to be examined as a witness.

### **Publics' concerns about the governance of GM insects**

6. Publics are those organisations and individuals who have an interest in GM insects, including researchers, communities who may be directly affected by GM insect trials, civil society organisations, industry and individual members of the public. Publics may also be referred to as stakeholders, citizens or the public.
7. It is well established in the academic literature that publics want to talk about a broader range of issues than narrowly defined scientific risks at the end of the innovation process. Publics want to talk about the governance of GM insects – this includes all the non-scientific issues related to the innovation process from the lab to commercial release, not simply the scientific assessment of risk. These governance issues are sometimes described as the political, social, ethical and/or economic issues.
8. Publics' hopes and concerns about GM insects remain relatively unexplored, particularly for agricultural applications of GM insects, despite the fact that these applications will very likely be the first GM animals to pass through the EU regulatory framework.
9. The scientific community is concerned that the emergence of GM insects must be handled carefully and transparently to avoid a potential public backlash, although there is no existing social scientific evidence of this potential. These concerns have been raised in a *Nature* editorial, in scientific papers and by the World Health Organization (WHO). Scientists' fears are based on an assumption that publics' reaction to GM insects will be shaped by their experience with GM crops. I agree that publics' concerns are likely to be shaped by experiences with GM crops and there is the potential for public rejection of GM insects, particularly within agricultural applications.
10. At present, very few civil society organisations are actively engaged with agricultural applications of GM insects. Genewatch (UK) and the Pew Initiative (US) are notable exceptions. Some civil society organisations have been involved with governance of GM animals and GM mosquitos and may get involved in governance of agricultural applications of GM insects in the future. These groups include Food and Water Europe, GM Freeze, Soil Association, Testbiotech, European Beekeeping Coordination, Center for Food Safety and Friends of the Earth.
11. Media interest in GM insects has been growing in recent years. Media articles have reported on scientific developments of GM insects, particularly on concerns over releases in the Cayman Islands, Brazil, Florida and New York. In general, these articles report on the science and offer little coverage of the governance issues. Interviews with civil society groups such as Genewatch, are generally limited to matters of science and risk.

### **The role of publics in regulatory risk assessment**

12. Risk analysis comprises three stages: assessment; management; and communication. Calls for public inclusion in risk assessment, where scientific experts determine risks, have mounted in recent years. These calls have come from academics as well as the European Commission's Scientific Committees, US National Academy of Sciences, Codex Alimentarius Commission and the WHO.



13. Calls for public inclusion in risk assessment respond to increasing evidence that risk assessment is not an objective, science-based process free from values, and therefore restricting decisions solely to scientific experts cannot be justified.
14. In practice, publics are not involved in risk assessment in the way prescribed by the European Commission's Scientific Committees, US National Academy of Sciences, Codex Alimentarius Commission and the WHO.
15. Theoretically and in practice, the role of publics vis-a-vis experts in risk assessment is contentious. Some experts argue for a role for publics and others are clearly opposed to blurring the lines between assessment and management.

### **Publics' involvement in establishing the EU risk assessment framework for GM animals**

16. In 2013, EFSA established the risk assessment framework for GM insects under the *Directive for the Deliberate Release of Genetically Modified Organisms* with the publication of the *Guidance on the Environmental Risk Assessment of Genetically Modified Animals* (the 'Guidance'). This Guidance is a risk assessment policy and as such, involves value judgements that include establishing the scope of future risk assessments (the kinds of impacts deemed to be within/outside the scope), what counts as evidence and how much is needed, the interpretation of evidence, how uncertainties should be addressed, and how precaution should be applied.
17. Codex Alimentarius Commission ('Codex') rules require the European Commission, the 'risk manager' to establish risk assessment policy in advance of risk assessment and in consultation with publics. Despite the EU's commitment to Codex rules, the Commission asked EFSA (the risk assessor) to develop the Guidance.
18. To meet its statutory obligation to stakeholder engagement, EFSA holds science-based public consultations: governance issues, including ethical and socioeconomic issues are outside its remit. Risk regulatory agencies in the USA (USDA and FDA) and Brazil (CTNBio) also hold science-based public consultations in their risk decision-making.
19. The public consultation held in the development of the Guidance was ineffective at capturing the full range of affected publics, resulting in an official complaint to the European Ombudsman about the independence of experts on the GM Insects Working Group and, more importantly, had minimal impact, particularly owing to the timing of the consultation at the end of a long, expert-driven process.
20. More importantly, the consultation was science-based therefore EFSA's experts did not consider non-scientific issues, even though participants' comments addressed governance issues.
21. By framing the Guidance as a scientific document, value-choices were hidden from publics and policy decisions were made by independent scientists without democratic

accountability. Frustration with this ‘cloaking’ of values was clear in EFSA’s public consultation and the issue has been raised frequently in the academic literature.

### **Publics’ involvement in the approval of the GM diamondback moth in New York, USA**

22. In 2014, the United States Department of Agriculture (USDA)’s Animal and Plant Health Inspection Service (APHIS) granted Cornell University’s application to release the GM diamondback moth in order to test its efficacy as an agricultural pest management tool. In the process, APHIS published an environmental assessment of the GM moth and held a science-based public consultation involving 286 participants (plus 19,869 signatures).
23. Analysis of the publics’ comments shows, overwhelmingly, that publics are concerned about governance of the GM moth and GM insects more broadly. Comments included the following concerns: Governance (mentioned 389 times); environment (118 times); animal integrity (42 times); human health (23 times); psychological (6 times); and, economic (once).
24. Publics’ concerns about governance included:
  - Trust and legitimacy, particularly trust in regulators, industry and scientists due to their close relationship and the focus on economic rather than social benefits from the technology;
  - Evidence and the burden of proof, particularly related to acceptable risk decisions;
  - GM technology more generally, the ‘unnaturalness’ of GM moths and the possible ‘slippery slope’ leading to the approval and normalising of other GM animals/insects;
  - Consideration of the GM moth in contrast to alternative pest management tools.
25. APHIS was unresponsive to these concerns and issued a permit for the release of the GM moth. This decision involved value-judgements about the acceptability of risk based on assessment of the environmental and human health risks and rendering the majority of the publics’ comments impotent.

### **The WHO’s ‘Guidance framework for testing of GM mosquitoes’**

26. The WHO’s Guidance Framework advocates the opening up of both scientific research and regulatory frameworks to publics to build trust and make substantive improvements to the development and deployment of GM mosquitos.
27. The Guidance Framework was developed for GM mosquitos as a human health intervention tool and, as such, it does not address governance of GM agricultural insects which are unlikely to garner the same levels of public support.
28. The WHO adopts an RRI approach, arguing scientific researchers are responsible for engaging with publics, responding to their concerns, and in case some instances, allowing publics’ concerns to shape the decision of whether a trial should proceed or not.
29. The Guidance Framework makes frequent mention of public consultation yet there is an assumption that these mechanisms allow publics to raise the issues that matter to them.

It fails to address the practical challenges of engaging publics through science-based consultations.

30. The WHO advocates a ‘science-based regulatory framework’ that provides for public stakeholder input, arguing that such a framework will “strengthen public confidence in and acceptance of GM mosquito biotechnologies, their developers, and the government agencies that regulate them.” (WHO, 2014: 94). I disagree with the WHO on this point. A science-based approach that restricts publics from raising concerns about governance will undermine public confidence and jeopardise public acceptance. This is particularly the case when science-based consultations are presented as legitimate mechanisms of public engagement.

**How appropriate are current EU and UK GMOs regulatory frameworks in addressing the issues raised by GM Insects? Are there lessons to be learnt from the regulation of GM insects in other countries such as Brazil?**

31. Although the full range of issues raised by GM insects has yet to be established, it is clear that the current EU and UK regulatory frameworks are *not* able to address the issues raised by GM insects and do not create opportunities to discuss them. Similarly, Brazilian and US regulatory frameworks do not allow for consideration of these issues.
32. Regulatory processes for GM insects are science-based and therefore restricted to scientific issues. The experts I interviewed who were involved with the EFSA Guidance agreed that the average person does not have the scientific knowledge or expertise to be able to comment on the scientific issues. In addition, GM insects raise issues that are broader than science and are related to governance. Currently, there are no opportunities in regulatory frameworks to discuss these issues.
33. Organisations, including the WHO state that regulatory processes include meaningful public involvement. Implicit in these statements is the assumption that public consultations are legitimate and open and publics are able to raise their concerns. However, regulatory processes include science-based public consultations that are limited to the risk assessment stage of risk analysis and restrict publics’ input to science.
34. The success of GM mosquitos in Brazil rests to a large degree on the Brazilian politicians and policy makers’ urgent need to come up with an alternative way to address an existing dengue epidemic coinciding with Oxitec’s initiative to introduce the technology in Brazil and the desire of its Brazilian partners to transfer useful development skills and capacities.
35. Oxitec’s public engagement in Brazil can be best characterised as a unidirectional public education campaign to publicise the trials, with the use of a van with a loud speaker and mosquito mascots. This approach to public engagement does not fit well with RRI approaches or those described in the WHO Guidance Framework.

**How can the gap between regulatory approaches and public concerns over GMOs be addressed? Is there a role for ‘responsible innovation’ approaches? What are the critical factors in effective public engagement from lab to final release?**

36. When GM crops emerged in the UK in the 1990s, a gap emerged between regulatory approaches and public concerns. Publics were deemed to have a deficit in knowledge and as such needed education about science. This ‘deficit model’ has been discredited leading to a shift in thinking about the relationship between regulatory approaches (science) and public concerns (society), driven in part by the Select Committee’s 2000 report, *Science and Society*. This shift translated into a significant rise in public engagement efforts, particularly in regulatory risk assessment and more recently, in scientific research through RRI. Publics are now promoted as valuable contributors to science.
37. This shift in thinking can be seen in the EU’s Scientific Committees, WHO and Codex recommendations for public input into risk assessment. However, the tension between science and society in the case of GMOs is still very apparent at the EU and UK level and I am not aware of a legitimate case of public input into risk assessment or risk assessment policy. Publics’ role in regulatory risk governance is limited to risk assessment where they are unable to discuss the issues that matter to them.
38. My interviews with scientists and policy-makers involved with biotechnology suggest the deficit model of public engagement remains entrenched.
39. Scientific research may be more responsive to publics’ concerns than regulatory authorities. For example, the majority of concerns articulated in the science-based consultation into the GM diamondback moth were ignored by the regulatory authority, but Cornell University and researchers redefined their research strategy following the consultation. However, Cornell University described the reasons for the change as scientific suggesting it may be difficult for scientists to openly respond to publics’ concerns about GM insects.
40. If risk assessment and scientific research are opened up to public input, they need to be able to respond to such input openly.
41. RRI has the potential to pluralise expertise and open up innovation to a broader range of voices and values in order to align the research system with the needs of society. RRI offers useful guidance on how to engage with publics in scientific research yet it is an emergent framework and we need to explore its potential and its efficacy in steering innovation toward society goals. As yet, RRI has not been applied to risk assessment. I am convening an expert workshop in November to consider this application.
42. The WHO Guidance Framework takes an RRI approach to scientific research involving GM insects (from the lab to release), yet it does not apply the same approach to regulatory risk frameworks governing the release of GM insects.

43. The critical factors in effective public engagement are well researched. Engagement must be conducted 'upstream' in the innovation process (starting in the design of research funding priorities). It must be a two-way conversation involving all interested parties with the freedom to discuss the full range of issues related to GM insects. It must be able to impact or shape the innovation process. Engagement should start with the societal or environmental issue that GM insects are proposed to contribute to and examine GM insects alongside alternative proposed solutions. It should not be an educational exercise to bring publics' thinking in line with a predefined government policy.
44. It may be helpful to think about an institution, mechanism or space to allow consideration of the governance or political issues related to GM insects.
45. In the case of GM crops, an argument has been made to support the exclusion of non-scientific issues from regulatory frameworks on the basis that the non-scientific issues should be addressed by consumers in the market place (although this model fails to work when labels are not provided). However, it is unclear how this model could work in the case of GM insects as they are unlikely to be available to individual consumers in both the human health and agricultural contexts.
46. We know very little about the benefits of GM insects. Scientific research is prone to hype: the benefits of scientific research are likely to be over-promised and this places pressure on technology to deliver on expectations. There is a need to research what the potential benefits of GM insects might be and create a 'space' to discuss these benefits in the context of alternatives.
47. We need to recognise that decisions about the potential role for GM insects in human health and agriculture are political and not scientific. Publics must be able to discuss these broader issues up front before a particular innovation trajectory is locked-in.

*22 September 2015*

**Work cited:**

WHO (World Health Organization) (2014) Guidance framework for testing of genetically modified mosquitoes. Geneva: WHO

Dr Sarah Hartley, University of Nottingham, Sciencewise, and the British Ecological Society (BES) – Oral evidence (QQ 16-25)

**Dr Sarah Hartley, University of Nottingham, Sciencewise, and the British Ecological Society (BES) – Oral evidence (QQ 16-25)**

[Transcript to be found under Sciencewise](#)

## **Innovate UK – Written evidence (GMI0008)**

### **The Innovate UK response to the House of Lords Select Committee inquiry into Genetically Modified (GM) Insects.**

1. Innovate UK is the UK's innovation agency, a non-departmental public body sponsored by BIS. It is the prime channel through which the Government incentivises innovation in business. Innovate UK is business-led. Our governing board and executive team is comprised of experienced business innovators and experts. We work with people, companies and partner organisations to find and drive the science and technology innovations that will increase productivity and exports and grow the UK economy.
2. We are working to:
  - accelerate UK economic growth by nurturing small high-growth potential firms in key market sectors, helping them to become high-growth mid-sized companies with strong productivity and export success;
  - build on innovation excellence throughout the UK, investing locally in areas of strength;
  - develop Catapults within a national innovation network, to provide access to cutting edge technologies, encourage inward investment and enable technical advances in existing businesses;
  - turn scientific excellence into economic impact and deliver results through innovation, in collaboration with the Research Community and Government; and,
  - evolve our funding models to explore ways to help public funding go further and work harder, while continuing to deliver impact from innovation.
3. In line with our strategy 'Concept to Commercialisation'<sup>67</sup> we operate across Government and advise on policies which relate to technology, innovation and knowledge transfer. We also support Government departments to become more efficient by supporting them in developing innovative solutions through harnessing the creativity that businesses can offer.
4. Innovate UK was established in July 2007 (as the Technology Strategy Board), we have committed more than £1.5 billion to date; for every £1 we invest, the private sector more than matches that investment, doubling the power of public sector money. We have directly supported over 6,500 companies and created or protected some 35,000 jobs. We work with nearly every University in the UK to stimulate the commercialisation of leading-edge academic research and innovation.
5. Innovate UK welcomes the Committee's inquiry into Genetically Modified Insects as such a technology is likely to be of interest to the UK academic and business community in service of positive public health and agricultural sustainability outcomes.

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<sup>67</sup> Available at <https://www.gov.uk/government/publications/innovate-uk-strategy-2011-to-2015-concept-to-commercialisation>

6. As the UK's innovation agency Innovate UK helps UK companies understand UK and global market opportunities. These opportunities are often in emerging fields where as well as new scientific approaches, there are often ethical and legislative considerations too. We are keen to consider the results of this inquiry which we hope will help form the scope of our strategy and potential future investments in the translation and development of GM insect technologies. Set out below is our response to the questions raised by the Committee.

**1. Which human diseases, across the world, could be addressed through GM insect technology? Are there any human disease risks in Europe, particularly the UK, for which GM insects are under development?**

7. We look to others more expert in the field to answer this particular question on the scope of opportunities.

**2. What are the possible livestock and agricultural crop applications of GM insects across the world? Of current livestock disease risks and agricultural insect pests that could be addressed through GM Insects, which should be the highest priority for Europe?**

8. This is an important question, as it will inform on the level and timing of the preparedness of the regulatory framework for potential developments in GM insect technologies. Answers will provide potential opportunities for science and for business to commercialise solutions in this area.

**3. Are there likely to be opportunities provided by GM insects that cannot be provided by other approaches, such as biological control methods? How could GM insect approaches be complementary to existing Integrated Pest Management (IPM) programmes?**

9. It is most likely that GM insects will provide new opportunities for the control of insects and the diseases and issues that they cause, which not only include those relating to human health but also importantly to those that threaten crop and livestock productivity.

10. Integrated Pest Management programmes that use a variety of approaches are generally preferred by practitioners over single solution methods of control. Integrated systems are more likely to avoid problems of resistance, and as all elements have different modes of action it means that by adjusting the active elements of a programme of control, a level of customisation can be achieved. Currently insecticides remain the main contributor to insect control whether as part of an integrated programme or as single control technique. However, with concerns about contamination of land and water bodies and effects on non-target species, as well as resistance, the options afforded by alternative or complimentary strategies are an important approach to pursue. This is especially the case if the use of insecticides can be lowered and effective control can still be achieved – this may be a possibility if GM insects are added within an integrated approach.



11. Where environmental and other factors are constantly in flux, the ability to use all available methods of control (including those using GM techniques) is important to establish and maintain. It is also important not to become totally reliant on one form of control if for some reason that method of control becomes unavailable or ineffective.
12. We can conclude that even though IPM approaches currently exist, there are concerns including those around resistance, and we need to look at new approaches, including the need to explore if GM can be added to the current portfolio of options. This in turn could result in growth opportunities for UK businesses.
13. Given that some insects cannot be controlled sufficiently with current control programmes (integrated or not), including those that use biological control, there seem to be opportunities for new techniques including those offered by genetic modification.
- 4. How appropriate are current EU and UK GMOs regulatory frameworks in addressing the issues raised by GM Insects? Are there lessons to be learnt from the regulation of GM insects in other countries such as Brazil?**
14. The regulatory framework is critical to permitting practices that are beneficial whilst effectively managing any risks. The current regulations pre-date the existence of GM insects and do not seem to effectively accommodate this technology. It is appropriate that the regulatory framework is addressed as it was designed to oversee the growth of GM crops.
15. It also seems apparent that the techniques for producing insects with altered characteristics are the focus for regulation rather than the phenotype that results. For example, the production of infertile male insects through radiation treatment is not regulated whilst there is a high level of examination of GM techniques that might bring about the same result. We would argue that any regulation of GM insects should focus on the risks and benefits of the phenotype produced (in this example the infertile male insect), rather than solely the method through which it is produced e.g. a GM technique versus radiation.
16. Additionally rather than a single consideration of risk, this should be balanced against potential benefits based on an evidence-based assessment. In evaluating risks and benefits current alternatives should be considered and reassessed if and as the landscape changes. It is also clear that where developments in science are moving quickly the regulatory framework needs to anticipate such progress rather than be reactive to innovation.
17. Where regulations in other countries and geographies exist these should be studied, understood and applied, if it is deemed appropriate and if they match the UK's requirements they may be incorporated into our regulatory framework.

**5. Do the World Health Organisation (WHO) guidelines on the release of GM mosquitoes provide the basis of an effective regulatory framework? How should issues regarding the emergence of resistance be considered?**

18. We cannot comment on the WHO guidelines, as they are outside our frame of technical specialisation and expertise as Innovate UK

**6. Do the European Food Safety Authority (EFSA) guidelines on the environmental risk assessment of GM Insects for commercial use sufficiently address the different risks from population suppression and population replacement approaches? How should the ecological risks and human benefits that might arise from the application of gene drive techniques to population replacement approaches be assessed?**

19. We cannot comment on the ESFA guidelines, as they are outside our frame of technical specialisation and expertise as Innovate UK.

**7. How is research into the development of GM insects currently funded? Are there opportunities to attract more private investment into this area?**

20. Private companies currently fund some of the applied research in this area, with support for a number of these projects coming from grant awarding bodies such as BBSRC, to enable early-stage developments, and where appropriate Innovate UK, to help business translate research into innovative technologies and products. Research is also conducted in collaboration with Government funded world-leading establishments such as The Pirbright Institute, which specialises in research and surveillance of viral diseases in farm animals and viruses that spread from animals to humans.

21. We are aware of one or two UK companies leading the world in GM insect research (including Oxitec in the UK, which both Innovate UK and BBSRC have funded) and that they are attracting private investment. We recognise however that the application of such research is likely to be in countries where the regulations allow the use of GM insects i.e. outside the EU. UK businesses will have to be prepared to do much of the trials to prove efficacy in those countries where the release of such insects are permitted. This means that whilst some of the research and development is conducted in the UK, most of the application will be conducted elsewhere.

22. Innovate UK may be a potential investor in such research and commercialisation if the investment were to lead to growth, productivity and be beneficial to the UK economy. The level of investment would depend among other considerations, and indeed on outcomes of this inquiry. If the inquiry were to support this approach we may consider specific funding in this area to promote commercialisation of UK-based research.

**8. Given the possible public health benefits of GM insects, should the Government be funding their commercialisation? Would this result in a conflict of interest with regard to regulation of releases? If so, how might this be managed?**

23. There seems no reason why the Government should not fund commercialisation of GM insects if the public health and/or animal health benefits are demonstrated.

24. To avoid potential conflicts of interest, it would be important for the regulation of GM insects to be handled by a separate inspectorate than those supporting commercialisation. Ensuring appropriate 'checks and balances' in the Government system would protect integrity and the interests of the UK population.

**9. How could the UK benefit economically from both developing GM Insect technology and its use within the UK?**

25. The UK has one of the most advanced networks of researchers in agriculture and health and already has the expertise and infrastructure to benefit from investment in this area. Indeed the business Oxitec who are active in this field are UK based and are a commercial spin-out from the UK academic system. The UK has the opportunity to benefit economically from the research and development, licensing and application of GM insects where the regulatory and market dynamics enable the deployment of the technology. The UK has the capability in the underpinning science and technology to benefit economically whether that deployment is within the UK, EU or elsewhere. However, where deployment is only possible in overseas markets, the UK risks losing its world-leading talent to the markets of greatest need/value for GM technology. Whilst the focus for Innovate UK is on the economic benefit, it would seem likely that there would be benefits beyond economic ones e.g. societal, given the animal and human health implications, which would be both in the UK but also in other countries which may be of interest to Government departments such as Department for International Development.

26. At the present time, UK companies can apply for co-funding from Innovate UK into the development of GM insects assuming all the criteria for funding (including regulation of such research) are met, but clearly they cannot take the commercialisation to full deployment any further in the UK market due to the interpretation of the current regulatory framework.

**10. How can the gap between regulatory approaches and public concerns over GMOs be addressed? Is there a role for 'responsible innovation' approaches? What are the critical factors in effective public engagement from lab to final release?**

27. As with all complex scientific issues, we would support effective public engagement and dialogue so that the evidence base is fully understood and the consumer can understand for themselves the risks and benefits of GM. This needs to be conducted by trusted third parties whose neutrality is clearly recognised.

Evidence submitted on behalf of the Innovate UK by:  
Dr Ruth McKernan, CBE, Chief Executive, Innovate UK

*17 September 2015*

Innovate UK, Biotechnology and Biological Sciences Research Council (BBSRC)—Research Council UK, and Professor Tim Dafforn, Department for Business, Innovation and Skills (BIS) – Oral evidence (QQ 1-15)

**Innovate UK, Biotechnology and Biological Sciences Research Council (BBSRC)—Research Council UK, and Professor Tim Dafforn, Department for Business, Innovation and Skills (BIS) – Oral evidence (QQ 1-15)**

[Transcript to be found under Biotechnology and Biological Sciences Research Council \(BBSRC\)—Research Council UK](#)

## **Institute for Science, Innovation and Society (InSIS) – Written evidence (GMI0030)**

*Authors: Dr Javier Lezaun and Christiaan de Koning, MPhil, University of Oxford.*

### **SUMMARY**

1. In this memorandum we provide a pragmatic perspective on the governance issues related to the development and deployment of genetically modified insects (GMIs).
2. There is at the present time no clear regulatory pathway for GMIs, and regulatory systems are particularly weak in the countries that could benefit the most from this technology.
3. In order to address this problem, we recommend the following lines of action:
  - a. **Address public concerns in the development phase of the technology.**
  - b. **Evaluate GMI-based interventions alongside alternative courses of action, and consider the potential lock-in of any GMI deployment.**
  - c. **Establish a transparent process for contained releases, including protocols for site selection.**
  - d. **Enhance mechanisms for post-release monitoring.**
  - e. **Initiate a public dialogue on second-generation GM insects, i.e. gene-drive or self-sustaining varieties, before the release of these organisms becomes a real possibility.**

### **ABOUT THE INSTITUTE AND THE AUTHORS**

4. The Institute for Science, Innovation and Society (InSIS) at the University of Oxford is a research group specialized in the governance of new and emerging technologies. Its work covers a wide range of scientific and technological innovations. Its research on climate geoengineering, for instance, was instrumental in the elaboration of the 'Oxford Principles,' which were endorsed by the House of Commons Select Committee on Science and Technology in 2010.<sup>68</sup>
5. Since 2008 InSIS has conducted research on the governance of new biotechnologies, including transgenic animals and mosquitoes. The Institute's BioProperty research group, funded by the European Research Council, has monitored the design and testing of transgenic mosquito varieties for vector control interventions. This work has included extensive interviews with scientists and regulators around the world, and a close study of past and planned releases in Brazil, Panama, Mexico and the United States.
6. Dr Javier Lezaun and Mr Christiaan de Koning have composed and submitted the

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<sup>68</sup> Rayner, S., Heyward, C., Kruger, T., Pidgeon, N., Redgwell, C., & Savulescu, J. (2013). The Oxford principles. *Climatic Change*, 121(3), 499-512.

following evidence on behalf of InSIS.

- Dr Javier Lezaun is Deputy Director of InSIS. His research focuses on the governance of scientific and technological innovation. He has published widely on the regulation of genetically modified organisms, and the role of public deliberation in the governance of new technologies.
- Mr Christiaan de Koning, MPhil, is a doctoral candidate at the University of Oxford's Saïd Business School. His doctoral research explores the governance and commercialization of emerging biotechnologies. Over the past two years he has been conducting empirical research on field trials of GMIs, and has interviewed a broad range of key actors in the UK, the EU, Brazil and Panama.

## **LACK OF REGULATORY PATHWAYS FOR GMI TECHNOLOGIES**

7. There is at the present time no consistent, internationally recognized regulatory framework for the testing and release of transgenic insects. While several countries have grappled with this question over the last decade, particularly in Latin America, they have developed *ad hoc* approaches, there is little exchange of information and 'best practice' across regulatory jurisdictions. In light of the importance of this technology, and of its significant cross-border implications, this state of affairs is unsatisfactory.
8. Countries, like those in the European Union, that have a detailed regulatory pathway for genetically modified organisms (GMOs), developed those in relation to genetically modified food crops and the biotechnologies that were available in the 1990s. Extending these regulations to GM insects requires a significant degree of fine-tuning and modification (for instance a re-evaluation of the guidelines for 'contained release,' and new criteria for the evaluation of environmental impact). Yet there is little appetite in these countries for reopening the political debate on the governance of novel biotechnologies.
9. Regulatory jurisdictions without a central authority in charge of assessing new GMO releases have struggled to deal with the complex challenges posed by GMIs. Even the United States found it difficult to chart a regulatory pathway for the release of transgenic mosquitoes when it was first approached by Oxitec Ltd. about this possibility in 2008. For resource-poor countries with limited regulatory resources – the key constituency for vector control applications of the technology – GMIs will represent a very problematic object of governance. In Mali, for instance, more than 30 agencies have been involved in approving the release of new GM mosquito varieties.
10. The process initiated in 2009 by the World Health Organization to develop a set of principles for the evaluation of GMIs has yielded a Guidance Framework for testing GM mosquitoes (2014). While this document offers high-level assessment criteria, it still requires a significant degree of adaptation to specific national and local conditions.
11. The challenges mentioned above pertain to 'first generation', self-limiting transgenic construct (e.g. sterile varieties). The difficulties increase exponentially, however, when we considering the development of self-sustaining, gene-drive systems. These 'second generation' varieties will present a radical challenge to existing regulatory frameworks.

For one, they will likely require forms of pre-release testing and post-release monitoring yet to be developed.

12. The lack of clear regulatory pathways adds a critical uncertainty to the viability of genetic insect control as a commercial enterprise. Private investment in this area has been very limited, even for agricultural pest control applications that might represent a significant market opportunity. With the recent purchase of UK-based Oxitec Ltd. by US synthetic biology firm Intrexon the sector has lost its most visible player.

## PRINCIPLES FOR A ROBUST REGULATORY APPROACH TO GMI TECHNOLOGIES

13. The experience gathered over the last decade in several Latin American countries offers some insights for the development of an effective governance system for GMI technologies. There has been a steep learning curve from the first open release in the Cayman Islands in 2008. Large-scale releases of GM *Aedes aegypti* mosquitoes have taken place in Brazil since 2010 in the context of that country's dengue control programme.<sup>69</sup> Significant releases have also taken place in Panama. Mexican authorities developed a particularly robust pathway for the contained release of transgenic *Aedes aegypti* in the southern state of Chiapas.<sup>70</sup> Several important lessons can be drawn from these experiences.

14. *Recognize public concerns and address them in the development process.* GMIs raise a number of significant issues and concerns in public opinion. These concerns are diverse, and vary from context to context. They are not necessarily a function of the insects being "genetically modified": in contexts where mosquitoes are an everyday vector of disease, any release of laboratory specimens into the environment is due to be cause for concern, regardless of how people feel about biotechnology. Some of these concerns can be addressed in the development phase – for instance those concerning off-target effects, sex selection (male-only releases), or the compatibility of GM species with local varieties.

15. *Evaluate GMIs alongside alternative approaches to the problem in question.* GMI technologies will not and should not be judged solely on their own technical merits. Application of genetic methods of insect control should be evaluated alongside alternative courses of action. If GM insects are to be released as part of a dengue control campaign, for instance, their effectiveness will need to be compared and contrasted with alternative approaches to dengue (e.g. the availability and efficacy of a dengue vaccine). The assessment of GM insects should also include a careful evaluation of alternative methods for vector control (e.g. drainage, spraying, bed nets, etc.). It is essential to conduct rigorous multi-technology evaluations, particularly because the deployment of GM insects will have significant lock-in effects,<sup>71</sup> For instance, deploying GM insects as a method of vector control against tropical diseases is likely to further weaken mosquito

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<sup>69</sup> Lezaun, Javier, Christiaan de Koning, Sarah Hartley, Lea Velho and Andre Campos. "Political responsibility and innovation: genetically modified mosquitoes in Brazil" (Forthcoming, in *Journal of Responsible Innovation*).

<sup>70</sup> Ramsey, Janine M., J. Guillermo Bond, Maria Elena Macotela, Luca Facchinelli, Laura Valerio, David M. Brown, Thomas W. Scott, and Anthony A. James. "A regulatory structure for working with genetically modified mosquitoes: lessons from Mexico." *PLoS Negl. Trop. Dis* 8, no. 3 (2014): e2623.

<sup>71</sup> Lezaun, Javier, and Natalie Porter. "Containment and competition: Transgenic animals in the One Health agenda." *Social Science & Medicine* 129 (2015): 96-105.

control programmes, and could contribute to the dismantling of public infrastructures that are already severely under-resourced. Genetic insect control applications in agriculture could reinforce the cultivation methods that exacerbated the pest problem in the first place. Any plans to move forward with this technology must thus be based on a careful consideration of alternative courses of action and of the long-term implications of technological selection..

- 16. *Establish a transparent process for contained releases.*** A robust and publicly accountable system for the governance of contained releases is key not only to the safety of subsequent open releases, but also to the public legitimacy of the technology as a whole. Yet it would be a mistake to simply implement the existing protocols for contained release of GMOs. These rules were often created to deal with GM crops, but insects raise a very different set of public issues and concerns, as well as very specific biosafety challenges. Furthermore, if we have learned anything from the experience of GM crops in Europe is that ‘field trials’ are a key battleground, and that what scientists interpret as a ‘limited’ or ‘contained’ release is often interpreted very differently by relevant constituencies. It is for instance critical to create a transparent site selection procedure, and to involve concerned local communities early on in the process. The experience of Mexico is significant in this regard. Researchers and regulators initiated a debate with local communities in Chiapas about the possibility of conducting a contained release study of GM insects there three years before the actual testing took place. The issue was openly discussed in the local assembly prior to the construction of the research facility. Community concerns were factored in in the design phase, before the mosquitoes were shipped to Mexico.
- 17. *Develop new mechanisms for post-release monitoring.*** Once again, the experience of GM crops is only of limited value in this regard. Transgenic insects pose particular issues with respect to environmental impact – for one, their traceability poses a significantly larger burden. We need better tools for the monitoring of GM insects in the environment, and the development of these tools needs to be addressed in a public and straightforward manner by the relevant scientific and regulatory institutions.
- 18. *Start a public discussion on next-generation GMI technologies.*** It is urgent to start a meaningful public dialogue on second-generation transgenic insect varieties, i.e. those varieties that incorporate gene drive systems and are thus expected to spread in the environment. This is a suite of technologies that is advancing quickly in laboratory work. Yet there is very little public awareness of their potential role, let alone a robust governance model for it.

4 November 2015

*Cite as: Lezaun, J., and de Koning, C. (2015) Memorandum on regulatory pathways for genetically modified insects.*



**Professor Anthony James, University of California – Written evidence (GMI0004)**

I am writing in response to your inquiry into Genetically Modified Insects. Specific answers to the questions follow.

**1. Which human diseases, across the world, could be addressed through GM insect technology? Are there any human disease risks in Europe, particularly the UK, for which GM insects are under development?**

At this time, mosquitoes, mosquito-borne pathogens and the diseases they cause are the most straightforward to address through GM insect technology. This is due to the significant advances brought about by the application of molecular biological, genomics and transgenesis technologies to these insects, in addition to the relative ease of rearing and maintaining these organisms in the laboratory. Also, the scale of the disease burden caused by these insects makes them worthy targets. Whole genome sequences are available, as are reliable methods for making engineered strains for use in population suppression or population modification strategies.

The specific major disease targets are malaria, dengue fever and Chikungunya fever. The significant risk in Europe and possible the UK is Chikungunya fever transmitted by the invasive mosquito species, *Aedes albopictus*.

**2. What are the possible livestock and agricultural crop applications of GM insects across the world? Of current livestock disease risks and agricultural insect pests that could be addressed through GM Insects, which should be the highest priority for Europe?**

This is outside my area of expertise, but in conversations with specialists, blue-tongue viruses come up often. Little work has been done to advance genetic manipulation of the species of flies that transmit these pathogens.

**3. Are there likely to be opportunities provided by GM insects that cannot be provided by other approaches, such as biological control methods? How could GM insect approaches be complementary to existing Integrated Pest Management (IPM) programmes?**

Yes, GM technologies, specifically those that achieve population modification of vector insects, offer the potential for high benefit-to-cost ratios by providing sustainable interventions. They can consolidate disease intervention and prevention efforts by providing barriers to pathogen and pathogen-competent vector reintroduction, and allow resources to be focused on new sites while providing confidence that treated areas will remain disease-free. These approaches are expected to work well with IPM approaches once the more-conventional approaches have achieved their regional goals.

**4. How appropriate are current EU and UK GMOs regulatory frameworks in addressing the issues raised by GM Insects? Are there lessons to be learnt from the regulation of GM insects in other countries such as Brazil?**

A lot of work still needs to be done in this area and it not only in the EU and UK. I am referring specifically to the circumstances created by the fragmented regulatory jurisdictions of multiple international, national and local agencies, and how this lack of coherency puts at risk the development of new technologies for which specific review and approval pathways do not exist. For example, we developed recently criteria for selecting collaborators and sites for efficacy and safety field trials of a transgenic mosquito strain designed to suppress populations of the dengue vector mosquito, *Aedes aegypti*. These criteria combined rigorous science with good ethical and legal practices. Specific site-selection criteria were developed in four categories, Scientific, Regulatory, Community Engagement, and Resources, in anticipation of open-field releases. The issue of how to get regulatory approval for the testing of a new technology when there was no dedicated agency to receive and review our applications was not trivial. Applying our checklist criteria, we identified Mexico as the only country at the time that had a horizontally- and vertically- integrated regulatory structure that could assure complete and ethical approval. Brazil may be there now. And yes, many lessons to be learned from these efforts.

**5. Do the World Health Organisation (WHO) guidelines on the release of GM mosquitoes provide the basis of an effective regulatory framework? How should issues regarding the emergence of resistance be considered?**

This publication is a good start. It would be best to develop it further with a specific GM product and disease target in mind. This way the important details will emerge and it will be possible to rank-order in an operational manner those factors that are significant. For example, resistance is likely to be more important in some circumstances than in others. It would be potentially counterproductive and a waste of resources to emphasize it as an issue before the specifics of a given situation were known.

**6. Do the European Food Safety Authority (EFSA) guidelines on the environmental risk assessment of GM Insects for commercial use sufficiently address the different risks from population suppression and population replacement approaches? How should the ecological risks and human benefits that might arise from the application of gene drive techniques to population replacement approaches be assessed?**

I would make the same argument here as I would for the WHO guidelines. The test of the robustness of existing regulatory structures will come from their application to a specific proposed product with a well-defined objective. This provides the opportunity to evaluate if the theoretical issues articulated in the various guidelines are sufficient or over-excessive, and whether or not there are additional concerns that need to be addressed.

**7. How is research into the development of GM insects currently funded? Are there opportunities to attract more private investment into this area?**

While basic research funding for both is available for both governmental and private organizations, I would say that considering the potential benefits and the scale of the problems, both are woefully underfunded. Business models for public health applications

are neither well-developed nor widely available for review. One idea was to make a good product and hope that a government would see its value and choose to support trials.

**8. Given the possible public health benefits of GM insects, should the Government be funding their commercialisation? Would this result in a conflict of interest with regard to regulation of releases? If so, how might this be managed?**

This is an area where new thinking is needed. The new technologies, in particular, those applied to public health issues, likewise have fostered demands for new administrative and support structures to carry them out.

**9. How could the UK benefit economically from both developing GM Insect technology and its use within the UK?**

Speaking in the context of public health, reductions in health care costs for treating ill people and reduced costs for prevention.

**10. How can the gap between regulatory approaches and public concerns over GMOs be addressed? Is there a role for 'responsible innovation' approaches? What are the critical factors in effective public engagement from lab to final release?**

This requires a lengthy answer for which I do not have time. Communication and trust are the key elements. The work of James Lavery and colleagues is a good place to look for the critical factors.

*1 September 2015*

Professor John Mumford, Imperial College London, Dr Jack Stilgoe, University College London, and Professor Paulo Paes de Andrade, Federal University of Pernambuco, Brazil – Oral evidence (QQ 39-47)

**Professor John Mumford, Imperial College London, Dr Jack Stilgoe, University College London, and Professor Paulo Paes de Andrade, Federal University of Pernambuco, Brazil – Oral evidence (QQ 39-47)**

[Transcript to be found under Professor Paulo Paes de Andrade, Federal University of Pernambuco, Brazil](#)

## **National Institutes of Bioscience (NIB) – Written evidence (GMI0012)**

**This submission is made on behalf of the eight UK National Institutes of Bioscience (NIB) funded strategically by BBSRC, namely The Roslin Institute, John Innes Centre, Institute of Food Research, Institute for Biological, Environmental and Rural Sciences (IBERS), Rothamsted Research, The Pirbright Institute, The Babraham Institute and The Genome Analysis Centre (TGAC).**

**The views expressed are independent of the Research Councils.**

### **1. (a) Which human diseases, across the world, could be addressed through GM insect technology?**

Most current approaches aim to affect target insect populations or species in a contained, species-specific way. In relation to human disease, such approaches are most obviously applicable to vector-borne diseases. Although different approaches have been proposed, are under development or in trials, they share key features – in particular they all depend on mating between modified insects and unmodified ones. This minimises off-target effects, however it is also likely to limit the application of such methods if a disease is transmitted by a large number of vector species. West Nile virus might be an example of a pathogen for which application of a genetics-based vector management method could be problematic, as it may rely on many vector species to spread between animals and humans. Conversely, dengue and chikungunya are attractive from this perspective with only one or a few significant vector species.

In some cases, the insects themselves are the disease agent rather than acting as a vector for a microbial pathogen. For example the larval stage of the New World screwworm, *Cochliomyia hominivorax* is the causative agent of screwworm myiasis disease. Some of these insects are excellent potential targets for genetic pest management (see below).

Other potential applications have been suggested, including the use of biting insects to deliver vaccines. While this might be interesting in particular cases, perhaps to vaccinate hard-to-reach wildlife disease reservoirs, we do not know of any substantial investment in this area.

GM insects are also used extensively in the laboratory to better understand fundamental aspects of the biology of disease vectors and other insects. Studies using GM insects, largely *Drosophila melanogaster*, have helped elucidate many underlying processes of normal and pathological states. However, we assume that the Committee's interest relates primarily to field/environmental applications and will not further discuss laboratory-only use.

### **(b) Are there any human disease risks in Europe, particularly the UK, for which GM insects are under development?**

Europe has *Aedes aegypti* and *Aedes albopictus* populations in several countries. These mosquitoes are the primary vectors of dengue and chikungunya viruses; GM strains of both

have been developed and successful field trials have been carried out in several countries for one strain of *Aedes aegypti*. Dengue is now endemic in Madeira (part of Portugal) and autochthonous (locally transmitted) cases of dengue occur sporadically in metropolitan France and other countries. A major outbreak of chikungunya in the Indian Ocean had severe effects on La Réunion (a French overseas *département*) and a smaller outbreak subsequently occurred in northern Italy. *Aedes albopictus* is continuing to spread north in Europe; risk maps from the European Centre for Disease Prevention and Control (ECDC) indicate that it may eventually establish in southern England. Historically, malaria was endemic in much of Europe, including the UK, and was only eliminated from Italy in the 1950s. Opinions differ as to whether malaria and other such vector-borne diseases are likely to re-emerge as a consequence of global warming. In addition to *Aedes* species, GM approaches are also under development for *Anopheles gambiae*, the major vector of malaria in sub-Saharan Africa, and for some other *Anopheles* species.

## **2. (a) What are the possible livestock and agricultural crop applications of GM insects across the world?**

The list of potential target pest species and problems is potentially very long. Increased globalisation has accelerated the rate of introduction of new invasive pests, so the list of pest problems continues to lengthen. Many of these may be good targets for sterile-insect methods, especially as invasive pests may lack a complex population structure even if present in the native populations from which they are drawn. When the damage is primarily due to direct feeding, e.g. of immature stages on host plant or animal, genetics-based population suppression methods may be appropriate. Where the pest causes harm indirectly, for example by transmitting a virus, methods aiming to reduce the ability of the target population to transmit the pathogen may also or alternatively be appropriate. This might be achieved, for example, by spreading a synthetic “virus resistance” (reduced vector competence) gene through the target population, an approach known as “population replacement” though the target population is not strictly replaced<sup>72</sup>.

Spread and long-term persistence of an engineered gene, for example the synthetic virus resistance gene in the example above, are likely to require the use of a gene drive system. Several designs have been proposed. These vary in several respects, one key property being the relative invasiveness of the system. Some gene drive systems are predicted to spread irreversibly through a target population, others cannot be reversed but can be overwritten, i.e. changed but not removed, others again are expected to stay confined to specified target populations and not spread significantly to non-target populations of the same species. Since many pest species are present in more than one country, and may be of different pest status in different areas, invasiveness and trans-boundary establishment are likely to be key regulatory issues and may limit the deployment of some systems.

Combinatorial use of gene drive systems has also been proposed whereby a less invasive system is used to spread a novel sequence through a target population; this novel sequence is then the target for a highly invasive genetic system<sup>73</sup>. Spatial confinement (“non-

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<sup>72</sup> Alphey L (2014) Genetic Control of Mosquitoes. Annual Review of Entomology 59: 205-224.

<sup>73</sup> Esvelt KM, Smidler AL, Catteruccia F, Church GM (2014) Concerning RNA-guided gene drives for the alteration of wild populations. eLife 3.

invasiveness”) is then conferred by the first system while the second may carry a deleterious gene potentially leading to elimination of the target population – but in this combination not of the species.

An additional potential application is in resistance management. In the context of an integrated pest management (IPM) programme, genetic pest management (GPM) methods can potentially help manage resistance to other control methods within the IPM programme. This has primarily been explored in the context of managing resistance to engineered plants, e.g. *Bt* crops<sup>74,75</sup>, but has wider application. The concept is as follows: in a GPM programme, modified insects are released to mate with wild pest insects. The numbers released (relative to the number in the wild population) vary by application but can be quite significant. Where some or all of these hybrids – progeny of mating between wild and released insects – survive and are fertile, there will be some introgression (spread) of genetic background traits (i.e. genes other than the transgene itself) from the “factory” population of modified insects into the wild population. So long as the factory population is susceptible to other control methods – for example an insecticide – “pushing” these susceptibility alleles (genes) into the wild population will tend to dilute and counter the spread of any incipient resistance genes in that wild population. Simulation modelling indicates that this could provide powerful synergy between GPM methods and other methods in an integrated programme, or even simply help reverse resistance in a population for otherwise-effective methods that have been rendered obsolete by the spread of resistance alleles.

In addition to livestock and agricultural applications, at least one other potential application of GM insects is gaining significant attention: use for conservation biology. Invasive species are a major problem for biodiversity and conservation. The best-known examples perhaps relate to rodents inadvertently introduced to naïve island habitats, but similar issues arise with insects. For example, avian malaria and avian pox transmitted by the mosquito *Culex quinquefasciatus* threaten several unique and endangered bird species in Hawaii with extinction. The self-dispersing and species-specific nature of genetic control methods make them highly attractive in this context.

**(b) Of current livestock disease risks and agricultural insect pests that could be addressed through GM Insects, which should be the highest priority for Europe?**

Even restricting to Europe there are still many candidates. Several tephritid fruit flies, especially Mediterranean fruit fly and olive fly, cause severe economic damage and are hard to control by current methods (primarily chemical insecticides, which are themselves under threat due to deregistration and emerging resistance in the pest insect).

In the UK, the Spotted Wing *Drosophila* (*Drosophila suzukii*) and the diamondback moth are potentially suitable targets, as are disease vectors such as thrips and whitefly. As the technology becomes routine, the costs and timescale of development and deployment are

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<sup>74</sup> Alphey N, Bonsall M, Alphey L (2009) Combining pest control and resistance management: synergy of engineered insects with *Bt* crops. *J Econ Entomol* 102: 717-732.

<sup>75</sup> Alphey N, Coleman PG, Donnelly CA, Alphey L (2007) Managing insecticide resistance by mass release of engineered insects. *J Econ Entomol* 100: 1642-1649.

likely to reduce, making it economically attractive for a wider range of targets – although this will largely be dependent on regulatory policies.

Introduced pest species can cause such harm and economic dislocation that there is a strong case for a proactive strategy based on horizon-scanning for threats and early development of suitable control tools, held in readiness against need. New invasions are by definition numerically and geographically limited and thus, highly vulnerable to genetics-based approaches. However, the development and regulatory timescales are such that starting development only after an incursion has been detected is likely to be too late, or at best unnecessarily expensive as the incursion will have considerable time to spread before actual deployment of the genetic strain. New World screwworm provides a classic example of timely intervention – an incursion into Libya, threatening Africa and Europe, was eliminated by use of sterile males from the large control programme in the Americas<sup>76</sup>. In this case, they used radiation-sterilised males, but the principle is clear. Had the US programme not been in existence, there would have been no defence. Government would need to consider funding mechanisms for this – as for vaccines, developing a GM insect for use in case of a future outbreak is unlikely to be commercially attractive due to the uncertainty over actual sales. Also, the conventional path to regulatory approval, involving cage and field trials of increasing scale, would need substantial modification for such proactive development as the pest is not yet present in the intended deployment area at time of development.

### **3. (a) Are there likely to be opportunities provided by GM insects that cannot be provided by other approaches, such as biological control methods?**

A major difference between biological control as traditionally practiced<sup>77</sup> and the use of GM insects is that with GM insects – as for classical Sterile Insect Technique – the control agent is a modified version of the pest species, rather than being some other species. The mating-based nature of the intervention (the control agent interacts with the wild pest population primarily or exclusively through mating) means that the use of GM insects is exquisitely species-specific. A major concern and limitation of classical biological control is off-target effects, in particular whether the released biocontrol agent will attack other species in the receiving environment than the intended one. While this must be a consideration for any intervention, the use of modified insects is much more specific and certain in this regard than other methods.

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<sup>76</sup> Lindquist DA, Abusowa M, Hall MJ (1992) The New World screwworm fly in Libya: a review of its introduction and eradication. *Med Vet Entomol* 6: 2-8.

<sup>77</sup> Biological control means different things to different people. Clearly GM insects are biological agents, as are radiation-sterilised insects, for example. However the term “biological control” is usually applied to the use of microbial entomopathogens (e.g. *Bacillus thuringiensis* strains, entomopathogenic viruses or fungi) – “microbial biological control”, or predators or parasitoids of insects. The use of predators or parasitoids is further classified as “classical biological control” where the control agent is expected to establish as a self-sustaining population after one or more releases, or “augmented biological control” where the control agent is only expected to be present at useful numbers if additional individuals are periodically released. Sterile-male releases fit the “augmented biological control” paradigm very well, but are nonetheless not usually considered as “biological control”, similarly for gene drive systems although a reasonable analogy can be drawn with classical biological control. Proponents of the use of artificial *Wolbachia* infections have attempted to promote or market it as biological control, even though there is little similarity with those methods normally described as microbial biological control.



Biological control of invasive pests is based on the notion that in moving to another area, invasive pests escape from other species – predators, parasitoids and pathogens – that adversely affect them in their native area. A typical start point for biological control is therefore to identify the native origin, and prospect there for potential control agents. These must then be exhaustively tested for potential effects on species in the new environment prior to actual use. For GM insects no such prospecting is required as the control agent is simply a modified version of the pest itself. On the other hand, other technical issues and regulatory requirements may mean that the timeline to deployment may not always be faster than for biological control.

**(b) How could GM insect approaches be complementary to existing Integrated Pest Management (IPM) programmes?**

IPM involves rational combination of the best available methods. In general, methods that are not technically incompatible and do not suffer from potential cross-resistance are likely to be candidates for inclusion in IPM. IPM tends to use biological control; genetic methods are fully compatible with this. Genetic control methods are also normally compatible with the use of chemical or biological toxicants, for example insecticidal chemicals or plant-incorporated protectants such as in Bt crops. One exception would be the use of adulticides in combination with the release of adult modified insects, though it is likely that this could be easily addressed by coordinated timing or placement of the two treatments. Cross-resistance between any of these interventions and GM insect approaches seems highly unlikely.

Specific synergies may also arise that would particularly favour the use of GM insects in IPM, for example:

- (i) Resistance management: some GM insect methods are designed to lead to significant introgression of genetic background (non-transgene) from the released insects into the factory population<sup>78</sup>. This can be a powerful tool with which to counter the potential spread of any resistance factor against other components of the IPM programme, for example plant-incorporated protectants or insecticidal chemicals.
- (ii) Control dynamics: most control methods may be able to reduce the target population but become less efficient as the target population diminishes, i.e. find it harder and harder to get the last ones. In contrast, sterile-male methods become more efficient as the target population diminishes – a key parameter is the ratio of sterile males:wild males; for a given release rate of sterile males, as the target population diminishes this ratio improves. An optimum control strategy from a cost-effectiveness perspective may therefore comprise use of sterile males as a major IPM component after initial suppression of the target population by conventional means.

**4. How appropriate are current EU and UK GMOs regulatory frameworks in addressing the issues raised by GM Insects? Are there lessons to be learnt from the regulation of GM insects in other countries such as Brazil?**

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<sup>78</sup> Alphey N, Coleman PG, Donnelly CA, Alphey L (2007) Managing insecticide resistance by mass release of engineered insects. *J Econ Entomol* 100: 1642-1649.

**UK so far:** On a pragmatic level, the UK framework for laboratory use of GM insects seems to work well. Moving outside the laboratory, even to secure field cages appears to be considered “deliberate release”, which may not be appropriate. For deliberate release as normally understood, i.e. release into the environment without physical confinement, the regulatory framework has not to our knowledge been tested in that there have been no formal requests for permission to undertake deliberate release of any GM insect in the UK. With the proviso that it has not been tested, the UK system may be adequate to regulate trial releases, at least of self-limiting genetic systems. Even at this stage though, some specific issues seem problematic. One is the Environmental Information Regulations that implement the Aarhus convention regarding public participation in environmental decisions. This can lead to a large number of Freedom of Information Act requests from pressure groups. While these may appear to be directed at government agencies, e.g. regulatory agencies, answering them will normally involve action by the developer. For an SME this is a significant burden, furthermore the cost asymmetry – very cheap for the pressure group, much more costly for the agency and developer – allows this tool to be misused for harassment and fishing exercises.

**EU market - regulatory failure:** From an EU perspective, there has been an application under deliberate release regulations for a small trial of a modified olive fly in Spain. The regulation of trials is a national decision and may be handled adequately, as seems to be the case in Spain, depending on the country. However any larger scale use would require EU approval; at present this seems so unlikely, and so costly and protracted if in fact possible at all, as to present a huge barrier to all but the most deep-pocketed developer. To be fair, to our knowledge no one has tried to put a GM insect product on the market, but the precedents, especially from GM plants, are extremely negative. This has at least three negative effects. Firstly, most developers will simply not be able to afford the costs, even if they could tolerate the timescale. This means that no university or SME will even attempt to introduce a GM insect method in the EU, no matter how beneficial. Secondly, the time and cost are such that a developer would need to see a large return. For a commercial developer this means a large and valuable market, which excludes many areas for which GM insect methods might be very valuable, for example niche crops, public health or conservation. Thirdly, the only developers with sufficiently deep pockets, at least in the commercial sector, are large multi-national companies. An overly onerous regulatory system will therefore put the technology, or at least its use, into the hands of such companies exclusively.

More generally there are a number of features of an appropriate regulatory system that are not ubiquitous, including:

**Product vs process:** while many countries regulate novel products in this area according to details of how they are made (regulating by process, here regulating products differently if they are GMOs), this is inappropriate for several reasons: (i) this inevitably leads to problems around the boundary of the definition of the process. For example, genetic control methods based on the use of *Wolbachia* require the insertion of over a million bases of poorly characterised foreign DNA into the recipient modified insect, encoding thousands of unknown genes. If any one of these genes were inserted, that would make the recipient a GMO, but because the whole package can be inserted without using recombinant DNA

methods, the recipient is not considered a GMO and is therefore subject to entirely different, and much less stringent regulation; (ii) similar products may be subject to very different regulatory regimes. For example, the products of site-directed mutagenesis are not considered GMOs. If such methods become more efficient, one could imagine a situation where two strains of the same insect are made with the same section of modified DNA – one modified using recombinant DNA methods, the other not. These insects would be indistinguishable by any means, yet subject to entirely different regulatory regimes; (iii) more generally, a credible, reputable regulatory regime needs to be consistent and proportionate. There does not seem to be a scientific basis for applying an entirely different regulatory regime to GM insects as compared with the novel genome or ecosystem associations of *Wolbachia* or classical biological control strategies, for example. Though the UK and EU regulate based on process, this is not universal – Canada considers “novelty”, the USA regulates by product rather than by process. Of course this does not preclude consideration of construction method in a risk assessment if there is a scientific basis for this.

**Regulatory authority and process:** it is important that developers and other stakeholders know who will regulate a given product, that they are credible and independent (both of the developer and of any other pressure group) and that a rigorous, independent, timely scrutiny will be conducted through science-based risk assessment. This has been a positive feature of the system in Brazil (CTNbio), for example. This requires the involvement a wide range of stakeholders, including those sceptical of the technology or product, to identify as wide a range of risks and benefits as possible, followed by review and decision-making by independent experts. Though many hazards may be considered initially, only those with a credible mechanism whereby the proposed action could cause the proposed harm should form the basis of a regulatory decision. The costs and uncertainty of regulatory timescales and outcomes for genetic methods in Europe are prohibitive at present.

**Benefits:** the regulatory system needs to include consideration of potential benefits as well as of potential risks. This might seem obvious, yet this is not the case in Europe, where only risks may be considered. Without considering benefits, one is implicitly comparing the proposed action with a non-existent risk-free alternative – a Utopian fallacy. Benefits, and therefore risk-benefit, could be considered explicitly. An alternative, widely used in the US system, is to compare the proposed action (e.g. a release or series of releases of a GM insect to control a target pest population) with one or more alternative scenarios, including “stay as we are” – the so-called “no action” alternative, and perhaps a scenario in which currently-used methods are applied more intensively. Consideration of the relative risks of each of these scenarios at least implicitly includes consideration of the potential positive as well as the potential negative outcomes of the proposed action relative to the current situation.

**Co-existence:** producers who wish to be able to take advantage of new methods need to be able to do so, without excessive adverse effects on those who do not – and vice versa. In the context of genetic technologies in agriculture, non-users may include “organic” farmers. For chemical insecticides that are banned under organic rules, this is achieved by setting a low-but-non-zero residue threshold (e.g. one-tenth of the limit for conventional farmers) to allow for the possibility of spray drift or similar from neighbours. In contrast, anti-GM pressure groups impose or threaten a zero threshold for similar adventitious presence of any

GMO, asserting that a single GM insect found on an organic crop might then lead to loss of organic status and consequential financial loss<sup>79</sup> – and presumably a basis for a law suit against the developer and/or user of the GM insect. Regulators or politicians need to impose co-existence rules to allow both adopters and non-adopters to operate and thrive alongside one another.

**5. (a) Do the World Health Organisation (WHO) guidelines on the release of GM mosquitoes provide the basis of an effective regulatory framework?**

The WHO guidelines<sup>80</sup> are not a regulatory framework, nor is the WHO a regulatory agency in this context. The guidelines make a number of general observations and recommendations that may well be useful to developers and/or regulators. However, as the Foreword to the guidance notes:

“Because of the breadth of different genetic approaches that are under consideration and conditions under which they might be used, it is not possible to provide an exact formula for evaluation of all [*genetically modified mosquito*] GMM technologies. It will be necessary to determine the specific needs on a case-by-case basis. Thus, the guidance framework presented here does not offer precise instructions for testing GMMs, but rather aims to support informed and thoughtful process development.”

**(b) How should issues regarding the emergence of resistance be considered?**

Any control intervention places some selective pressure on the target population that may lead to an evolutionary response (“resistance”). This may affect long-term effectiveness and so should be considered in relation to effectiveness – which may or may not be part of the regulatory process, as discussed below. Effectiveness is likely to be a major consideration for the end-user, and so through normal mechanisms for the developer, e.g. for a commercial product, market mechanisms. If the emergence of resistance might predictably lead through a credible pathway to a specific hazard then it would also be an issue for a regulatory agency to consider. If there were considered to be no or few alternatives to a specific intervention, there might be a public-good argument for ensuring its continuing effectiveness beyond the potentially short-term interests of the developer; this could also be the basis for regulatory intervention.

**6. Do the European Food Safety Authority (EFSA) guidelines on the environmental risk assessment of GM Insects for commercial use sufficiently address the different risks from population suppression and population replacement approaches? How should the ecological risks and human benefits that might arise from the application of gene drive**

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<sup>79</sup> See, for example, an open letter dated June 10, 2015 from Friends of the Earth [USA], Center for Food Safety, Food & Water Watch, Northeast Organic Farming Association of New York and GeneWatch UK, cited in a New York Times article (31 August 2015) which also cites a contrasting opinion from a legal expert, Susan Schneider of University of Arkansas School of Law.  
[http://documents.foodandwaterwatch.org/doc/DBM\\_letter\\_FINAL\\_6.10.15.pdf#\\_ga=1.174218663.465980230.1441097155](http://documents.foodandwaterwatch.org/doc/DBM_letter_FINAL_6.10.15.pdf#_ga=1.174218663.465980230.1441097155)  
[http://www.nytimes.com/2015/09/01/science/replacing-pesticides-with-genetics.html?rref=collection%2Fsectioncollection%2Fscience&action=click&contentCollection=science&region=stream&module=stream\\_unit&contentPlacement=1&pgtype=sectionfront&r=2](http://www.nytimes.com/2015/09/01/science/replacing-pesticides-with-genetics.html?rref=collection%2Fsectioncollection%2Fscience&action=click&contentCollection=science&region=stream&module=stream_unit&contentPlacement=1&pgtype=sectionfront&r=2) which also

<sup>80</sup> WHO/TDR (2014) Guidance framework for testing of genetically modified mosquitoes. Geneva: WHO. 132 p.

### **techniques to population replacement approaches be assessed?**

The EFSA guidelines<sup>81</sup> were developed with a specific focus on GM technologies and products then seen as likely or feasibly entering the EU market within ten years of time of writing. Note that “entering the market” in this context does not include field trials. Gene drive technologies were considered unlikely to reach the market on that timescale, given the regulatory difficulties and the fact that no gene drive system capable of spreading in a wild type background had been demonstrated in any pest insect. This conclusion still seems reasonable though perhaps a little less certain with the recent demonstration of relatively easily constructed, highly invasive gene drive system in a model insect<sup>82</sup>.

Key issues of persistence and invasiveness are certainly mentioned in the EFSA guidelines, though without a great deal of detail. This is appropriate given the nascent state of the technology, and the corresponding uncertainty regarding the specific characteristics of any product that might in due course emerge. The potential for spread, particularly trans-boundary spread, persistence and reversibility, for example, vary dramatically from one proposed system to another. It would therefore seem unwise to try to develop a comprehensive regulatory framework at this stage, rather guidelines such as these should be applied as the basis for a science-based risk assessment by a technically competent regulatory agency, which is then used as the basis for the regulatory decision. With the experience gained from handling several such cases it may be possible to produce more prescriptive guidelines, at least for that class of technology.

The EFSA guidelines focus on commercial use or “placing on the market”, however it is possible that gene drive systems may not initially or primarily be developed for commercial purposes. Highly invasive gene drive systems may not lend themselves readily to a purely commercial business model; research in this area at present appears to focus on philanthropic and/or public funding for development with a view to a very limited release programme giving long-term effects (e.g. genetic changes and/or population crash affecting an entire species). If this is undertaken by the developer, it may not meet the definition of “placing on the market”, which present as trials even though these might have long-term, irreversible and trans-national effects – though this is all hypothetical at present. In contrast, while several academic or government groups are developing sterile-male type methods or components, all field releases to date have involved a UK company, Oxitec Ltd.

### **7. (a) How is research into the development of GM insects currently funded?**

The overwhelming majority of research using GM insects relates to laboratory-based use of *Drosophila melanogaster* for basic-science purposes, funded by government or philanthropic agencies. Research into development of GM insects for field use is also largely funded by government or philanthropic agencies at present, mostly in the UK, Europe and USA; the UK has particular strengths in this area. The principal exception is Oxitec Ltd, a private company spun out of the University of Oxford in 2002. Over several funding rounds, Oxitec attracted

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<sup>81</sup> EFSA Panel on Genetically Modified Organisms (GMO) (2013) Guidance on the environmental risk assessment of genetically modified animals. EFSA Journal 11: 3200.

<sup>82</sup> Gantz VM, Bier E (2015) The mutagenic chain reaction: A method for converting heterozygous to homozygous mutations. Science.

£29m of equity-type funding, largely from investment funds and high-net-worth individuals, both UK-based and overseas. Grants from UK funding agencies, especially BBSRC and TSB/Innovate UK, provided crucial early support. In August 2014 takeover by Intrexon Inc for \$160m, was announced. Intrexon is an NYSE-listed company which has recently acquired several other synthetic biology companies.

**(b) Are there opportunities to attract more private investment into this area?**

A key problem for private investors is regulatory uncertainty. This makes it very difficult to understand an investment proposition. Long timescales and high costs of regulation, even if clear, necessarily restrict for-profit investment to large high-margin markets. While these may exist for genetic pest management methods, for many applications the size may be too small (many specialty crops) or commercial returns too low (many public-good applications, e.g. public health or biodiversity) for a commercial model to be viable in the face of a protracted and expensive regulatory system; uncertainty (of cost, timescale and/or outcome) further exacerbates this. This seems regrettable as few credible risks seem to have emerged, either in theory or in practice, for the few GM insect products that have so far reached field trials.

It is harder to see how to attract private investment into the development of invasive genetic systems. This is for several reasons including (i) difficulty in developing a business model; (ii) regulatory uncertainty – it is unclear at present how to regulate genetic systems expected to spread across national borders and for which the ability to reverse or “recall” is at best untested, so the time and cost requirements of getting permission for release are extremely hard to estimate.

**8. Given the possible public health benefits of GM insects, should the Government be funding their commercialisation? Would this result in a conflict of interest with regard to regulation of releases? If so, how might this be managed?**

Where the potential benefit of use relates to a function normally seen as a responsibility of government, it is reasonable to see governments as the customer/user and in some cases it might well be appropriate for that government to fund development as well, especially where there is no obvious business model or incentive for commercial development. This might apply to public health or conservation applications, for example. It might also apply to some agricultural applications, particularly in the context of invasive pests, or where area-wide control is seen as an infrastructure investment.

Governments have to regulate their own activities in many ways, so while regulation of government activities in relation to GM insects might potentially provide some conflict of interest, there is plenty of precedent for how to resolve this. It would be helpful, if not essential, to have a credible science-led regulatory agency substantially free from political interference and independent of the developers and users of the technology.

**9. How could the UK benefit economically from both developing GM Insect technology and its use within the UK?**

**As user:** Relative to many other countries, the UK does not have major insect problems, whether in agriculture or public health, or other sectors. Perhaps the most promising near-term application is the control of invasive pests, for example Spotted Wing Drosophila or oak processionary moth. However, most attractive commercial targets would be major, stable, pest problems where the value of a new control method is clear – and likely still to be there after the developer has gone through the regulatory process. In contrast, invasive pests are best tackled while the incursion is small, so the control tool should ideally be developed ahead of need – when there is by definition no market – and applied only to a limited area and hopefully for a limited duration, i.e. until the incursion is successfully eliminated. Prompt action may benefit the whole country, but it may be difficult for a commercial developer to realise that value from the many beneficiaries, especially those remote from the initial incursion. On the other hand, it may be possible to undertake small-scale programmes under some sort of experimental-use permit, thereby avoiding the much greater costs of full EU-wide registration.

**As developer:** design and development of GM insects and GM insect based control methods represent an emerging, knowledge-intensive and potentially high-value industry. Total value is hard to estimate, but it could potentially address a number of multi-billion-dollar problems in agriculture and public health around the world. Could the UK become a leader in this industry? What are the potential sources of comparative advantage, if any, for the UK, as a developer of GM insect technology?

*Current position:* The UK has a clear lead in the commercial development of GM insect technology through Oxitec Ltd. Though an agreement for Intrexon Inc to acquire Oxitec was announced in August 2015, Oxitec’s research facility is expected to remain based in the UK. The UK also has a number of leading academic research groups active in this area, including those led by Luke Alphey (The Pirbright Institute) and Austin Burt and Andrea Crisanti (both Imperial College), world-leading developers of GM insects, respectively focusing on self-limiting and self-sustaining methods. More generally, the UK has a strong bioscience sector in universities, research institutes and small and large companies. However, there is competition in the US and elsewhere, notably China where there has been considerable recent investment in this area. Furthermore, the current regulatory – and perhaps political – situation makes it hard to test GM insects in the UK. This has a knock-on effect on potential markets as there is an expectation that a developer would first test a product “at home”. Developers that can do this will have an advantage over those that cannot.

*Market:* as noted above, the domestic market for this technology is limited. This precludes a common route for small companies of starting with a local market then expanding. If the government were to encourage the development of GM insect technology for those specific, otherwise intractable problems for which it seems appropriate, this would catalyse and underpin the development of an export industry which would likely otherwise struggle to gain traction.

**10. How can the gap between regulatory approaches and public concerns over GMOs be addressed? Is there a role for ‘responsible innovation’ approaches? What are the critical factors in effective public engagement from lab to final release?**

Given resources expended failing to resolve this question in the context of GM crop plants it would be naive to think that anyone has definitive answers to these questions. Nonetheless, we present some observations below.

Public confidence in a product is related to confidence in those who have approved its use. Developers, especially private-sector developers, are commonly seen as tainted by conflicts of interest, so regulatory agencies become key. Transparency, expertise, science-based assessment, apolitical, independent assessors – these all help. However, if regulators make decisions contrary to the wishes or beliefs of those with strongly-held views they may simply dismiss the decision-makers as part of a conspiracy, subverted by the developers or other actors.

Perceived benefit may be important. This forms part of the answer to questions such as “why are you doing this?”, “why should I let you do it?” or “what’s in it for me?” It is striking that the most rapid progress with GM insects has been with a product targeting the dengue mosquito, *Aedes aegypti*. Dengue is a major human disease with no specific drugs or licensed vaccine. It affects rich and poor alike; with an estimated 390m infections and 50-100m cases per year, in endemic countries most citizens will have been affected or have friends or family members who have. Furthermore, government information campaigns exhort the citizens to control the mosquito by cleaning up potential breeding sites. Most people in such countries will therefore recognise the motivation behind the development and use of the product, even if they are not comfortable with specific aspects. It may also be important that the risks and benefits are seen to be equitably distributed. The importance of benefits in relation to public perception highlights the absurdity of not including consideration of benefits in the regulatory process, as discussed above.

A wide range of other factors are likely to be important, including transparency, familiarisation, the nature and funding of pressure groups (pro and anti), public attitudes to science in general, the nature and credibility of backers, interlocutors and commentators, etc.

17 September 2015

<http://www.nib.ac.uk/>



## **Nuffield Council on Bioethics – Written evidence (GMI0020)**

### **KEY POINTS**

- Genetic modification techniques, such as gene drives, have been embraced with enthusiasm by many researchers, but also provoked debate about future uses, including ecological engineering.
- Questions about GM research and innovation should be considered in the context of alternative ways of responding to human priorities, and in accordance with broader social values.
- Public engagement around GM insects should learn from the polarised public debate about GM foods. One aspect of this may be to understand what different people mean when they invoke ideas about naturalness in discussions about developments in science and technology.

### **BACKGROUND**

The Nuffield Council on Bioethics is a UK independent body that examines and reports on ethical issues in science and medicine. We welcome the opportunity to comment on the House of Lords Science and Technology Select Committee inquiry into Genetically Modified (GM) Insects in relation to their use in human disease control as well as livestock and agricultural crop applications.

The Council identified the ethical issues surrounding GM insects in 2014 as a possible topic for future investigation as part of our horizon scanning activities.

The Council has carried out or is carrying out a number of projects that are relevant to discussions about GM insects:

#### ***Genome editing***

The Council has recently started a new project on genome editing. The first stage of the project will look at developments such as the CRISPR-Cas9 system and gene drives, which allow precise, targeted changes to be made to DNA molecules in living cells, assess the impact of the technologies in research and the kinds of ethical questions that arise. This will result in a 'platform' report that will be followed by one or more report(s) looking at specific applications.

The Working Group is chaired by Dr Andy Greenfield and met for the first time in September 2015. The early stage of our project means we are not able to comment on specific applications such as GM insects. However, issues that our project will look at include:

- The meanings and significance of 'genome' in societal contexts

- Genome editing in the context of developments in science and society, for example debates about GM, assisted conception
- Issues around ease, efficiency and economy of use of the CRISPR-Cas9 system, and questions around dual use, and bio-hacking
- Drivers and responses to developments in genome editing, including ‘science push’/‘policy pull’, commercial drivers, civic responses, and framings.
- Questions of individual liberty and dignity
- Issues of cross-border and intergenerational justice and questions of global public interest.
- Questions of domestic inequality, for example in terms of access to scientific careers or the distribution of benefits of biomedical research

We intend to publish the first stage of this work in the first half of 2016, when work on the first ‘applications’ report will commence. We would be happy to advise the Committee on the state of our work as it develops over the coming months. Further information about the project is available online: <http://nuffieldbioethics.org/project/genome-editing/>

### ***Naturalness***

The Council is currently undertaking a project exploring how different ideas and understandings of ‘naturalness’ affect public and policy debates about science and technology, including GM. The project includes a review of media articles, political debates, reports from civil society and scientific organisations, and previous Council reports. The report will be published in late 2015.

A review of academic research exploring public perceptions of naturalness has also been carried out and is available at: <http://nuffieldbioethics.org/project/naturalness/evidence-gathering/>

The findings will be discussed over the autumn with journalists, policy-makers and parliamentarians, Government officials, scientists and representatives from civil society groups, and with members of the public. A report setting out our findings will be published in November 2015.

Further information about the project is available online: <http://nuffieldbioethics.org/project/naturalness/>

### ***GM crops and emerging biotechnologies***

The Council has published three relevant reports on GM and emerging biotechnologies.

- *Genetically modified crops: the ethical and social issues* (published in 1999) – available online: <http://nuffieldbioethics.org/project/gm-crops/>
- *The use of GM crops in developing countries: a follow-up discussion paper* (published in 2003) – available online: <http://nuffieldbioethics.org/project/gm-crops-developing-countries/>

- *Emerging Biotechnologies: technology, choice and public good* (published in 2012) – available online: <http://nuffieldbioethics.org/project/emerging-biotechnologies/>

## COMMENTS FOR THE COMMITTEE

### Regulation

- 1 GM techniques offer one way among others of responding to human priorities. We conclude that questions about GM research and innovation should be considered in the context of alternative ways of responding to human priorities, and in accordance with broader social values. Rather than considering GM technologies in isolation on a case by case basis, the Council recommends a broader approach where risks and benefits of biotechnologies, such as GM, are assessed on a comparative basis. This should include assessing the risks involved in doing nothing (which in itself is not an ethically neutral act) and investigating alternative options (which may be technological, social or organisational), in order to address the same societal priorities or concerns.
- 2 Some view the issue of GM insects as purely a matter of risk-benefit analysis. Proponents of the technology consider it a useful tool in the fight against insect-borne diseases and for pest control. Possible benefits of GM insects include fewer effects on non-target species than pesticides, the ability to cover areas that may be inaccessible to conventional methods, and the reduction in the amount of insecticides and other potentially harmful chemicals being used. In terms of risks, concerns have been raised regarding the release of GM insects into the environment, including the development of resistant pathogens or insects, the elimination of one species leading to the dominance of another, the transfer of the inserted genes into other species (horizontal gene transfer), and the potential harmful effects of GM insects on human health and the ecosystem.
- 3 In previous written evidence to the Committee for its inquiry on GM crops and the application of the precautionary principle in Europe, the Council highlighted the inappropriate application of the precautionary principle to emerging biotechnologies. We concluded that regulatory design cannot provide all the answers to securing benefits or averting harms from emerging biotechnologies, such as GM insects. In part, this is because emerging biotechnologies do not fit easily into risk-based regulatory models but require instead an approach guided by caution which, in turn, requires a continuous and reflective engagement with broader societal interests. We are currently awaiting the Government's response to the Committee's report which referred to the Council's recommendations.

### Public debate

- 4 The use of gene drive technology in GM insects means it might be difficult to restrict their spread once they have been released into the environment. This may have important implications for consumers who wish to avoid contact with genetically modified organisms (GMOs), and may revive the ecological concerns of earlier GMO

debates, around unintended consequences of environmental release. Gene drive technology therefore opens up a new dimension to public engagement initiatives compared to others that have focused on non-replicating insects.

- 5 There may be opportunities to learn from the polarised public debate about GM foods. Some people may express their concerns about GM technology by describing it as ‘unnatural’, meaning they think it is wrong or unacceptable. Ideas about naturalness, and what people mean when they say something is ‘natural’ or ‘unnatural’ are important to consider when thinking about public debate about GM. Some people use the terms ‘nature’, ‘natural’ and ‘unnatural’ in a value-laden way, i.e. to imply that something is wrong or right, acceptable or unacceptable. Within this, our analysis found that people invoke ideas about naturalness to imply a range of different ideas and meanings. Others are sceptical about the existence of any robust distinction between the natural and unnatural, alongside doubts about any link between naturalness and value.
- 6 Our initial findings suggest that there is a danger of people speaking past each other when they talk about naturalness in the context of developments in science and technology. Greater clarity about what people mean when they invoke ideas about naturalness may help the public, policy makers and scientists have more constructive debates about science, technology and medicine. Our report, to be published in November 2015, will set out a range of different ideas about naturalness and how they affect public debates about science, technology and medicine.

*September 2015*

Nuffield Council on Bioethics and Buglife, The Invertebrate Conservation Trust – Oral evidence (QQ 56-64)

**Nuffield Council on Bioethics and Buglife, The Invertebrate Conservation Trust – Oral evidence (QQ 56-64)**

[Transcript to be found under Buglife, The Invertebrate Conservation Trust](#)

## **Oxitec Ltd – Written evidence (GMI0016)**

This document represents written evidence provided by Oxitec Ltd. to the House of Lords Select Committee on Science and Technology Call for Evidence on Genetically Modified Insects. Oxitec was acquired by Intrexon Corporation, an NYSE-listed public company with operations in North America and Europe, in August 2015. Oxitec's primary operations, including its research and development facilities, continue to be based in the United Kingdom.

### **Executive summary**

Specific applications of genetically modified (GM) insect technology have the potential to contribute significantly to global solutions for pest control in public health and agriculture. The UK is already a global research leader in this field but moving forward, benefits will be realised only if there is an enabling policy environment and public acceptance.

[Oxitec](#) Ltd., which originated from Oxford University, is a pioneer in the field. To our knowledge we are the only company in the world producing and distributing GM insects. We have developed a genetic-based approach to controlling pest insect populations, without toxins or pesticides, building on the proven successes of the radiation-based Sterile Insect Technique (SIT) that has been used worldwide for over 50 years. For more than a decade the Oxitec approach has employed tools of modern biotechnology in producing genetically modified (GM) male insects, for use in sterile release programmes. The offspring of these males inherit a self-limiting gene and have no continued presence in the environment, thereby reducing the pest population in a manner targeted exclusively toward the insect species, and avoiding the off-target effects and broad environmental consequences of applying chemical insecticides.

Oxitec's flagship product, a [GM \*Aedes aegypti\* mosquito](#) used in controlling the principle vector of Dengue fever and Chikungunya virus, has received biosafety approval for commercial release in Brazil, and has been evaluated in open release trials in several other countries. In every case the disease vector was reduced by >90%; an unprecedented level of control in comparison to current methods. To date more than 100 million Oxitec mosquitoes have been released worldwide with no reported adverse effects on human health or the environment.

Historically, malaria has been reported in the UK, and *Aedes* mosquitoes have vectored outbreaks of dengue and chikungunya in Europe within the last decade. Climate modelling predicts that insect vectors of human disease could further expand their range in Europe. Therefore the use of self-limiting GM insect technologies to control vectors of human disease could be foreseen in Europe.

On the agricultural side, the use of self-limiting GM insects has enormous potential for controlling damaging pests in a safe and species specific manner. In 2014 the United States Department of Agriculture (USDA) granted an environmental release permit for an Oxitec [Diamondback moth strain](#), and in the same year, the National Biosafety Technical Commission of Brazil (CTNBio) approved a similar release trial for an Oxitec [Medfly strain](#).

These most recent regulatory milestones are allowing Oxitec to build on previous safety data collected in contained conditions and generate additional data in environmental situations that support product safety and demonstrate efficacy. All of this has been accomplished from a small home base in the UK by effectively leveraging partnerships with private and academic collaborators internationally, and funded principally through private investment and various individual, global and domestic funding initiatives.

Moving forward, Integrated Pest Management (IPM) solutions will be instrumental in addressing pest pressures that are mounting in the face of increasingly ineffective chemical controls. IPM solutions have smaller environmental footprints and help to manage resistance in pest populations. The use of self-limiting GM insects is fully compatible with IPM, and is foreseen as playing an integral part of IPM approaches across applications, as well as in some crops, a standalone replacement for chemical controls.

Self-limiting GM insects are not the same as GM crops, which society has politicised in the EU. The majority of commercially available GM crops have been designed with traits for resistance to insect attack or herbicide damage, thus giving them a “fitness” advantage over other varieties. It is the fitness advantage of GM crops which confers an ability to persist in the environment over time. Self-limiting GM insects are the complete opposite, being engineered with the greatest fitness *disadvantage* of all; not being able to reproduce effectively, and are therefore unable to persist in the environment.

Regulation should enable an evaluation of GM insects that is balanced and proportionate whilst maintaining protection for human health and the environment, such that informed decisions can be made about their use. Science-based risk assessment should give foremost consideration to the properties of the final product rather than the technology that underlies its development. Differentiating for example approaches which are expressly designed not to persist in the environment (e.g. self-limiting), from those which have intended persistence as a feature of their design (e.g. population replacement), could significantly streamline the evaluation processes. A balanced and proportionate regulatory approach should also give appropriate consideration to potential benefits as weighed against risks, and potentially the cost of not using the intervention. The European regulatory approach to the oversight of GMOs is focused entirely on evaluating potential risks associated with GM technology, whereas other jurisdictions internationally have embedded mechanisms to balance risk evaluation within the broader context of benefits and alternatives. In informing regulatory approaches, international and regional guidance for risk evaluation, such as that from the World Health Organization (WHO) and the European Food Safety Authority (EFSA), should also consider fundamental differences in the core technologies used in GM insects (e.g. self-limiting vs persistent) as a key parameter in risk evaluation.

As the UK is a leader among knowledge-based economies, with centres of innovation and academic excellence, we have cultivated an environment for investment in science. Informed government policy rightfully accounts for a breadth of civic interests, however, a disproportionate weighting given to pressure groups has the potential to create an innovation and economic void. Large multinational companies have already removed their agricultural biotechnology research outside of the UK and EU because of this climate, and the recent proposed ban in Scotland on GM crop production continues the dangerous

precedent in this regard. It is sincerely hoped that developers of GM insects will not also be driven to leave the UK.

Proportional and balanced consideration of disparate interests is critical and one such mechanism to facilitate this could be an ombudsman role for information accountability; to offer a neutral forum for the independent validation of pressure groups claims so that we may all have access to the facts. Such a mechanism would provide the public with an impartial assessment when questions surrounding the adoption of new technologies enter the public domain.

Given more than a decade of first-hand experience in the field of GM insects for safe and sustainable pest control, we welcome the opportunity to provide written evidence to the House of Lords Select Committee on Science and Technology. We appreciate the need for evidence-based discussion so that the UK is not left behind in understanding, regulating and applying new advances for global health and food security.

**1. Which human diseases, across the world, could be addressed through GM insect technology? Are there any human disease risks in Europe, particularly the UK, for which GM insects are under development?**

i) In the UK insect-borne disease is sometimes considered as a threat affecting predominantly tropical countries. However this is not the case. Invasive mosquito species that carry disease are not new to the UK, and malaria cases have been recorded from Roman times up to the end of the 1<sup>st</sup> World War<sup>83</sup>. History teaches us what happened before can happen again. With global climate change modern records show that invasive species that carry human diseases are gaining footholds in Europe and the UK. The incidences of the disease they carry have also increased concomitantly with the arrival of these insects. Where the insect goes the disease follows.

ii) In the EU there has been a steady increase in invasive mosquitoes. In 2012-13, a Dengue outbreak in Madeira caused more than 2000 local cases, leading to over 80 cases being exported to mainland Europe (Lourenco and Recker, 2014). One of the species that transmits Dengue – the Asian tiger mosquito - has moved as far north as central France. In October 2014, France confirmed 4 cases of locally-acquired Chikungunya in the southern city of Montpellier<sup>84</sup>. Chikungunya had been previously reported as well in the north-east of Italy in 2007, where 217 cases were identified (Liumbruno *et al*, 2008). A recent modelling exercise performed and published in the journal BMC Public Health, in 2014, concluded that there is a significant probability that climate change will open the doors to dengue in mainland Europe (Bouزيد *et al*, 2014).

iii) Being resident in the UK it is sometimes easy to forget that one of the biggest killers on the planet is still infectious disease, and that some of the most important infectious diseases globally are transmitted by a single class of insects, the mosquitoes. Vector-borne diseases<sup>85</sup> account for more than 17% of all infectious diseases, causing more than 1 million deaths

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<sup>83</sup> The history of Malaria in England [http://malaria.wellcome.ac.uk/doc\\_wtd023991.html](http://malaria.wellcome.ac.uk/doc_wtd023991.html)

<sup>84</sup> <http://www.who.int/mediacentre/factsheets/fs327/en/>

<sup>85</sup> Vectors are living organisms that can transmit infectious diseases between humans or from animals to humans. Mosquitoes are the best known disease vector.



annually<sup>86</sup>, a global health challenge which could be addressed by supporting the development and implementation of new tools and solutions. Oxitec technology has proven to be significantly more effective than chemical pesticides alone in controlling mosquito disease carrying vectors<sup>87</sup>, and is based on toxin-free genetic technology that leaves zero chemical residue after applications cease. The Oxitec technology relies on a ‘self-limiting’ gene which means that any insect carrying the gene, or the offspring of male insects released into the environment, are destined to die and do not persist in the environment. This genetic engineering technology is completely different to most GM crops, where the majority have been designed with traits which confer resistance to insect attack or herbicide damage, thus giving them a “fitness” advantage over other varieties. Self-limiting GM insects on the other hand, are given the greatest fitness disadvantage, as they are engineered to die after environmental release and mating. Self-limiting GM insects by nature are less ‘fit’ than their wild pest insect counterparts and are unable to persist in the environment. The core science used in all Oxitec insect applications has been described in many peer-reviewed publications (<http://www.oxitec.com/category/publications/>).

iv) Oxitec has had huge success in controlling the principal mosquito vector of Dengue fever (*Aedes aegypti*), with significant reductions in the target vector mosquito population being seen in all trials to date<sup>3</sup>. Dengue is a serious flu-like disease with complications that can leave long-lasting joint pain or result in haemorrhagic fever and mortality. There is no cure for dengue and the development of effective vaccines has been problematic. The World Health Organization (WHO) estimates<sup>88</sup> around 390,000,000 infections a year of Dengue, and ten-fold more are at risk of infection; half a million of these cases require hospitalisation, of which 2.5% of cases lead to mortality of mainly children.

v) The World Health Organisation (WHO) has classified human diseases that are transmitted by insect vectors. The table below identifies key diseases and their insect vectors that could potentially become invasive and threaten the health of people in the UK (sources; Medlock and Leach 2015; Vaux and Medlock 2015; Bouzid *et al* 2014; ECDC 2014<sup>89</sup>).

| Arthropod vector (Common name) | Arthropod vector (Species) | Disease  |
|--------------------------------|----------------------------|--|
| Mosquito                       | <i>Aedes</i> sp.           | Dengue fever<br>Rift Valley fever<br>Yellow fever<br>Chikungunya<br>Zika virus |
| Mosquito                       | <i>Anopheles</i> sp        | Malaria  |
| Mosquito                       | <i>Culex</i> sp            | Japanese encephalitis<br>Lymphatic filariasis<br>West Nile fever               |
| Sandflies                      | <i>Phlebotomus</i> sp.     | Leishmaniasis<br>Sandfly fever ( phlebotomus fever)                            |

<sup>86</sup> <http://www.who.int/mediacentre/factsheets/fs387/en/>

<sup>87</sup> Examples: Harris *et al* 2012; Carvalho *et al* 2015

<sup>88</sup> WHO dengue fact sheet <http://www.who.int/mediacentre/factsheets/fs117/en/>

<sup>89</sup> [http://ecdc.europa.eu/en/healthtopics/vectors/vector-maps/Pages/VBORNET\\_maps.aspx](http://ecdc.europa.eu/en/healthtopics/vectors/vector-maps/Pages/VBORNET_maps.aspx)

|                 |  |  |
|-----------------|--|--|
| Ticks           |  | Crimean-Congo haemorrhagic fever<br>Lyme disease<br>Relapsing fever (borreliosis)<br>Rickettsial diseases (spotted fever and Q fever)<br>Tick-borne encephalitis<br>Tularaemia |
| Triatomine bugs |  | Chagas disease   |
| Tsetse flies    |  | Sleeping sickness (African trypanosomiasis)  |
| Fleas           |  | Plague<br>Rickettsiosis  |
| Black Flies     |  | Onchocerciasis (river blindness)   |

**2. What are the possible livestock and agricultural crop applications of GM insects across the world? Of current livestock disease risks and agricultural insect pests that could be addressed through GM Insects, which should be the highest priority for Europe?**

i) Modernisation of global agricultural systems has always been dynamic and embraced technological advance. Large-scale mechanization, biological selection, and the use of chemicals have been some of the key drivers of revolutionary change. As challenges with the early generation solutions to agricultural pests arise, such as resistance to chemicals or undesirable effects of residues, we must look to new generations of pest control solutions for continued modernization and effective pest control. The Food and Agriculture Organization (FAO) estimates that global food production must increase by 70% to meet the demands of 9.1 billion people by 2050<sup>90</sup>. Otherwise we are facing serious threats to global food security that if left unmet will have a broad destabilising effect. The challenge of sustainable agriculture is set on a backdrop of less arable land and fresh water with increased pressure from pests and global climate change.

ii) Current pesticide registrations are decreasing due to more stringent oversight of environmental impacts, such as neo-nicotinoids being banned due to concerns about their effects on bee health, while new active ingredients are becoming harder to identify. Insect pests are becoming resistant to applied chemistries, including some biotechnology traits that protect against insects in row crops such as corn, soy and cotton.

iii) Self-limiting GM insect technology for agricultural pests offers an alternative approach to pest control and is especially powerful where those pests are or have become resistant to other crop protection products. Oxitec recently published a paper with lead researchers at Cornell University (Harvey-Samuel *et al*, 2015) demonstrating the effectiveness of GM diamondback moths, carrying the Oxitec self-limiting gene, at both controlling populations, and reducing resistance genes carried in pest populations (in this instance against a pest moth that causes \$4-5bn in damages and control costs every year for crops such as canola, rape, broccoli, cabbage, and other brassicas in the UK and around the world). Oxitec’s core technology is transferable to any insect pest that has the following characteristics:

<sup>90</sup>[http://www.fao.org/fileadmin/templates/wsfs/docs/expert\\_paper/How\\_to\\_Feed\\_the\\_World\\_in\\_2050.pdf](http://www.fao.org/fileadmin/templates/wsfs/docs/expert_paper/How_to_Feed_the_World_in_2050.pdf)

- o Sexual reproduction
- o Ability to rear the insects in rearing facilities
- o Ability to genetically transform the insect
- o Simple lifecycle with non-damaging males (ideally)

These characteristics are present in many of the most significant global pests of agriculture. In Europe, agriculture is under a heavy burden from invasive and local insect species that are difficult to control with pesticides, where application is limited by label instructions driven by maximum residue limits, and of course where de-registrations are driven by health and environmental considerations.

iv) Oxitec has demonstrated solutions for a number of these pests including the olive fly which has devastated the olive growers in Europe<sup>91</sup>, the Mediterranean fruit fly which is considered the world's most damaging fruit pest, and *Drosophila suzukii* (spotted wing drosophila) which is now affecting soft fruit growers in the UK. This pest was inadvertently introduced to Europe in 2009 and now threatens a £1.8 billion UK industry including strawberries and raspberries<sup>92 93</sup>.

v) In livestock, GM insects (and other arthropods) could be effective in controlling a range of vector-borne diseases, including tsetse fly-vectored trypanosomiasis in cattle (and humans), and brown ear tick-borne *Theileria parva* (which kills >1 million cattle per annum in Africa<sup>94</sup>). The house fly, *Musca domestica*, is a nuisance and pathogen-transmitting pest of livestock around the world, estimated to cause US \$375 million per annum in agricultural losses in the US alone (Geden and Hogsette, 2001). The stable fly, *Stomoxys calcitrans*, is a painful biter of cattle and other animals, compromising animal welfare and causing very significant losses in cattle farming (US \$2.2 billion in the US) (Taylor *et al* 2012).

vi) In Europe, house fly and stable fly are significant and difficult-to-control pests and the self-limiting GM insect approach could provide an effective management solution. In addition, midge-borne viruses – most notably bluetongue virus – have emerged in Europe in recent years, and represent a significant threat to livestock production across Europe, including the UK<sup>95</sup>.

### **3. Are there likely to be opportunities provided by GM insects that cannot be provided by other approaches, such as biological control methods? How could GM insect approaches be complementary to existing Integrated Pest Management (IPM) programmes?**

i) Biological control is principally deployed commercially in smaller scale and protected horticulture, and in the home gardening sector; biological alternatives are currently lacking for major applications<sup>96</sup>. Establishing parameters, such as balancing the population of the biological control agent and pest population can be difficult, and the costs of rearing

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<sup>91</sup> <http://www.nytimes.com/2014/12/04/world/europe/amid-bugs-hail-floods-and-bacteria-italian-olives-take-a-beating.html>

<sup>92</sup> <http://www.cabi.org/isc/datasheet/109283> (describes *D. suzukii*)

<sup>93</sup> [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/141608/hort-report-31jul13.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/141608/hort-report-31jul13.pdf) (UK horticulture report showing UK soft fruit industry)

<sup>94</sup> <http://www.parasitesandvectors.com/content/7/1/91>

<sup>95</sup> <http://rstb.royalsocietypublishing.org/content/364/1530/2669#sec-3>

<sup>96</sup> <http://www.biocomes.eu/biological-control/>

biological control agents are often high as well. Self-limiting GM insects in mass release programmes analogous to the Sterile Insect Technique (SIT) (Dyke, 2005), offer species-specific, environmentally sustainable pest management that can dramatically reduce the pest population far below the levels of control seen with other biological control methods. Self-limiting approaches, such as provided by Oxitec, have been demonstrated as extremely efficacious at reducing pest populations to very low levels. Oxitec’s approach is complementary with other pest control strategies in the context of Integrated Pest Management (IPM), or Integrated Vector Management (IVM) approaches, and the economics of combination approaches are likely to be favourable according to Oxitec in-house models. The use of self-limiting GM insects offers a unique ability to manage, reduce and potentially eliminate insects that carry pesticide resistance genes, extending the longevity of chemical controls.

ii) In addition to the potential to control insect pest species already present in an area, including invasive environmental species beyond agriculture and public health applications, self-limiting GM insects could be used in programmes to prevent new incursions of invasive insect species. At its core, the functionality of the system relies on the universal mate-seeking behaviour of male insects. The potential to hold in readiness, self-limiting GM insects of species which pose a risk of invasive entry, for scale up to control potential infestations, or to establish control barriers<sup>97</sup> represents an opportunity that cannot easily be realised with current controls or biological organisms. Invasive species can be itinerant in nature and having a self-limiting GM insect as a control measure against incursions, especially when it is at low levels, could help protect the UK from potential phytosanitary and zoonotic pest incursions. Currently there may be significant public, regulatory and technical issues in testing and registering a GM insect to control a pest that is not already present in the country.

#### **4. How appropriate are current EU and UK GMOs regulatory frameworks in addressing the issues raised by GM Insects? Are there lessons to be learnt from the regulation of GM insects in other countries such as Brazil?**

i) The EU GMO regulatory frameworks and UK implementing regulations cover both contained use (effectively limited to use in physical structures) and deliberate release of all GMO’s and therefore have a broad remit. For the purposes of contained use the regulations work well in the UK, with centres involved in genetic modification being registered by the Health and Safety Executive (HSE) and inspected periodically. There are further additional requirements under UK phytosanitary and animal disease protection legislation that have to be complied with for the genetic modification of plant and animal disease vectors. One such example is the requirement for mosquitoes to be registered under the Importation of Animal Pathogens Order, 1980 as they are “potential” vectors of animal disease, even if they are imported to the country as dead specimens. This appears to be anti-intuitive and requires significant compliance resourcing as each transfer of specimens has to receive permission from the Secretary of State.

ii) The deliberate release and “placing on the market” EC Directive 2001/18 is not fit for purpose i.e.; ensuring potential adverse effects on human health and the environment from

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<sup>97</sup> Example: A permanent barrier of sterile new world screw-worm (radiation based) is maintained over eastern Panama to protect pest free areas to the north <http://www-naweb.iaea.org/nafa/ipc/screwworm-flies.html>

genetically modified organisms are accurately assessed. Directive 2001/18/EC on the deliberate release into the environment of genetically modified organisms has been shaped predominantly by experiences of GM crop assessment and the politicisation of the process has led to dramatically increased data requirements. As can be seen from the EFSA Guidance document on GM animals this thinking is already spilling over to GM insects. Consequently any potential regulation for the use of GM insects at the EU level is currently likely to be prohibitively expensive, protracted, unpredictable and so resource intensive that any developers are unlikely to try such a registration. The current regulatory framework is therefore neither enabling nor proportionate for GMO's and especially not for GM insects that are expressly designed not to persist in the environment (self-limiting applications). Not only is the regulation itself not enabling it sends a negative message to the rest of the world that has less experience – “ if this can't be regulated in the EU, how are we supposed to do it? “

iii) GM insects are being developed, and have received approvals for commercial scale use (e.g. self-limiting GM mosquitos in Brazil) for the control of mosquito vectors of human disease where existing controls are failing to provide adequate protection to human health. These applications, were they to undergo evaluation in the EU would require a focus on vanishingly small potential risks, exclusive of potential benefits, as the current regulatory framework only allows consideration of potential risk scenarios. The utility of a risk/benefit analysis has been identified as well by the Advisory Committee on Releases to the Environment (2013) in their input to the EFSA consultation on guidance on the environmental risk assessment of genetically modified animals. Other health products are assessed on a risk-benefit balance in the EU; something missing from the EU and the UK systems for GMO's. The use of a risk/benefit framework in regulation of GM insects could facilitate a rational debate and proportionate analysis of risk.

iv) There are unmet needs in agriculture and horticulture as well for which self-limiting GM insects are being developed, such as for control of the massively destructive olive fruit fly (see Section 2). Even in light of the enormous impact olive fly had on European olive producers in 2014<sup>98</sup>, a recent application to Spain for a self-limiting GM olive fly was required to be withdrawn as the costs of confinement of the trial were prohibitive.

v) One of the principle benefits of self-limiting GM insect biocontrol is that it is species specific and only targets the pest of interest thereby avoiding the off-target effects and broad environmental consequences of applying chemical insecticides. The focus of the EU legislation fails to take into account these potential environmental benefits, when obvious synergies exist with other EU legislation. The Sustainable Use Directive (2009/128/EC) specifically requires farmers and horticulturalists to reduce their environmental reliance on chemical controls and develop Integrated Pest Management (IPM) alternatives. The Department for Environment, Food and Rural Affairs- Chemicals Regulation Directorate (DEFRA/CRD) have a major R&D programme that helps promote IPM <sup>99</sup>, however as CRD regulates pesticides and certain biological control agents but not GM insects, there is no coordinated approach to considering how non-chemical GM insect biocontrol agents could

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<sup>98</sup> <http://www.nytimes.com/2014/12/04/world/europe/amid-bugs-hail-floods-and-bacteria-italian-olives-take-a-beating.html>

<sup>99</sup> <http://randd.defra.gov.uk> (search using 'Integrated' keyword)

be integrated into sustainable agriculture approaches. Lessons should be learnt from the regulation of biological control organisms as the use of self-limiting GM insects in sterile release programmes is effectively analogous to releasing a biological control organism into the environment (e.g. Mumford 2012). Instead developers of new approaches to pest control, such as the use of self-limiting GM insects, are hampered by the large data requirements and a lack of risk/benefit proportionality, a result of the current focus on the GM aspect (i.e. the development process) of the product in the current EU regulatory framework. Another way of considering this is that the product itself should be regulated on the basis of its characteristics, and not the process (GM) of making the product.

vi) In the exportation of GM insects out of the EU, for example to collaborative international partners, the implementation of the transboundary movement regulation (TBM) 1946/2003 is a further burden to UK business. This is not because the intent of the regulation is undesirable; it is important that importing countries know that a GMO is being brought into their country for deliberate release, but this regulation has been based on requirements for trade in commodity goods and ensuing trade tariffs. Any import of a GM insect for field release or commerce already requires the relevant permits from the importing country prior to shipment– to require the exporter to also supply largely the same information to the same authorities again in a different format, is not only redundant and burdensome, but also confusing to the importing agencies as they receive this information twice in different formats. To implement the transboundary movement regulations in the UK and the EU it should simply be sufficient to notify authorities with the relevant import and field release permits received from the importing country as part of the TBM notification. This achieves the goal of the TBM regulations of advance informed consent, prevents confusion of the authorities and streamlines operations within business and government.

vii) Lessons learnt from others;

Globally, there are gaps and overlaps in approaches to the regulatory oversight of GM insects, as well as useful precedents from which perspective may be gained.

- Regulatory uncertainty, i.e. where governments need to pause for thought on how to regulate GM insects due to lack of precedent, provides a vacuum that is frequently exploited by pressure groups whose opposition to GM technologies does not appear to be science-based. The process of regulatory evaluation as the gatekeeper should be respected and the outcome honoured; a good example is the Australian regulatory system.
- Considerable uncertainty and delay can be added to the process as it is not always clear which legislative frameworks apply to GM insects. GM insect targets are principally pest insects, some of which are subject to plant and animal quarantine actions, resulting in a complex mosaic of sometimes conflicting requirements. This has been especially challenging with GM mosquitoes as opposed to agricultural pests, as there are frequently multiple agencies operating under different legal jurisdictions, and experience has shown that submitting an application is sometimes the most effective means to clarify the regulatory pathway. For agricultural pests, Oxitec encountered this in Spain, where the authorities took over 6 months to determine if they had the legal jurisdiction under the 2001/18/EC regulation to handle applications for GM olive fly. In Brazil a clear regulatory framework, based on

plausible scientific pathways to harm and subsequent evaluation allowed the assessment of the dossier for commercial release in approximately 9 months from submission to approval.

- It is frequently forgotten that unlike crop plants, target insects for GM approaches in pest control scenarios are, in their wild form, generally harmful to human or animal health, or agriculture, or are not environmentally neutral, invading from other countries and displacing native species. They are often already subject to controls using chemical, biological or other means. Consequently evaluation should consider a comparison to existing control measures, and additionally, the cost of taking no action. A good example of this is from the USA, where under the National Environmental Policy Act, agencies are required to issue an Environmental Assessment that takes into consideration the alternatives available alongside the GMO application. In an example, if GM mosquitoes were to be used in a sterile release based control program then they could be assessed against the current chemical controls (which are more damaging to beneficial insects and less effective on the target pest), as well as the availability (or lack) of therapeutic interventions such as vaccines. Comment periods for applications, would then provide the opportunity for public input to regulatory authorities based on a balanced presentation of risk data, as well as benefit scenarios. This was also a consideration in Brazil for the use of a GM mosquito (*Aedes aegypti* OX513A), where dengue fever is endemic and new solutions are urgently sought due to the increasing ineffectiveness of chemical control methodologies.
- GM insect biological control agents, such as those developed for population control in agricultural applications, could conceivably, depending on the specific design of the insect, result in low level presence of non-viable GM material on a small proportion of the harvested crop. Although regulatory tolerances for insect damage in product destined for both the fresh market and for processing are almost always in place, and buyer specifications in some cases may exceed regulatory tolerances, these tolerances are often not zero, and the low level presence of residual GM insect material may pose a challenge for food safety regulators. The US-FDA has in place the Early Food Safety Evaluation System for New Non-Pesticidal Proteins Produced by New Plant Varieties Intended for Food Use<sup>100</sup>. This system allows a prior food safety evaluation for GM crops in field trials under regulatory permit, such that any inadvertent traces in product destined for consumption, triggers a balanced regulatory response in light of a previously evaluated risk to human health. Such an approach to the evaluation of GM insects for use in agricultural pest control applications could be appropriate, especially at the early trial stage, as the potential for excessively damaging regulatory actions (product recalls, trade barriers) exists when food safety aspects remain unassessed and unapproved GM events enter the food supply. This may also require a change in legislation in the EU as the current threshold for tolerance of unapproved events is zero; not a biologically relevant parameter either.

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<sup>100</sup><http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/Biotechnology/ucm096156.htm#scope>



**5. Do the World Health Organisation (WHO) guidelines on the release of GM mosquitoes provide the basis of an effective regulatory framework? How should issues regarding the emergence of resistance be considered?**

i) The WHO guidelines on the release of GM mosquitoes (GMM) issued in 2014 have had a long and thoughtful gestation from a broad group of scientists skilled in various fields. They aim to support informed and thoughtful development processes drawing on evidence from other public health applications such as insecticides, vaccines and other tools including biocontrol methods and agricultural practices. Whilst they draw on these aspects they also include public engagement and transparency needs during the research. Several key aspects in the document are welcomed:

- the recognition of the enormous global health burden that mosquito borne diseases cause;
- the framing of the testing evaluation to be considered on a case by case basis;
- risk-benefit analysis being a forefront consideration for decision making;
- the recognition of national sovereignty in decision making; and,
- the recognition that self-limiting technologies carry lower risks than those of modified mosquitoes incorporating gene drives and intending to be self-perpetuating.

However there are several aspects to the guidelines that could potentially hinder the implementation of mosquito control programmes using self-limiting GM technologies were it to be used alone as a basis of a regulatory system.

ii) The guidance document could be interpreted as a potential checklist for regulatory authorities. Each country/regulatory jurisdiction could consider that each step has to be conducted entirely independently, in the local context, without referring to data generated in other countries. The purpose of generating data is predominantly to identify whether the genetic insert has resulted in unintended or adverse changes linked to the endpoints in the risk assessment. Redundancy in data generation does not increase the knowledge base on safety and adds expense, complexity and time to the potential deployment of these valuable innovations, especially as funding sources for GM mosquitoes are predominantly either philanthropic or venture capital based. One of the stated aims of the guidance was to provide consistency for regulators and users developing data, therefore data generated in one country should be portable (i.e. accepted by other countries). The need to use the WHO guidance as a framework in its entirety through Phase 1 – Phase 4 has in fact already been suggested by some countries with which Oxitec is working, despite having sufficient data on the potential for unintended and adverse changes to achieve commercial biosafety registration in another country, and that evaluation being available publically in the Biosafety Clearing House<sup>101</sup> of the Biosafety Protocol to the Convention on Biological Diversity.

iii) Although the principle that self-limiting GM mosquitoes present less risk than self-sustaining applications is sprinkled throughout the WHO guidelines, it is not clearly articulated that the two approaches should have fundamentally different considerations when evaluating risk. There are already robust risk mitigation options for self-limiting

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<sup>101</sup> Example for Oxitec OX513A in Brazil <https://bch.cbd.int/database/record.shtml?documentid=105833>



approaches including halting releases or using conventional vector control methods, and not all risk considerations are universally relevant to all GM mosquitoes. There is an implicit risk of over burdening these technologies with this guidance, as the separation of self-limiting and self-sustaining requirements not clearly delimited. There is also an overemphasis on the measurement of disease outcomes for self-sustaining technologies; the control of the vector, the mosquito itself, should be considered a positive driver for the use of these technologies at a wider scale without having to demonstrate epidemiological outcomes. No insecticide has to demonstrate an epidemiological outcome to obtain registration for wide-spread use.

iv) Overall, although probably not the intention, the WHO guidance document appears to present a restrictive, overly prescriptive, set of conditions for the analysis of GM mosquitoes that could load inappropriate testing burdens for certain applications (e.g. self-limiting technologies) as mentioned in the points above. Consequently meeting the requirements if taken in their entirety is unlikely to be affordable by either private or public entities that seek to conduct work in this area, thereby hindering the adoption of innovative solutions so desperately needed in the fight against devastating mosquito borne diseases.

#### **How should issues regarding the emergence of resistance be considered?**

vi) For self-limiting technologies one way of dealing with the emergence of resistance could be to address this at the level of mass-rearing and production. A robust quality management system that allows the continual assessment and improvement of quality to ensure product specifications (and therefore the customers' expectations) are consistent is desirable and may be required by regulators. This has already been instigated and implemented at Oxitec. Insect product lines are routinely checked against known baselines for the genotype and the phenotype as well as mating competitiveness. Deviations from the baselines are investigated, corrected where necessary and concluded. The quality system includes: in-process and laboratory quality controls, non-conformance control, equipment control, control of documents and records, change controls, staff training, and post-market surveillance methodologies which are audited both internally and externally. Therefore Oxitec is confident that product going out of the factory door meets quality standards and customer expectations. Furthermore as adaptive management of insect numbers and ongoing product assessment is part of product application in vector control programmes, any deviations in product performance could be readily identified and inform future actions.

#### **6. Do the European Food Safety Authority (EFSA) guidelines on the environmental risk assessment of GM Insects for commercial use sufficiently address the different risks from population suppression and population replacement approaches?**

##### **How should the ecological risks and human benefits that might arise from the application of gene drive techniques to population replacement approaches be assessed?**

i) The EFSA guidance on the environmental risk assessment of genetically modified insects has been developed as a tool to direct assessment activities under the legislative authorities of 1829/2003 EC on genetically modified food and feed, and 2001/18 EC on the deliberate release into the environment of genetically modified organisms. The risk assessment criteria thus elaborated in the EFSA guidance necessarily aligns with a regulatory framework which in itself may be less appropriate for certain GM insect applications, such as self-limiting approaches vs persistent population replacement (discussed in question 4 response).

ii) The EFSA guidance is evidently borne out of the decades of extensive experience regulators have gained from the assessment of GM plants, and resembles EFSA plant guidance (EFSA 2010) in both its specific areas of risk, and in process. Across the guidance document the established and tested GM-crop centric approach to defining areas of risk is consistently apparent at its core. Whilst this is convenient for regulators and allows some consistency at the agency, the use of such a framework to define risk assessment criteria for GM insects is a force fit; requiring that GM insects categorically be evaluated across seven specific areas of risk without consideration given to the final traits or characteristics manifested in the GM insect.

iii) In recent years, regulatory approvals have been secured globally (Brazil, Cayman Islands, Malaysia, and Panama) to allow evaluation of GM mosquitoes, which are self-limiting in the environment, in population suppression programs. We believe these applications demonstrate significant promise in addressing global health challenges posed by mosquito borne diseases, with consistent suppression of target mosquito populations in all trials to date (e.g Harris *et al* 2012, Carvalho *et al* 2015, additional data pending publication). Multiple agricultural applications for pest suppression approaches using the same core technology are ready for field evaluation, and regulatory approvals for field trials have been secured (USA - Diamondback Moth, Pink Bollworm; Brazil- Medfly). These pest population suppression approaches depend on mass rearing and continued release of insects engineered expressly not to produce viable progeny, nor persist in the environment. This method is essentially an adaptation of the Sterile Insect Technique (SIT), which uses radiation induced sterility and has proven efficacious in both population control and eradication programs for well over 50 years (Dyck *et al* 2005). This highlights the fundamental difference between population suppression approaches using mass reared genetically “sterile” insects, and population replacement approaches. The basis of genetic approaches to sterile insect release is engineered lethality, whereby insects are designed expressly not to persist in the environment, and require sustained releases in the context of a population control program; they are effectively “self-limiting” in the environment by design. Population replacement approaches seek to achieve the opposite result, that is, engineered environmental persistence. These fundamentally different approaches are entirely divergent in terms of the intended environmental fate of released insects, and the EFSA guidance does not recognize this in establishing the direction and ensuing evaluative criteria for the environmental risk assessment. Approaches to risk assessment in the regulatory context would best consider at the outset, the intended environmental fate of released insects and whether the engineered traits are manifested to achieve that intended outcome. Approaches from the assessment of biological control organisms could also be considered.

iv) Population replacement approaches have the intended endpoint of environmental persistence as a feature of their design and they should necessarily be subject to an environmental risk assessment approach having greater focus on areas of risk regarding environmental persistence of the GM insect. Across the defined areas of risk in the EFSA guidance, exposure in all risk areas should be evaluated with primary consideration given to the temporal backdrop when evaluating population replacement approaches. Population replacement strategies result in potentially indefinite exposure of the environment to the

introduced GM insect, where-as population suppression strategies using self-limiting genetic approaches generally result in transient exposure scenarios measurable in timeframes of days. As environmental persistence is an intended trait in population replacement strategies, resulting in prolonged exposure to the environment, the specific areas of persistence and invasiveness, and the interactions of the GM insect with non-target organisms, should require rigorous assessment over appropriate timescales.

v) At its core, population suppression technologies using sterile GM insect (i.e. self-limiting) approaches depend on the capacity of released male insects to a) mate with wild female insects, and b) pass on traits such that progeny are not produced or do not survive. Male GM insects used in current self-limiting approaches are not associated with vectoring disease, as in the case of mosquito applications (i.e. males do not bite), nor are they associated with crop damage in agricultural applications as it generally female oviposition, or egg laying, and subsequent larval development which results in crop damage. In evaluating solutions to insect pest pressures in the face of alternatives, the male release strategy employed in self-limiting GM insect approaches has an evident advantage as the males do not cause damage, yet the mechanism does not exist in the EFSA guidance to give this appropriate weight. Population replacement strategies using both male and female release need to be more rigorously assessed in regard to the environmental persistence of females, and risk weighed in the face of alternative approaches.

vi) Insect pests present significant challenges to both public health and agriculture, and promising solutions using self-limiting GM insects in release programs similar to proven SIT approaches are now available or well in the development pipeline. These solutions will be slow to positively contribute to public health outcomes and benefit agricultural and stakeholders if inflexible approaches to regulatory oversight in the context of risk assessment are not broadly examined with an eye for reform. Government policy makers and regulators must recognise that fully embracing solutions which can contribute to achieving broader government policy objectives in the areas of public health and agriculture requires adaptive approaches to regulatory oversight in risk assessment.

### **7. How is research into the development of GM insects currently funded? Are there opportunities to attract more private investment into this area?**

i) In comparison to the benefits that GM insects may bring, and the clear scientific lead that the UK has in this area, UK funding for research into this area has been very low in the UK, and vanishingly scarce for translational capability for development from laboratory to market. The main developments have been funded through the Grand Challenges in Global Health programme (funded by the Gates Foundation and others) and private investment. In our experience a small amount of early stage funding has been invested by the BBSRC and Wellcome Trust. Some grant funding has also been provided by the Technology Strategy Board (now Innovate UK), but the benefit can be substantially eroded for an SME as they lose the Research and Development tax credit on all grant related activity regardless of the level of grant funding. Overwhelmingly the majority of funding tends to be for early stage research and is extremely limited for translational activities. The consequence of this is a lack of funding leverage comfort in the eyes of investors. Further the lack of such funding bears testament to a politicised environment around GM activities in the UK/EU (especially where those developments are coming from the private sector), and this is a powerful

disincentive to fund activities in the UK/EU despite the UK having a scientific, entrepreneurial and operational competitive advantage.

ii) From an Oxitec perspective the vast majority of funding for R&D in this field has come from private sources and specifically includes high net worth individuals with international exposure who appreciate the dire need for new solutions to mosquito borne diseases and the limitations of a continued reliance on an increasing narrow range of chemical insecticides. The other main avenue is the Gates Foundation who have funded several programmes in this area within the framework of their objective of reducing the burden of malaria.

iii) There are many challenges for getting a new science application off the ground to benefit as many people as possible. Many years of funding are required before proof of concept is achieved. While there is a similar funding pathway to, say, health biotech companies the sheer novelty of the GM insect approach and the lack of benchmarks will put off many commercial investors. In Oxitec's case the primary initial funders were individuals and entities with a very strong social motive as well as a desire to earn a financial return. Even now that the company is realizing commercial scale biosafety approval, it took a company like Intrexon Corporation, a US based enterprise with both significant financial resources and a singular forward-looking vision for the planet, to secure Oxitec's ability to move these technologies forward.

iv) The major challenge here is that in Europe, society has allowed GM technology to become highly politicised in spite of the clear benefits the technology can bring. This politicisation of a technology genre means that any private investor must be prepared to lose their investment as the main barriers to advancement are not based around scientific, market need, economics or regulatory barriers but instead are political. Once political risk is added to the myriad of other challenges then new ventures become almost impossible to fund unless there is an overwhelming social conviction as to the importance of the technology from its investors. An example of the politicisation of this technology could be seen recently in the announcement of the proposed Scottish ban on GM<sup>102</sup>. What investor will invest in an area when multiple years of funding can be swept away in a single political statement?

v) However, the clear example of Oxitec hopefully will show entrepreneurs and investors that technical commercial and investor success can be gained in this area and it is to be hoped that new initiatives will come forth and the Oxitec benchmark will facilitate investment.

**8. Given the possible public health benefits of GM insects, should the Government be funding their commercialisation? Would this result in a conflict of interest with regard to regulation of releases? If so, how might this be managed?**

i) In our view Government and the UK would benefit from helping to fund commercialisation for a number of reasons;

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<sup>102</sup> <http://news.scotland.gov.uk/News/GM-crop-ban-1bd2.aspx>

- To keep a lead in a new technology area for the benefits of British science and the economy as a whole;
- to build capacity for combatting the likely health threat to mainland UK from invasive species as rising temperatures bring these species to the UK; and,
- to support public health of Britons and indeed others, in British overseas territories, which rely on tourism as the primary source of income.

ii) Britain is a knowledge-based economy with exceptional strengths in life sciences. We should support new technologies as they emerge to ensure British science gains a leadership position. Otherwise key leading positions (for example agricultural biotechnology, stem cell research, GM insects) will all be lost. Private investment cannot be relied on to bring these technologies through especially where there is a political dimension. In these areas it is society's failing that has allowed an un-level playing field so Government should assist to level it up.

iii) There is no conflict with regulation. Regulation should focus on the proportionate evaluation of safety and environmental aspects of a new product and equally consider the relevant risks and benefits. The UK can lead here too ensuring that the regulatory process that is developed is fit for purpose and proportionate. Developing a commercial proposition for the technology in a foreign country is doubly difficult if it is not supported in the home country.

iv) Just as we rely on Government to both regulate and fund public health care, Government may be involved in these different areas for GM insects and other services created for the public good.

### **9. How could the UK benefit economically from both developing GM Insect technology and its use within the UK?**

i) Britain can benefit from the direct economic returns in:

- Jobs;
- inward investment;
- exports;
- taxes; and,
- royalties for IP,

but it can also benefit from being recognised as a country that promotes both businesses and science and creates a climate for their development. At the moment Britain is renowned for invention and entrepreneurial flair but equally for underfunding of key technologies, a sensationalist media and ultimately selling our assets cheap abroad and losing out on the value created. There has to be a very positive policy to prevent this from happening.

ii) At the moment Britain, compared to other countries, does not have a major imminent health threat from invasive species, but it is likely to arrive as insects adapt to more temperate environments and as temperatures rise, providing more opportunities for incursion. The Asian Tiger mosquito is a threat that is now causing a major health concern in France for example. By developing the capacity to address such eventualities they will be available to help if and when needed.

**10. How can the gap between regulatory approaches and public concerns over GMOs be addressed? Is there a role for ‘responsible innovation’ approaches? What are the critical factors in effective public engagement from lab to final release?**

i) Firstly, we need to distinguish between actual genuine public concerns and pressure group political activities. There is very little evidence of any public concern in the UK over GM insects and the overwhelming majority of independent media coverage is positive. It is possible to find pressure group publicity and some sensationalist tabloid coverage but this is the exception. Looked at objectively, GM insects are being used to protect people from mosquito borne diseases, have the potential to reduce pesticide use, and contribute to sustainable agriculture. These are objectives that chime with public sentiment.

ii) The critical factor for any academic institution or company bringing forward a new technology is transparency and an ability to communicate with not only the science community but also with a broad stakeholder community such as politicians, media, local communities etc. The Science and Media Centre, has helped to ensure that science-based stories are reported accurately in the media by facilitating access to high-quality independent scientific experts relevant to the story. This initiative should be strengthened and broadened by Government as they play a critical role in UK society.

iii) Society sets up independent evaluation mechanisms primarily through the regulatory process to ensure that any innovation is developed through a step by step process where each new step is preceded by the requisite level of data and proof to warrant the next step. Where risk management decisions are taken by political entities, this politicises the process. We should be careful not to develop new processes such as oversight for “responsible innovation” which create another level of bureaucracy, potentially stifling innovation. Also, we should ensure that the processes in place should enable participation by smaller, resource-limited developers and companies. If we over-regulate we alienate entrepreneurial innovation and value creation.

iv) Given that new technologies such as GM insects are likely to emanate from small companies with few resources rather than from large multinationals, the UK should consider a mechanism to provide a balanced perspective when pressure groups put information into the public domain and make claims as to its scientific validity. Proponents of a new technology such as GM insects are subject to rigorous oversight by regulators, as well as scrutiny in the public domain; mechanisms to hold pressure groups accountable are needed to provide balance. In short, there are mechanisms in place that hold companies responsible and accountable - we need a mechanism to provide a similar accountability for pressure groups.

Perhaps the UK should consider a ‘science information ombudsman’ that could evaluate, from an independent perspective, pressure groups claims and go on record as to their veracity. The UK is a knowledge based economy with great expertise in life sciences - if the public loses faith in science it will be to the great detriment of our economy.

*18 September 2015*

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Oxitec Limited, Advisory Committee on Releases to the Environment (ACRE), and Dr Jeremy Sweet, Sweet Environmental Consultants – Oral evidence (QQ 26-38)

**Oxitec Limited, Advisory Committee on Releases to the Environment (ACRE), and Dr Jeremy Sweet, Sweet Environmental Consultants – Oral evidence (QQ 26-38)**

[Transcript to be found under Advisory Committee on Releases to the Environment \(ACRE\)](#)

## **Oxitec Ltd – Supplementary written evidence (GMI0029)**

This document represents supplemental written evidence provided by Oxitec Ltd to the House of Lords Select Committee on Science and Technology Call for Evidence on Genetically Modified Insects following the Oral Evidence Sessions of Tuesday October 20<sup>th</sup> with Witness(es): Professor Rosemary Hails, Chair, Advisory Committee on Releases to the Environment (ACRE); Dr Jeremy Sweet, Environmental Consultant, Sweet Environmental Consultants and Ms Camilla Beech, Head of Regulatory Affairs, Oxitec Limited

[Oxitec](#) was acquired by [Intrexon](#) Corporation (NYSE: XON), an NYSE-listed public company with operations in North America and Europe, in August 2015. Oxitec's primary operations, including its research and development facilities, continue to be based in the United Kingdom.

While there was an appreciation in the oral evidence session that the evaluation of the potential benefits of a GM insect application in addition to the assessment of potential risks to human health and the environment may be warranted in the decision making process, further considerations are noted below in this regard.

- A product-based approach to regulation is ideal, focusing on the traits of the final product rather than the process of development, specifically focusing on the novelty of the product as the regulatory trigger.
- As in the case of Brazil, USA, Canada, and Australia, among others, the technical evidence based scientific review of an application with regards to biosafety risk assessment should remain entirely independent of socioeconomic and economic risk or benefit assessment or political influence. Decisions made in this regard, on the basis of biosafety assessment should stand on their own scientific merit. The process should encourage a transparent dialogue between regulated parties and risk assessors thus facilitating a more predictable regulatory environment in terms of timelines and data requirements, and enable greater transparency in the process with respect to the public domain.
- Clearly articulated protection goals for environmental and human health would enable the development of measurement endpoints for which data could be generated to support risk assessment (i.e. what specific elements of the environment and human health does the regulatory system aim to protect)
- Socioeconomic and economic risk and benefits should be considered outside the scope of the biosafety assessment itself and be given consideration through other mechanisms in the overall decision making process.
- Policy considerations and ethical considerations of member states, should

be clearly articulated through a distinct mechanism at length from risk assessment to as to disable the possibility of shrouding political motivations with technical justifications (e.g. overstating environmental risk as a means to achieve politically motivated outcomes does not promote transparent evidence based scientific processes).

In the evaluation of benefits:

- Mechanisms should be established to ensure consideration is given to how GM insect applications may contribute to key objectives established in other EC directives, for example:
  - *Directive 2009/128/EC establishing a framework for Community action to achieve the sustainable use of pesticides* mandates Member States to take all necessary measures to promote low pesticide-input pest management, giving wherever possible priority to non- chemical methods.
  - *528/1999 EC laying down measures to improve the quality of olive oil production*, where- by in taking action against the Olive fly, it is required that special emphasis shall be placed on integrated biological control methods.
- Consideration should be given to how GM insect applications may be integrated into established EU, Member State or UK strategies in areas such as invasive species control or integrated pest management for example.
- Benefits should be assessed with respect to the potential to contribute to key objectives of international organisations for example the World Health Organisation (WHO) in the area of vector management for neglected tropical diseases, where-by a stated objective is *“To increase access to less hazardous and cost-effective tools and technologies for vector control, including pesticides”*

*On concerns raised about political influence in the regulatory process and mechanisms for public opinion/inputs.*

- European regulatory policy inherently accords civic interests a significant weight in the policy process, while interpretation of the precautionary principle in EU regulatory policy has effectively resulted in a lowest common denominator amongst member states for risk tolerance, that is, a disproportionately low threshold for risk compared to other international jurisdictions. Together these factors make the ground ripe for pressure groups to exert an undue influence on decision making in member states and the Commission.
- Political influence may be based on assumptions about overall public opinion being based on the loudest voices. While the dissenting voices are well organised, and networked, the average citizen does not have a forum for asking their questions, getting unbiased answers, and communicating

their values. Oxitec welcomes dialogue with all stakeholders and have taken all opportunities to conduct this interchange (door to door, broadcast, print and social media etc.) and to be as transparent as possible.

*30 October 2015*

## **Oxitec Ltd – Further supplementary written evidence (GMI0033)**

### **Case study of the Oxitec Olive fly application in Spain 2012-2015**

The olive fruit fly (*Bactrocera oleae*) is considered the most important pest of cultivated olives<sup>103</sup>. Infested table olives are not marketable, and the quality of olive oil is compromised due to the acidity imparted to the product by damaged fruit. Across the olive industry overall, there are thus very low tolerances for olive fly damaged fruit. The biology of the olive fly makes it an ideal candidate for a population suppression approach based on the release of sterile males (i.e. SIT analogous approaches). Preliminary market research revealed olive producers were very receptive to new solutions, subject to regulatory clearances, thus Oxitec Ltd invested significant resource in developing a candidate olive fly strain for evaluation in a suppression program. The Oxitec olive fly contains a self-limiting gene which means that it cannot establish itself in the environment and a colour marker gene to allow them to be easily distinguished from the pest insect.

Subsequent to preliminary studies under contained conditions, late in 2012 Oxitec made a regulatory submission to the Biosecurity Commission of the autonomous region of Catalonia (within the Generalitat de Catalunya-GENCAT) for a trial to be conducted outdoors within a netted enclosure. This application was made under the deliberate release regulations (Part B of 2001/18 EC). For an application under 2001/18/EC, the Spanish National Biosafety Commission (NBC) undertakes a biosafety review and advises GENCAT, whom then may take an autonomous decision on the application. The NBC identified two key areas in the 2012 submission for which they required additional data to inform a decision: further characterisation of the expression of the self-limiting trait, and exposure studies on non-target organisms. As well, they requested additional physical security measures for the site to mitigate the risk of an unintended release. Oxitec evaluated the request and determined that due to the timeframes required to generate the data, that the appropriate administrative approach would entail a withdrawal of the application and re-submission at a later date.

Oxitec subsequently undertook studies (both internally and with external providers) to further characterize the expression of the self-limiting trait as was recommended, as well as evaluate the impact on three different “non-target” organisms, representing three distinct potential exposure routes and two different ecological guilds of non-target organisms. In these studies, no adverse effects were observed in any case and it is Oxitec is preparing these for peer-reviewed journal submission.

In 2015, a new regulatory submission was made to GENCAT which included the data from the above noted studies, additional literature reviews, as well as site security measures. The trial site was isolated within a government research centre, and the study itself was a collaboration with the research institute (IRTA) owned by the Government of Catalonia, and attached to the Department of Agriculture. IRTA has been recognised as one of the best

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<sup>103</sup> <http://www.cabi.org/isc/datasheet/17689>

scientific research centres in Spain<sup>104</sup>, with a stated purpose which includes “...to contribute to the modernization, competitiveness and sustainable development of agriculture...” Despite having addressed the 2012 requirements of the NBC, concerns remained with the 2015 application regarding the confinement of the trial site. While additional confinement measures were presented, it appeared that GENCAT would only accept a fully-contained trial, and the application was subsequently withdrawn.

An application under the Contained Use Directive (2009/41/EC), may have been an acceptable route for the Oxitec olive fly trial in Spain, but as this had already been conducted<sup>105</sup> this option would not have contributed to the stepwise scientific evaluation of the insect.

The governments of the USA and Brazil have recently granted environmental release approvals (*outside* of netted enclosures) for self-limiting GM insect plant pests based on identical technology. While risk assessment is case-by-case by nature, and site specific considerations may be unique, it is difficult to rationalize the decision of the Spanish NBC given internationally accepted principles of evidence-based risk analysis.

23 November 2015

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<sup>104</sup> [http://www.irta.cat/en-us/RIT/Noticies/pages/IRTA\\_millorcentre\\_recerca.aspx](http://www.irta.cat/en-us/RIT/Noticies/pages/IRTA_millorcentre_recerca.aspx)

<sup>105</sup> Ant *et al.* *BMC Biology* 2012, 10:51 (<http://www.biomedcentral.com/1741-7007/10/51>)

Dr Professor Paulo Paes de Andrade, Federal University of Pernambuco, Dr Amaro de Castro Lira Neto, State Institute for Agronomy (IPA) and Dr Marcia Almeida de Melo, Federal University of Campina Grande – Written evidence (GMI0006)

**Dr Professor Paulo Paes de Andrade, Federal University of Pernambuco,  
Dr Amaro de Castro Lira Neto, State Institute for Agronomy (IPA) and  
Dr Marcia Almeida de Melo, Federal University of Campina Grande – Written  
evidence (GMI0006)**

**Transgenic insects from a regulator's perspective**

Having worked for a long time directly with the GMO regulator in Brazil (CTNBio) or in close contact with it, we had the opportunity to assess risks linked to many different organisms, including a GM *Aedes aegypti* developed by the British company Oxitec. This long and fruitful collaboration allows us now to contribute to the discussion on the safety and use of genetically modified insects. We hope that the answers to the questions raised by the House of Lords, in addition to suggestions of other important issues, will further promote meaningful discussions and lead to informed decisions in Britain.

**01 Answer to Questions**

**02** Although based in the scientific literature and in technical reports, the answers do not usually refer to these sources, as to avoid the unnecessary lengthening of the text.

**03 1. Which human diseases, across the world, could be addressed through GM insect technology? Are there any human disease risks in Europe, particularly the UK, for which GM insects are under development?**

**04** The answer must take into account the vector biology and should be restricted to vector-borne diseases. Those transmitted by one or more species of mosquitoes are the natural candidates to be controlled by the use of GM insects: malaria, yellow fever, dengue, chikungunya, zika. The difficulties inherent in multiplication of phlebotomine sand flies in insect facilities preclude the use of GM insects in the control of leishmaniasis. The reproductive behavior of all Chagas' disease vectors does not allow either an immediate use of technology. It might be applied, however, in the control of African trypanosomiasis, depending on environmental variables involved in the multiplication and spread of *Glossina morsitans*. Diseases transmitted by other arthropods do not seem appropriate to control by GM insects, at least in the current state of the art.

**05** As for the risks of vector-borne diseases in the UK, they have been reviewed and discussed at the University of Liverpool last year during the Second Conference on Vector-Borne diseases in the UK. Ticks, *Culicoides* and mosquitoes may pose some threat, but the risks for the general population are small, especially for mosquitoes, which are rather a nuisance than a threat. However, increasing incursions of mosquito borne diseases in the Southern EU have been reported and may turn to be a cause of concern in the near future

Dr Professor Paulo Paes de Andrade, Federal University of Pernambuco, Dr Amaro de Castro Lira Neto, State Institute for Agronomy (IPA) and Dr Marcia Almeida de Melo, Federal University of Campina Grande – Written evidence (GMI0006)

**06 2. What are the possible livestock and agricultural crop applications of GM insects across the world? Of current livestock disease risks and agricultural insect pests that could be addressed through GM Insects, which should be the highest priority for Europe?**

07 There is a very wide range of GM insects applications in agriculture and livestock. Of course, companies/developers will seek to invest in agricultural and livestock pests of major impact on global food production, mostly because the cost of registering the product only makes it worthwhile on those scales. Developers may dedicate themselves later to those with only regional or national importance. Pests of fruit and cruciferous plants are the natural candidates for a first attempt to use this technology in agriculture. The horn fly (*Haematobia irritans*) and other flies that attack cattle are candidates for the technology in livestock.

08 As for the European priority, we leave the answer to other colleagues.

**09 3. Are there likely to be opportunities provided by GM insects that cannot be provided by other approaches, such as biological control methods? How could GM insect approaches be complementary to existing Integrated Pest Management (IPM) programmes?**

10 From our perspective, the use of GM insects is a biological control. However, due to changes in reproductive behavior and the fact the control agent is from the same species that acts as a pest, GM insects can achieve a much greater success than the use of other predatory species, with possible lower or no environmental impact. In all cases, the use of GM insects should not overlook integration with the other pest control measures. Of course, it is essential to correctly articulate the various alternatives, especially regarding the use of insecticides.

**11 4. How appropriate are current EU and UK GMOs regulatory frameworks in addressing the issues raised by GM Insects? Are there lessons to be learnt from the regulation of GM insects in other countries such as Brazil?**

12 Both US and UK regulatory frameworks are based on existing laws and in some cases on existing agencies. This strategy may work, but is far from adequate to easily cope with the ever changing field of biotechnology. The agencies must keep a continuous dialog between themselves in order to adapt to the risk assessment of new products whenever a challenging new host or new technology is presented. In spite of these restrictions, the American system is working conveniently, both safeguarding health and environment and allowing the adoption of the technology. The main point underlying the success of the American system is the full independence of the risk assessment procedure against the other risk analysis steps, i.e., risk management and risk communication, and ultimately against political decisions. Once the three American agencies consider the GM product to have risks similar to the conventional, non-transformed counterpart, it is ready to be introduced in the North American market. No political interference is allowed, at least under normal circumstances.

13 The same independence is the cause of the rapid adoption of biotechnology in Brazil and, to a certain extent, also in Argentina, Australia and Canada. The Brazilian Biosafety Agency, namely CTNBio, is the sole Government Agency responsible for risk assessment and its decision can only be challenged by a Council of 11 Ministers, which



Dr Professor Paulo Paes de Andrade, Federal University of Pernambuco, Dr Amaro de Castro Lira Neto, State Institute for Agronomy (IPA) and Dr Marcia Almeida de Melo, Federal University of Campina Grande – Written evidence (GMI0006) has never happened in practice. Once considered safe by CTNBio, the new GM product automatically goes for further registration (for labeling, depending on the product etc), but its biosafety evaluation can't be questioned by any other agency.

14 In spite of being efficient, the Brazilian system is expensive and alternative, faster and cheaper pipelines should be developed. The only burning issue is the independence between the technical decision (based on risk assessment) and political issues derived from the public risk perception.

**15 5. Do the World Health Organisation (WHO) guidelines on the release of GM mosquitoes provide the basis of an effective regulatory framework? How should issues regarding the emergence of resistance be considered?**

16 The WHO guidelines are useful for research purposes, mostly as a guide for developers. But has no direct application in risk assessment and on regulatory issues. Indeed, the established risk assessment procedure, initially used for GM plants and extended to many other GMOs, is very effective and flexible and can be used to assess risks of almost any GMO, including insects.

17 We are not quite sure on how to interpret the question on resistance.

**18 6. Do the European Food Safety Authority (EFSA) guidelines on the environmental risk assessment of GM Insects for commercial use sufficiently address the different risks from population suppression and population replacement approaches? How should the ecological risks and human benefits that might arise from the application of gene drive techniques to population replacement approaches be assessed?**

19 The EFSA guidelines broadly follow the internationally agreed risk assessment procedure (embedded in the AHTEG Guidance, the EFSA guidance and many other official texts). There is no need to speculate on each specific transgenic animal, even as an example, as it distorts the aim of a general guidance. The guide was written for transgenic animals, not just for insects. As it is now, the guidance is useful for neophytes in risk assessment and may be of some help for those already used to the step-by-step procedure, which is not different between a plant and an insect. The specific questions raised by the application of such a risk assessment procedure will be answered either by the scrutiny of the available literature or by experiments. Such experiments, however, are meant to respond to specific risk assessment questions that are plausible science based pathways and are not meant to satisfy the scientific curiosity of someone or even a group of people.

20 The specific ecological risks derived from the gene drive technique will be assessed on the basis of sound, testable scientific hypotheses in the lack of sufficient data on the subject. This is by no means different of what happens to any other GMO expressing a specific trait. In conclusion, the current risk assessment frameworks, if properly used are adequate for GM insects

**21 7. How is research into the development of GM insects currently funded? Are there opportunities to attract more private investment into this area?**

22 This is a question outside our expertise.

Dr Professor Paulo Paes de Andrade, Federal University of Pernambuco, Dr Amaro de Castro Lira Neto, State Institute for Agronomy (IPA) and Dr Marcia Almeida de Melo, Federal University of Campina Grande – Written evidence (GMI0006)

**23 8. Given the possible public health benefits of GM insects, should the Government be funding their commercialisation? Would this result in a conflict of interest with regard to regulation of releases? If so, how might this be managed?**

24 Placing a new product to market is usually a task on the financial burden of the private sector. However, regulatory costs can be minimized by the Government if a clear benefit is foreseen, as long as the risks can be conveniently assessed. This provision must be clearly written in the regulation normative from the national GM authority. There will be no conflict of interest if risk assessment procedures are kept effective and accepted by partners in the EU and other regions.

25 On the other hand, public research funding should be encouraged for products with a clear application on burning health or agricultural/livestock issues.

26 However, none of these actions are effective alone and a streamlining of GMO approval is essential for those countries that have not yet adopted biotech in a large scale, with special regard to the independence of risk assessment to other risk analysis issues and to political questions (see also Question 4). Indeed, if the approval pipeline is made independent of political conflicts, there will be no need for a special approach for products with a high positive impact on public health or agriculture.

**27 9. How could the UK benefit economically from both developing GM Insect technology and its use within the UK?**

28 This is a question outside our expertise.

**29 10. How can the gap between regulatory approaches and public concerns over GMOs be addressed? Is there a role for 'responsible innovation' approaches? What are the critical factors in effective public engagement from lab to final release?**

30 Risk communication is a key element in the overall process of acceptance of a new product on the market. Unfortunately, we found that biotech companies and their partners do little in this particular area and when they do, miss a lot: they usually start risk communication only immediately prior to commercial release, they use an inadequate propagandistic language, do not reach the opposition with the right arguments, etc.. There is no doubt that risk communication, an integral part of risk analysis, should begin during the development of a product, particularly in steps involving the release of new GMOs into the environment, even in a controlled manner. If risk communication is well planned, it will result in a gradual change in the perception of risk and facilitate the adoption of the product.

31 The relevant actions to risk communication involve private or public companies, universities and the Government, as well as NGOs and other social organizations. The dialogue must be initiated professionally and conducted continuously until after the release of a new GMO. Costs need to be shared between the company (most interested part) and the Government. Language and transparency are essential factors that can't be minimized.

Dr Professor Paulo Paes de Andrade, Federal University of Pernambuco, Dr Amaro de Castro Lira Neto, State Institute for Agronomy (IPA) and Dr Marcia Almeida de Melo, Federal University of Campina Grande – Written evidence (GMI0006)

**32 Additional issue: The independence of risk assessment and other elements of risk analysis in the decision-making**

**33** Although mentioned before, we think it is worth to emphasize that a regulatory framework will only enable the adoption of biotech, and specifically GM insects, if the risk assessment decision taken by the National Authority (or authorities) can't be further questioned by other Government bodies. This is unfortunately not the case in Europe and an EFSA decision may be considered invalid by some Government authority of a given Party. The political refusal, however, is acceptable, but should clearly state that it is not based on risks, but on other issues (public perception, commercial problems, etc.). Such a clear separation may enlighten the public and contribute to a better public risk perception.

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*16 September 2015*

Professor Paulo Paes de Andrade, Federal University of Pernambuco, Brazil, Professor John Mumford, Imperial College London, and Dr Jack Stilgoe, University College London – Oral evidence (QQ 39-47)

**Professor Paulo Paes de Andrade, Federal University of Pernambuco, Brazil, Professor John Mumford, Imperial College London, and Dr Jack Stilgoe, University College London – Oral evidence (QQ 39-47)**

*Evidence Session No. 4*

*Heard in Public*

*Questions 39 - 47*

TUESDAY 20 OCTOBER 2015

Members present

Earl of Selborne (Chairman)  
Lord Hunt of Chesterton  
Lord Kakkar  
Baroness Manningham-Buller  
Lord Maxton  
Duke of Montrose  
Baroness Morgan of Huyton  
Baroness Neville-Jones  
Lord Patel (co-opted)  
Lord Peston  
Viscount Ridley  
Lord Vallance of Tummel

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**Examination of Witnesses**

**Professor Paulo Paes de Andrade**, Department of Genetics, Federal University of Pernambuco, Brazil, **Professor John Mumford**, Professor of Natural Resource Management, Centre for Environmental Policy, Imperial College London, and **Dr Jack Stilgoe**, Senior Lecturer, Department of Science and Technology Studies, University College London

**Q39 The Chairman:** I thank our three witnesses who have come to help us in the second session. We are being broadcast on the web, so could I ask you to introduce yourselves for the record? If any of you would like to make an introductory statement, do feel free to do so.

**Professor John Mumford:** I am John Mumford, I am a Professor in the Centre for Environmental Policy at Imperial College London. I have been a contributor to both the EFSA and the WHO guidelines on GM animals and GM mosquitoes. I manage the risk analysis part of a project called Target Malaria, which is funded by the Foundation for the National Institutes of Health in the US. A little more broadly, I have worked extensively with the International Atomic Energy Agency on the design and evaluation of sterile insect technique programmes around the world, so I have a lot of experience with radiation sterility; and I

Professor Paulo Paes de Andrade, Federal University of Pernambuco, Brazil, Professor John Mumford, Imperial College London, and Dr Jack Stilgoe, University College London – Oral evidence (QQ 39-47)

chair the Great Britain Non-native Species Risk Analysis Panel, which advises the three Governments in Great Britain on invasive species. In the course of that, we have overseen over 130 risk assessments of invasive species, so I have very practical experience of the risk assessment process.

**The Chairman:** Thank you. Dr Stilgoe?

**Dr Jack Stilgoe:** I am Jack Stilgoe, Senior Lecturer in Science and Technology Policy at University College London, where my particular interests are in the governance of emerging technologies rather than GM insects in particular. Relevant to this inquiry, I have been working with the research councils developing frameworks for what we and they call responsible innovation. Also relevant to declare, given your previous witnesses, I am on the steering committee of Sciencewise, the Government's public engagement with science arm.

**The Chairman:** Thank you very much. Professor Andrade?

**Professor Paulo Paes de Andrade:** I am Paulo Andrade, Professor of Genetics at the University of Pernambuco in Brazil. I am a former member of the Brazilian National Biosafety Council, from 2006 to 2012, and I was engaged in the risk assessment of the transgenic mosquito that we are dealing with here, and many other organisms, including plants, vaccines, yeasts, algae and other relevant organisms such as trees. I have a lot of experience in risk assessment as a risk assessor, but I do not have much experience as a risk analyst. I am not used to discussing political questions related to biosafety, but I am glad to be invited for a second time here. I was here in February; Lord Patel was the chair of the meeting and it was very pleasant.

**Q40 The Chairman:** We are particularly grateful to you because you have come from Brazil via Lisbon, and that is well beyond the call of duty. Thank you very much indeed for having joined us today. I must start with an apology: I am afraid that I have a medical appointment which I was not able to change, so for the last quarter of an hour or so of this session Baroness Manningham-Buller will take my place and take the Chair. I do apologise for having to leave early. Perhaps I may start by asking a rather general question, in order to set the scene. Do not feel you all have to answer this question. Is the current regulatory environment in the European Union and the United Kingdom, in your view, fit for purpose for GM insect technologies? In other words, has the right balance been struck between innovation and regulation?

**Professor John Mumford:** The answer, almost certainly, is that it varies, because there are many purposes; it may be fit for some and less fit for others. You are also asking about a balance between innovation and regulation. I am not sure one of its purposes is to promote innovation. The main purpose of the regulations, as I understand them, is to protect the environment and human health. We have to keep in context what those purposes are. But getting to the point that you are trying to make, it is certainly restrictive; it works against the introduction of innovation, as we have heard in the previous session. It is certainly very burdensome on the applicants—some would say rightly so; they should show that things are safe—but, on the other hand, we want the innovation, so you have to get the balance. It is very process focused. I would like to see a much more flexible system rather than one which is highly prescribed. In that sense, I think it is not quite fit.

**The Chairman:** Would you like to describe what would be the alternative to something which is process oriented? Would you prefer something that was product oriented?

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**Professor John Mumford:** The emphasis on the problem-formulation stage that is part of the European regulation was touched on in the earlier session. If that problem-formulation stage was more open, more fluid, involving more discussion between the applicants, the regulators and indeed the interested public at that early stage—this is prior to actually doing risk assessments—I suspect that quite a few of the issues could be designed out prior to an application going in. It would be much easier to do risk assessments on relatively safe products that have good design features already put into them. That is the kind of thing I mean regarding a bit more fluidity. We are starting to see that already in applicants being encouraged to talk to regulators at an early stage. We could formalise that fluid process to get them talking about what the public is concerned about and what the regulators are concerned about and what are the several options, because most applicants will have several pathways that they could follow in the development of their products.

**The Chairman:** Would either of the others like to add anything to that, or shall we move on?

**Professor Paulo Paes de Andrade:** I would like to emphasise that risk assessment is the core of the regulation in Europe, and should also be here in the UK, since the UK follows what the European Union decides in terms of risk of GMO regulation. I frequently see people putting issues of benefit together with issues of risk. Risk assessment is usually done by scientists—scientists are not risk assessors; they are not trained for it, but they learn with time. The language is different and the process is different, but it is scientifically driven. So, after a while, scientists learn how to do it. But scientists do not know how to evaluate the benefits, because that is an economic issue. The best element to use in deciding whether or not a product is useful is the market. If we leave that decision to any member or any group of people, we are putting the state in front of the economy and that is bad; that is socialism. I am not against socialist countries, but I am against socialism now, as it is. It is completely outdated. We have to think of the market as a decision element and not put benefits in front of risks; risk assessment is just biological and should be completely separated from benefits. I have heard this suggestion many times, and I know you may think it is useful, but it is very bad for risk assessors to discuss economic issues, because they are not prepared for that. Europe is mixing things, and although the main framework is good, doing it is not good in Europe; they are not experienced in evaluating and agreeing the economic use of some products. In the end, everything comes to a dead end and we cannot approve anything in Europe. One of the reasons is that Europeans try to balance benefits and risks. Just try to keep doing risk assessment; nothing else.

**Dr Jack Stilgoe:** May I quickly follow up on that? Though not specific to the matter of GM insects, there are important regulatory considerations to be taken on board that recognise that markets are rather bad at decision making under the conditions of uncertainty that emerging technologies tend to generate. Regulators, it strikes me, should rightly represent the public interest in ways beyond just questions of scientific risk. Those are the reasons why the European regulatory system has emerged to that end.

**Viscount Ridley:** I was a little puzzled by what you have just said, Professor Andrade. I can see what you are getting at—that state regulators are not best placed to measure benefits—but our problem in Europe is that nobody is measuring benefits; nobody is allowing benefits into the equation at all, it seems to me. We are discussing risks with the right hand and nothing with the left hand. Is that not the case?

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**Professor Paulo Paes de Andrade:** It is really a burden for the risk assessor because he or she cannot argue in terms of benefits. The technology is nice, there are no risks or low risks and the advantages are clear, but risk assessors should not talk about advantages—just say whether or not it is safe. If the product is accepted later on, that is a question of a political decision sometimes or just a market decision. In my country, it is just a market decision.

**Viscount Ridley:** Before anything gets near the market somebody has to speak up for the potential benefits.

**Professor Paulo Paes de Andrade:** No, not at all. Not in Brazil.

**Viscount Ridley:** How do we ever capture these benefits? How do we ever have a sensible conversation?

**Professor Paulo Paes de Andrade:** The company—the developer—captures the benefits.

**Viscount Ridley:** But if the company cannot come to market because of the regulators, we do not get the chance to do that.

**Professor Paulo Paes de Andrade:** No chances.

**Lord Peston:** I am a little bit lost. I start from the fact there is a problem: people are dying of malaria. That is the problem. They are dying of it. It is possible that science will develop and we can do something on the GM side so that they do not die of malaria. That is why we are in this field to start with. We are not there outside of the world; we are there because there is an actual problem. I do not understand your position, Professor Andrade. Are you telling all these people: “You have to die”? Is that your position? I cannot believe it is for one minute.

**Professor Paulo Paes de Andrade:** No, it is not my position.

**Lord Peston:** Therefore, the fact is that the benefits are very clear and cannot be avoided. You have to deal with the other problem which puzzles me. Are you going to tell all these people dying of malaria: “I am afraid you have to die, but you are dying in a rather nicer environment than you would have done”? Is that your position?

**Professor Paulo Paes de Andrade:** I must apologise for my bad English. Maybe I was not clear enough. Risk assessors should not consider benefits. The first point is that, for public health products, it is obvious that the Government should encourage the adoption of something which has low risks and also shows benefits. The Government should support that. The first point is low risks. We can imagine a product that can combat or control malaria, or the dengue virus in my country, but if it is dangerous for the environment it should not be released, or should be balanced against the benefits. However, if the risks are very, very low then anyone would support it. It is not a question of arguing, because the risks are so low. The first thing is to do the risk assessment. I am not really saying that people should die of malaria—not at all.

**Professor John Mumford:** Perhaps I could outline the process of risk analysis which might help to put Professor Andrade’s point in some context. It is a multi-stage process: you start with risk concern, you move on to risk assessment, you move on to risk management, and there are iterations and repeats as you go along. My understanding of what he is saying is that the risk assessment stage should be independent of values such as benefits. Those may enter at a later stage, at the risk management stage, where a decision is made, but not at

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the assessment stage. Assessment should be objective and management should focus on performance and benefits. The point made in the previous session by some of their Lordships is that that last stage is not happening adequately. There is plenty of emphasis on the concerns and plenty of emphasis on the risk assessments. The two could be tied together better, so that we were doing risk assessments related to real concerns—that would come out, as I was saying earlier, in the problem formulation stage—then decisions at the risk management stage would more actively consider benefits.

**Q41 Baroness Manningham-Buller:** Professor Andrade, we know you had a very successful programme against malaria in Brazil. Who in your system did the benefits bit? The risk assessment showed this was low risk. Who articulated, for the public and more widely, the benefits?

**Professor Paulo Paes de Andrade:** If it is not a GMO it is the registration agency; in Brazil it is called ANVISA, the national health authority. It evaluates if the product is good and effective and registers the product to be sold or used somehow in my country. If it is a GMO, it is first analysed for biosafety concerns by the National Biosafety Authority. Later, if there is any special question, it can be reassessed by the National Biosafety Council, which is composed of 11 state ministers. It has never met because the crops are just crops, and even for the insect the benefits are so large it was not necessary to put the 11 ministers together to discuss that.

**Baroness Manningham-Buller:** So public opinion was behind the health one. Also, for the other things you mentioned, such as vaccines and yeasts, you have not had any opposition to it?

**Professor Paulo Paes de Andrade:** No. The public has opportunities because we have public audiences—public hearings—where the public can put their concerns about the technology or the product before CTNBio makes a decision on the biosafety. Moreover, the ministers also represent the public, so there is a second opportunity to directly put the public opinion in the final decision.

**Lord Ridley:** On a point of fact, we have slightly taken as read that there were huge benefits here. Can you enumerate the impact on malaria, dengue or on mosquito numbers, or whatever, from the Oxitec experiments in Brazil?

**Professor Paulo Paes de Andrade:** The negative impacts are known. We had trials in Brazil, in two different cities, and they were very well conducted by the company and observed by CTNBio, and the negative impacts are known to be null. We have still to see the positive impacts because we are now adopting the technology at a pre-commercial level<sup>106</sup>. We have seen that the insect population has drastically reduced in a few months. But I do not know if it will impact dengue virus transmission. That will be seen in the future. We have to have large-scale experiments.

**Lord Ridley:** The mosquito impact is known, but we are still waiting to know the dengue effect.

**Professor Paulo Paes de Andrade:** That is it.

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<sup>106</sup> The positive impacts on the reduction of vector population is already very clear – what is still missing is the impact on disease transmission.



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**Q42 Baroness Neville-Jones:** In the light of this general discussion, perhaps there are some differing views, but there are other disruptive technologies. My question is: do you think it is possible to learn the way in which some of those are being managed—any improvements in the system for GM—and what kind of alternative regulatory regime would you really like to see, if you could design it?

**Dr Jack Stilgoe:** My strong sense is that past experiences with emerging technologies, both good and bad, can be extremely helpful in this regard, given that when it comes to assessing the risks and benefits of any new technology, necessarily there is vast uncertainty surrounding those assessments. Lessons of previous examples, good and bad, would include, for me, the European experience with GM crops and comparisons in other countries. The good news story I would draw upon would be the British experience with fertilisation and embryology and the way in which a solid governance regime has emerged alongside a hugely innovative research and clinical community there. However, the lesson from those, taken together, is that governance needs to improve. I do not like the presumption that we are dealing with balancing innovation and regulation, because what we would all ideally like is something like responsible innovation that is steered towards particular problems, whether those are problems of disease control or something else, and away from the risks and hazards that we might be able to identify. Numerous efforts have been made over the last couple of decades. The Royal Commission on Environmental Pollution—much missed—outlined in its final report some important lessons for what it called “adaptive governance”, where we presume that we do not know all the risks and the benefits that we face when we are running experiments and rolling out technologies, and so we put in place requirements to better monitor and understand the impacts of those experiments, whether those are field trials or the actual rollout of technology. So governance can improve in all sorts of different directions. I would finish by saying that, in my own work, the research councils have been looking very far upstream, so the issue is how scientists can get better involved in anticipating some of these concerns, engaging with members of the public and reflecting on those concerns.

**Baroness Neville-Jones:** Perhaps I may pursue that a tiny bit. I entirely agree with you about responsible innovation and that it is not so much about balancing as about the manner in which you actually combine those two considerations.

**Dr Jack Stilgoe:** Indeed.

**Baroness Neville-Jones:** How, specifically, to turn to GM, would you like to apply what you have just said as general principles to the situation we are in to get some forward movement? We are actually at something of an impasse.

**Dr Jack Stilgoe:** Indeed. GM is one of those situations where, if your concern is with upstream questions, as mine is, I am afraid it is one of those situations where you could say ‘you wouldn’t start from here’.

**Baroness Neville-Jones:** But we are here.

**Dr Jack Stilgoe:** We are indeed. Considering all the other interests involved in the current state of GM regulation and the European dimension of it, it is hard to know where one might go. It strikes me that that is a straightforward political fight that the UK needs to have with Europe as much as it is one about good governance.

**Baroness Neville-Jones:** Does anybody else have any thoughts on this?

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**Professor John Mumford:** I am thinking of a completely different example, but one where the upshot at the end was that governance was changed. Thirty years ago, in Australia, there was objection to the introduction of biological control agents. Some people argued that they were going to lose out as a result of the introduction of biological control agents which might do harm to some interests they had. As they had a harm-based regulatory system at the time, if anybody said they were going to suffer some harm the whole thing stopped. This was clearly untenable, in the end; it did not represent what society wanted. The system was changed and the Biological Control Act was introduced in Australia. It set up a system of public inquiries to determine who benefits, who loses, how much the losers will lose and how they should be compensated. That system has been in place and has been much more effective. I think it covers one of the points that Jack Stilgoe is making—that you need to introduce a governance system that actually meets the purpose. That is an example of where they did it. They simply changed it.

**Baroness Neville-Jones:** Would a trait-based system serve the purpose, in your view?

**Professor John Mumford:** Yes, I would much prefer to see a trait-based system. That is different from having a governance system, but we need trait-based systems with good governance, so I would like to see both.

**Dr Jack Stilgoe:** The only qualification I would add to the discussion about trait-based regulation—sometimes called product-based versus process-based regulation—is that there are reasons why one might want to put in place a process-based regulatory scheme. They are to do with the uncertainties that we might be unable to predict in terms of the products, whether those are the products themselves or the products of that particular innovation in terms of the consequences and ramifications of those traits, and actually paying attention to the processes might better take you into a precautionary approach to governing those uncertainties.

**Q43 Lord Hunt of Chesterton:** I sat on a Lords Committee on animals in scientific procedures. It was very interesting that the Home Office's view, as is broadly accepted in the United Kingdom, is that essentially you must be very, very careful about animal experiments, whereas in the United States they do many more experiments on animals. My wife is asthmatic; all her drugs are tested on primates in America. That could never be done in the United Kingdom. Similarly, perhaps you can also see this in America with GMOs; they have used them very widely and have not worried about the loss of biodiversity in hedgerows and other things—they have a view about looking at food for people. What you feel about the European aspect of this is that we are extremely conscious of perhaps the biodiversity element. That is why it is such a strong political driver. The question really is that the public debate, it seems to me, is very limited. We did not have a strong public debate, really, about animals in scientific procedures. We have not had a strong, meaningful public debate on these issues here, certainly not on the continent of Europe. We had a meeting last week and put to our panel: how should there be a more intelligent public debate on this? They said: this is an area for experts; experts should talk about it. I was not completely happy with that answer. What is your answer to that question?

**Dr Jack Stilgoe:** I had a look back through last week's evidence and I did not get that message from it—maybe I was looking for different things. As I mentioned, I am on the steering group of Sciencewise, and last week you had Sir Roland Jackson, representing

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Sciencewise, talking about the sorts of public debates that are commissioned through that process. Clearly, not everything can be a topic of public debate, which is why I think it is important to learn from previous experiences in this regard. I would want to see experts, certainly, prompting that debate, but not presuming that their knowledge or wisdom is complete in that regard. That is why I think that the dialogue between experts and the public—whether that is the public in Britain or specifically the public in the local communities where trials are happening or problems are prevalent—is absolutely vital. There are all sorts of mechanisms through which one might take those forward.

**Lord Maxton:** What drives public opinion?

**Dr Jack Stilgoe:** There is a sociology degree in that.

**Lord Hunt of Chesterton:** Why is it different in different countries? That is the point. Why is it so different in Europe and the United States?

**Dr Jack Stilgoe:** My other response to that question is that public opinion may be a relatively small part of the experience there. If you take the GM crops comparison, perhaps a more stark example would be French agriculture relative to US agriculture. Other committees have done countless inquiries on this. However, GM crops suit American agriculture in a way that they simply do not in France, and one could equally explain it in those terms. Actually, caricaturing the public as anti-science or anti-technology in Britain or Europe—this was discussed last week, I think—is an enormous mistake, because all the evidence suggests that they are simply not.

**Lord Hunt of Chesterton:** I did not say that; it is different aspects of the science—that is the point. People give the environment a different emphasis.

**Dr Jack Stilgoe:** There is no straightforward explanation, I think.

**Lord Maxton:** We have talked about GM crops and GM insects, but of course there is human genetic modification as well. Where does that fit into all this?

**Professor Paulo Paes de Andrade:** In my opinion, comparing Brazil and Britain, it is obvious that the debate in Britain is dependent now on the alternative media. There is a lot of debate on GMOs in alternative media, with no access or no influence of the Government or of scientists. Scientists do not have time for that, and I think people from the Government also do not, so the discussion goes on over the internet. It has enormous influence on the risk perception of the public in general. We have somehow to interact with this huge cloud of information, but I do not know how to do it. In Brazil the internet does not have that much influence, and the large media—the official media—can still have a lot of influence. We use journals, papers and television, and the discussion then is a bit more scientific than what runs in the underground, and this may be the difference. In the United States it is just the opposite, because they have such internet facilities; everybody has a mobile that can access the internet, and they have a lot of opposition to biotechnology, but the Government decided on a scientific basis, and they really separated risk assessment from the other decisions. That is the trick there.

**Q44 Baroness Morgan of Huyton:** Perhaps I can come in now rather than later, since we are talking about this issue. How have we managed to have, I would say, a pretty reasonable public debate about embryology and its wider aspects in the United Kingdom that has involved the scientific community, the medical community and the media? Somehow that

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has worked, and yet we fail in this area. Are there lessons from that which we should apply to this? One of my concerns about last week's evidence was about taking it issue by issue by issue, rather than saying: "Let's have a larger public debate about the risks and benefits of this new technology", which arguably we have done in the field of embryology.

**Dr Jack Stilgoe:** I think the issue-by-issue-by-issue thing is exactly what recent reports, such as the Royal Commission's and also the one from the Nuffield Council on Bioethics, have tried to get past, which is the idea that actually these things tend to raise similar questions over and over again, and we are slowly getting better at understanding how to come to terms with them. In the debate about embryology, I would say the reason that worked was that it asked a broad set of questions early, prompted by the first clinical use of IVF. It involved experts from a wide variety of disciplines: Mary Warnock and others led the discussion, as well as the scientists and clinicians involved. It was public and it was done before there had been an entrenchment of particular positions. With GM crops, the benefits were presumed from the start and the risks were presumed to be relatively negligible, which meant that those with interests in GM crops were taken by surprise by the additional set of concerns presented by European citizens. Perhaps I may also remind the Committee of the large amount of work done by social science in precisely understanding the roots of public concerns on GM crops; there was a vast amount of evidence that the Commons Committee went over.

**The Chairman:** We will, in a later session, be hearing from the Nuffield Council on Bioethics, and we will have an opportunity to address those issues, as indeed we did last week.

**Lord Vallance of Tummel:** Tell me if I am wrong, but my instinct is that public concern is in two very different areas. One is to do with tail-end risks—low probability, high impact, although they may not put it that way—but the other is a moral dimension. I suspect that these have to be dealt with in two very different ways. Perhaps with embryology it was done properly, but I think if you do not address both upfront you are not going to get the right answer from the public. Am I wrong?

**Dr Jack Stilgoe:** I do not think one can easily, necessarily, separate those things because quite often people's perception of the risk is bound up with the extent to which they trust the morality of the person they feel is making the intervention. I think, absolutely, it is important to consider the ethical dimension as well as the calculable risk dimension of the construction of those concerns.

**The Chairman:** Lord Hunt, have we dealt with your question?

**Lord Hunt of Chesterton:** Yes, Lord Chairman.

**The Chairman:** Could we move on to Lord Ridley? Perhaps I may also ask Baroness Manningham-Buller if she will take over from me.

*Baroness Manningham-Buller took the Chair.*

**Q45 Viscount Ridley:** Just to comment on the last conversation before moving on to my question, I am very interested in what Professor Andrade says about social media, and so on, and I think we probably should try and follow up on that. Those of us who have experienced

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the anti-GM crowd on Twitter know what you are talking about. The WHO has come out with some guidelines on GM insects and so has the European Food Safety Agency. Given our written evidence, it seems the WHO guidelines are not particularly problematic but the EFSA ones are much more so. The Royal Entomological Society described them as “probably overbearing and inhibitory to innovation”. Is that a view the panel shares?

**Professor John Mumford:** Having contributed to both of them, I know that they are certainly very different. They were for different purposes, and I think the outcome reflects that. For EFSA, they required a document that would explain to applicants and the public how the process worked, and it was very prescribed by the way that the deliberate release directive is written. All the sections within it address, section by section, point by point, what is in that regulation.

**Viscount Ridley:** That regulation was originally written for crops rather than insects.

**Professor John Mumford:** Exactly, yes. In fact, we spent a great deal of our time, in the insect section that I worked on, trying to interpret what was a crop-directed set of instructions to explain to insect applicants and the insect-interested public how this system would work, and we tried to do that with quite a lot of examples. As we looked into it there was huge variation in the potential GM insect applications. There are some that are very similar to GM crops—a silkworm with higher productivity kept in captivity is not that dissimilar to growing wheat—whereas others are released entirely into—

**Viscount Ridley:** Except that we do not eat silk.

**Professor John Mumford:** Yes, that is true. We also looked at honeybees and, potentially, GM honeybees. We also looked at vectors, and in fact as vectors seemed to be the most likely applications in the short term we put a lot of effort into those. We found one of the key differences there was to think about populations, very long timescales and very large spatial scales. We put emphasis on the use of models. We tried to be instructive to applicants by saying what an applicant should provide and how they should provide it. It was very, very specific, with very highly detailed bits about the parts of the directive. In the WHO guidance it was, in some senses, much easier because we were focused entirely on GM mosquitoes. There were two basic strategies—and several different technologies within those two strategies—of replacement and suppression that we could address. As it was much more specific, that made it easier. We were also aiming at looking at the whole process from start to finish, not just at the risk assessment stage but thinking why would you start with this and how you would go step by step through to a decision to implement in the end. We were able to think about a continuum, from the early stages where you focus on biosafety through to a later stage where you are starting to think about the economic benefits and wider social benefits, and so you could take everything step by step. We could not do that in the EFSA guidance because we had to start and stop with the risk assessment stage, so it was after concerns and before decisions, so there was not much scope in the middle.

**Viscount Ridley:** Just to pin you down, do you think those EFSA guidelines are inhibitory to innovation?

**Professor John Mumford:** Not in themselves. I think the process that makes decisions subsequent to a risk assessment is inhibitory—the process after the risk assessment stage. The EFSA guidance is about the risk assessment stage for environmental and public health

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risks. It is not about decision-making. It is simply saying, “As expressed and articulated in the directive, here are a number of concerns that have been proposed; here are examples of why they are a problem, how we might assess them and factors to take into account”, and then it stops. There is nothing in it about how a decision would be made, so there is no value judgment at all at the end.

**Viscount Ridley:** One further point: you mentioned the distinction in the WHO guidelines between population suppression and population replacement. Is that distinction sufficiently captured in the regulations that are coming forward generally? Does more work need to go into teasing apart the differences there?

**Professor John Mumford:** I would say it is not captured at all. In fact, it is a fundamental conflict within the regulation that there are seven large areas of technical concern within the deliberate release directive, and persistence is one of those seven. Obviously, with the self-sustaining mode of action for some of these methods, you are starting from an assumption that the whole mode of action is a concern. That is an inherent conflict within the regulation. I think it would be difficult in designing a regulation to allow for every possible strategy that might develop in the future. I do not say it is a fault of the regulation, but it is a problem with it.

**Viscount Ridley:** It is not well future-proofed?

**Professor John Mumford:** No, and it is one of the things we tried to explain in the EFSA guidance.

**Lord Maxton:** I am not quite clear on this. You give scientific, technical advice, or that is given, but no decision. How many times has your advice been ignored by those who take the decisions?

**Professor John Mumford:** Nobody has made an application, other than on the olive fly in Spain, that is related to GM insects.

**Lord Maxton:** No one else has come to you so far?

**Professor John Mumford:** In Europe, yes. It has been different in other places. We have had releases and acceptance of releases in Brazil, trials in cages in the US and releases in the open for mosquitoes in a number of other countries.

**Q46 Duke of Montrose:** Much of the GM insect technology is focused on mosquitoes because of the various human diseases which come from mosquitoes. Have the difficulties encountered there led to work being put off work on other insect problems, such as tsetse fly and other tropical diseases? Is there much going on in GM technology?

**Professor Paulo Paes de Andrade:** At least in my country there is a lot going on in mosquito control based on GM technologies, but we are certainly behind England now. We do not expect to have a product in the near future, at least not for mosquitoes, but we may have for other animals, especially fish.

**Viscount Ridley:** What kind of fish?

**Professor Paulo Paes de Andrade:** It is freshwater fish, which is edible, not salmon but another fish. It is a Brazilian fish. It is more difficult for us. It would be better to have just salmon because it is not Brazilian—it is not even from the South Atlantic—so we can leave it free; it does not matter. The Brazilian fish is more complicated.

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**Viscount Ridley:** You are not trying to suppress the population of fish; you are trying to encourage it?

**Professor Paulo Paes de Andrade:** Not at all. We want the opposite; we want to encourage the population.

**Professor John Mumford:** There are applications of GM fish, though, to control invasive fish. In Australia, for example, there has been interest in the use of GM carp to control wild, invasive carp.

**Viscount Ridley:** We will come to this later in the inquiry, but is the use of this technology for dealing with invasive species promising, distant or a big part of the story? It is obviously not a health issue but it is quite an important ecological issue.

**Professor John Mumford:** It certainly has some potential. The invasive species are, like everything else in the environment, very variable, and it depends on the timing of them. Some of the GM technologies that are being considered require concentrations of a population to control; it would depend whether the invasive species were widely spread or focused. It may depend on whether they were intermittent. Many invasive species have very, very low stages in their population and then surge seasonally. Those kinds of populations may not be particularly well suited to a biologically based approach.

**Q47 Lord Patel:** My question is about the developing science and the regulatory framework that will be required for the benefits of this science to be harnessed. The US National Academy of Sciences has set up a committee to look at the state of the genomic science now—technology such as gene drive and gene editing, using technologies such as CRISPR, which is used to gene edit, which could actually end up applying to humans, but let us not go there just now. Do you think the UK, to inform those concerned with regulation and those who might be concerned with public involvement too, should set up such a committee to assess the state of the science and where it is likely to go?

**Dr Jack Stilgoe:** I am a former employee of the Royal Society's Science Policy Centre, which would be the obvious place to locate such an equivalent. The magic of such exercises tends to be in how they are framed. The National Academy has taken an approach of looking at this issue beyond just the immediate problem, or an immediate suggested solution, and looking more broadly at the issue of genome editing, particularly germline editing, and I can see the wisdom of that. The Royal Society's contribution in the last couple of decades has been to be a broader source of expertise than the National Academy's, and I think it does that job extremely well. The question would be whether one starts from a problem, and one might want to start with the problem of disease control, or whether one looks at a particular, suggested technological solution of concern and starts the inquiry from there. I do not think there is any easy answer to that question. Similarly, as I have said before, there are plenty of lessons that can be learned from similar inquiries and efforts that are going on elsewhere by the Nuffield Council and others.

**Lord Patel:** We are likely to end up in a situation where the science—let us focus on GM insects just now—is the same; the gene drive, gene editing, is the technology that is used for GM modification of insects. When it comes to public understanding of whether this science is harmful or not or whether it can be beneficial, both to crops and human health, the regulation will thwart any further development, as we heard in the last evidence session. Do

Professor Paulo Paes de Andrade, Federal University of Pernambuco, Brazil, Professor John Mumford, Imperial College London, and Dr Jack Stilgoe, University College London – Oral evidence (QQ 39-47)

we need to be ahead of that and, as the US National Academy of Science has done, inform them of what the science is likely to deliver?

**Dr Jack Stilgoe:** I think there is, as I say, value in doing those sorts of exercises. I think they work best when one does not presume in advance what the public understanding of the issue is or what the public fears are. Instead, you go out and ask people. That I think should be a part of any good inquiry, and that is something that the Royal Society and other organisations have been doing now for decades, and doing it very productively.

**The Chairman:** Professor Mumford, do you agree with that reply?

**Professor Paulo Paes de Andrade:** May I add some words on that?

**The Chairman:** Yes.

**Professor Paulo Paes de Andrade:** I think that the scientific discussion is very welcome but that scientists are not the right people to talk about risk communication; they are usually very bad communicators indeed. What happens is that they discuss among themselves, they come to conclusions and they put out nice words, but words that sometimes cannot be completely understood by the general population. Moreover, they are not risk assessors, so if they meet to discuss risks they possibly will make bad mistakes. I really encourage scientific discussion but I do not agree that scientists should discuss risks by themselves. They should sit together with experienced regulators to learn from them how to do risk assessment before stating whether or not something is risky.

**Lord Peston:** I accept that, in a democracy, we have to have meaningful public involvement. I accept that as a Member of the House of Lords, which is totally undemocratic. My worry is that most members of the general public have no idea of the concepts of risk or uncertainty—the great Frank Knight distinction; uncertainty being the really hard one, because it essentially amounts to “the unpredictable always happens”—let alone that the general public believe that if you toss a coin, and it is a fair coin, and it comes up three heads in a row, the probability of it coming tails next time has gone up. What worries me enormously is, why do we have experts if we have to consult the public on matters where they simply do not understand what the problem is in the first place? Dr Stilgoe, I am addressing you because you know a lot about all this. I know we have to bring the public in somewhere but, wearing my professorial hat, I am very worried about what they can say other than: “We are worried”.

**Dr Jack Stilgoe:** The quick answer—as I said, this runs the risk of being another degree course—would be that the reason why one needs to talk, and should talk, to people outside conventional experts is that people are experts in different things. As my former boss, Lord Rees, former member of this Committee, was fond of saying: “Experts are depressingly lay outside their own specialisms”. Also, when it comes to matters of GM insects, they are not simple, technical problems. They are riven through with all sorts of political questions which are actually legitimate points of public discussion and should be rightfully informed by expertise. However, the idea that any single or even group of experts will be able to come up with a complete understanding, let alone a complete understanding that determines a decision, I think, is just a misunderstanding of science.

**Lord Peston:** I am not disagreeing with you. I get things wrong, and have done all my career to an enormous extent. In fact, mostly my wife will tell you if I say what is going to happen, bet against that if nothing else. If you take a different field, such as pharmaceuticals, where



Professor Paulo Paes de Andrade, Federal University of Pernambuco, Brazil, Professor John Mumford, Imperial College London, and Dr Jack Stilgoe, University College London – Oral evidence (QQ 39-47)

all these sorts of problems arise and we have very strict regulations, on the whole we do not seem to get the public involved. Why is this area different?

**Dr Jack Stilgoe:** I would say there are all sorts of channels of public involvement throughout all sorts of regulations.

**The Chairman:** Lord Patel, I think you wanted to finish off your area of questioning.

**Lord Patel:** It was not directly related but I wanted to ask Professor Andrade whether they have used GM insects to increase sugar cane crops in Brazil.

**Professor Paulo Paes de Andrade:** GM technology for sugar cane?

**Lord Patel:** Yes, insect modified.

**Professor Paulo Paes de Andrade:** Insect modified?

**Lord Patel:** Yes.

**Professor Paulo Paes de Andrade:** Not yet. I do not know of anyone working on that.

**The Chairman:** Thank you all very much for your evidence; we are very appreciative of it. We are particularly grateful to Professor Andrade for having come a long way to help us. I do not know if any of you have any final comments you want to make. If you think of something after the meeting you wish you had said, please send it in; otherwise, we will draw to a close. Thank you very much indeed.

## The Pirbright Institute – Written evidence (GMI0019)

1. The use of genetically modified insects, whether via population suppression or population replacement, represents a potentially valuable tool to add to the arsenal of control strategies available for the control of human disease. It is most suitable for use where all of the following conditions are met:
  - a. One species of insect is exclusively or almost exclusively responsible for transmission, because the technique only directly affects the target species.
  - b. The insect vector can be readily reared and mass-reared in captivity.
  - c. Only one sex is responsible for the impact of the insect species. Captive-reared insects may exhibit reduced mating fitness compared to wild populations and so high numbers of modified insects must initially be released. This may itself increase the species' impact in the short term if this condition is not met.
2. Suppression of the target species could theoretically have secondary ecological effects by removing (possibly unrecognised) beneficial effects of the species, for example by occupying an ecological niche that could be replaced by a species capable of causing greater problems, or by representing a necessary food source for species performing valuable ecosystem services. However, in practice many important mosquito vectors of disease are invasive species and this risk is low for such species as they are recent arrivals.
3. High impact human diseases which also have a high potential to be substantially reduced in impact by the appropriate use of these approaches include dengue, Japanese encephalitis, chikungunya, yellow fever, and lymphatic filariasis. Outbreaks of dengue and chikungunya have recently occurred in Europe. It is unlikely that the *Aedes* mosquitoes which transmit the pathogens causing these diseases could establish successfully in the UK, although introduced populations may survive for short periods (and were responsible for the only recorded outbreak of yellow fever in the UK (in Swansea in 1865).
4. Globally, some potential livestock applications of GM insect technology include control of nuisance insects causing direct impact via blood loss and stress, for example *Stomoxys* stable flies. The north American bluetongue vector species *Culicoides sonorensis* may also represent a suitable target.
5. The use of insects modified by GM technology, exposure to radiation or modification of bacterial symbionts provides opportunities that cannot be provided by other approaches and complement other control technologies. GM modification offers a more robust, predictable and controllable method of insect modification than either radiation or the modification of bacterial symbionts.
6. Caution is required when deploying such technologies that any subpopulation differences in the vector species are understood, as differential suppression of a subpopulation could change the epidemiology of the disease. For example, suppressing a subpopulation with increased preference for indoor biting would increase the proportion of transmission occurring outdoors, as has occurred with differential suppression (via other control techniques) of *Anopheles* malaria vector mosquitoes.

7. Current UK and EU regulatory frameworks are primarily designed with GM plants in mind, and do not really reflect the difference in risks associated with the release of modified insects. Among these differences are the fact that transgenic insects are not intended for consumption and generally cannot enter the food chain directly, and also that horizontal gene transfer is extremely rare or absent in insects, whereas it is common in some plant species. The current UK and EU approach to GM product licensing is based around consideration of risk rather than a risk-benefit analysis and also assessments of the risk associated with technologies rather than other aspects.

8. Currently, funding for research in this area is a mixture of competitive public-sector, private sector investment and industrial partnership awards. The benefits of using GM insects for the control of disease are likely to be felt as a public good rather than benefiting a specific stakeholder. In many cases the greatest potential beneficiaries (i.e. those bearing the greatest burden of vector-borne disease) are poor or in developing areas of the world. As such I believe government involvement would be sensible. There would be no greater conflict of interest than currently exists in reviewing medical

9. A recent public discussion of the use of these technologies in London in February (report available at

[http://www.pirbright.ac.uk/Pub\\_Engage/docs/GM%20insects%20event%20report.pdf](http://www.pirbright.ac.uk/Pub_Engage/docs/GM%20insects%20event%20report.pdf))

suggested that public support for the use of GM technologies, particularly for the control of human disease, is higher than might be expected from high-profile media reports on opposition to GM crops by a small number of individuals. Public concern about the use of GM is lower for products that do not enter the human food chain. In addition, a major aspect of public concern about the use of GM products relates to concern about the extent to which such technologies facilitate unethical practices by large corporations. Responding to perceptions of public concern by increasing the burden of regulation of GM technologies has the potential to exacerbate this problem. Before any actions are taken based on a perception of public concern over the use of GM insects for disease control, two questions need to be answered: firstly, to what extent is the general public concerned about this use? Secondly, is this concern about the technology itself or the potential for its abuse by the private sector?

*18 September 2015*

## Dr Rupert Read, University of East Anglia – Written evidence (GMI0002)

1. My name is Dr Rupert Read. I am chair of the Green House think tank and a philosopher writing, as part of a cross-disciplinary group that includes Nassim Taleb (author of THE BLACK SWAN), about the risks of GMOs from a statistical perspective. Our recent paper, entitled 'The Precautionary Principle (with Application to the Genetic Modification of Organisms)' outlines more comprehensively our position towards GMOs, and I would encourage the Committee to read it fully and consider the argument before compiling your report. A link to it can be found at this web-address: <http://arxiv.org/pdf/1410.5787v1.pdf>. I am writing primarily to answer question 4 in your list in your call for evidence, and to address an issue that is unfortunately not present in your list, as I will explain:

2. In our paper on the Precautionary Principle and GMOs, we argue that traditional risk management analysis is not applicable in cases where there is a risk, however small, of 'ruin'. 'Ruin' is a term that is used for irreversible, non-geographically localised damage. An obvious example of 'ruin' would be ecocide brought about through human-triggered climate change or nuclear war. In these instances, even if one calculates a very small probability of 'ruin', and a large probability of societal gain, it is still the wrong decision to go ahead with the risk. We argue that society is not used to computing the risks of 'ruin' because of our lack of experience when it comes to existential risks. However, due to humanity's increasing ability to affect our environment in ever more drastic ways, the possibilities for 'ruin' are much more prevalent today than ever before and therefore we need to adapt our risk management strategy accordingly (See point 5, below). This is *particularly*, so, in cases where there cannot be a strictly meaningful numerical calculation of the risk involved, due to endemic epistemic uncertainties.

3. We argue that GMOs fall into the category of risking ruin due to their uncontrollability when released into non-contained environments, the difficulty of keeping particularly virulent GMOs even within partially-contained environments, and the possibility of GMOs mixing with non-GM varieties and causing new and dangerous mutations or even species, and the endemic uncertainties in the engineering procedures involved (Much has been learnt in recent years for example about how gene-expression often exceeds the knowledge that geneticists have of the genes they are observing or manipulating). The risks we identify map directly onto GM insects, as well as crops, although I should note that with insects the risk of 'global' consequence is obviously higher, as the restriction of insects to one geographic region is much harder. Scenarios such as 'terminator'-style genes spreading outside the intended domain of application, or of insect equivalents to 'super-weeds' (see e.g. <http://www.sciencemag.org/content/274/5285/180.short>), or of pure 'black swans' (or, as it were 'black mosquitos' etc.) are non-calculable (Their probability, while we might reasonably estimate it as 'low', cannot be numerically pinned down), making silent risks, hidden dangers, present within the introduction of GM insects particularly salient.

4. It is often levelled at those sceptical of GMOs that we need to provide empirical evidence of danger, but our paper illustrates that, in cases of potential 'ruin', the onus must be on those proposing the risk to provide evidence that the risk does not encompass the possibility, however small, of 'ruin'. This is because often the way in which evidence of

danger is gathered is through past experience of damage caused. In cases of 'ruin' this is obviously not desirable, as, by the time one collects this evidence, there will not be an opportunity to later adapt our risk management strategy accordingly... Our 'Precautionary Principle' bridges the gap between lack-of-evidence and policy-outcome by using the distinction between 'local' (acceptable, amenable to cost-benefit-analysis etc.) and 'global' (potentially-ruinous) risks. Because of the uncontainability factor of GM insects, the impact is global and therefore there must be firm and irrefutable evidence of their safety before they are utilised. Such evidence is not available yet, and indeed it is difficult to see how it could become available in the foreseeable future (See point 6, below).

In other words: my argument is that the idea of being 'evidence-based' in the form in which that idea is most commonly understood at present is inadequate, and in particular that an approach to the question of GM insects that was 'evidence-based' only in the sense of looking for evidence of harm from GM insects would be gravely inadequate. Absence of evidence of harm is not evidence of absence of harm. Evidence of absence of harm is what ought to be sought, and comprehensively so; in the absence of it, the Precautionary Principle should be invoked, and research on GM insects outside very strictly controlled laboratory environments ought to be prevented.

5. So: The potential global impacts of uncontained GM Insects make them one strong candidate for being halted until investigated very thoroughly (and very cautiously) indeed. The other reason for scepticism comes from an empirical observation that risk of 'ruin' is unlikely to happen to slowly evolving ecosystems. Historically ruinous events generally have exogenous catalysts from ('outside') ecological systems, such as extreme volcanic instability or asteroid hits. However, the greatest threats of 'ruin' that exist today come through top-down human manipulations, which in effect mimic such exogenous catalysation: quick advances in technology that have been implemented before being thoroughly risk-examined (I.e: climate change (and geoengineering), nuclear proliferation and GMO/GM Insects would be key cases). This is what differentiates GMOs from selective breeding, a technique used for thousands of years by farmers. It is the scale of the advance that makes GMOs more dangerous, as we cannot gradually see the consequences (as we can through selective breeding) in order to adjust our modifications accordingly. It is these features that make GMOs — in this case, GM Insects — a legitimate candidate for the application of the Precautionary Principle.

6. In summary, my argument can be distilled into two key points: 1) When there is legitimate suspicion of risk of 'ruin', however small, one should not proceed to undertake the risk. 2) GMOs and GM insects fall into the category of warranting legitimate concern of potential risk of 'ruin'. Because of the concerns above outlined, I believe that current legislation and regulation is not adequate in the UK for GMOs and that, unless a radically more stringent criterion is added for GM insects, we should not be proceeding to research and deploy them. The only exception I would make is for research in such highly-contained laboratory environments that there is no risk of contamination of the natural environment. (For a list of rejoinders to common objections to the position I have outlined please see the end of the paper which I have linked at the beginning of this evidence submission.)

*18 August 2015*

## Research Councils UK (RCUK) – Written evidence (GMI0017)

**Research Councils UK (RCUK)** is the strategic partnership of the UK's seven Research Councils. Our collective ambition is to ensure the UK remains the best place in the world to do research, innovate and grow business. The Research Councils are central to delivering research and innovation for economic growth and societal impact. Together, we invest £3 billion in research each year, covering all disciplines and sectors, to meet tomorrow's challenges today. Our investments create new knowledge through: funding research excellence; responding to society's challenges; developing skills, leadership and infrastructure; and leading the UK's research direction. We drive innovation through: creating environments and brokering partnerships; co-delivering research and innovation with over 2,500 businesses, 1,000 of which are SMEs; and providing intelligence for policy making. Find out more about our work at [www.rcuk.ac.uk](http://www.rcuk.ac.uk)

This evidence is submitted by the Research Councils and represents their independent views. It does not include, nor necessarily reflect the views of the Knowledge and Innovation Group in the Department for Business, Innovation and Skills (BIS). The submission is made on behalf of the following Research Councils:

- Biotechnology and Biological Sciences Research Council (BBSRC)
- Medical Research Council (MRC)
- Natural Environment Research Council (NERC)

### EXECUTIVE SUMMARY

Insects are responsible for a significant proportion of vector-borne infectious diseases of humans, animals and plants as well as being significant herbivorous pests of plants in their own right. Other than the uses of pesticides in agriculture, no effective large-scale control measures exist currently to reduce or prevent the spread of such diseases. As the UK Parliamentary Office of Science & Technology noted in 2014<sup>107</sup>, several non-endemic viral diseases that are spread by biting insects pose a risk to UK and mainland Europe livestock. This is due to climate change and other factors such as globalisation and trade. In agriculture and livestock production, even single outbreaks of insect-borne diseases can have significant economic impact. Insect-borne disease in humans is also a major and persistent challenge across the world and increasing in several instances.

Controlling disease-transmitting insects is already part of the existing global strategy for vector-borne diseases. GM insect technology offers a targeted alternative to the less specific control measures (mostly chemical agents) used currently for insect control and also to the often challenging route of developing vaccines for the diseases that insects transmit.

GM insect technology developed in the UK could contribute to the development of our national capability in plant and animal health, and our 'bioeconomy'. The world faces challenges in feeding a growing a population, climate change and scarcity of natural

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<sup>107</sup> <http://www.parliament.uk/documents/post/postpn360-gm-insects.pdf>

resources. Research and innovation will be key to meeting such ‘grand challenges’ and we will need every tool at our disposal to tackle the increasing threat of insect pests to human and animal health and our food supply. GM is not a panacea; there will be situations in which GM is the best approach to combating insect pests or insect-borne disease, situations where other approaches are more appropriate, and situations requiring a combined approach as part of an integrated pest management or disease prevention strategy.

Aspects of GM insect research are within the respective remits of BBSRC, MRC and NERC. We have invested in such research through our usual competitive routes, from GM insects as a technology to the use of GM insects to investigate other research targets. We also support underpinning research such as understanding how GM insects would survive and function in the natural environment. The Research Councils are supportive of a responsible innovation approach and have utilised such approaches. We believe that public engagement should aim to inform research so that it advances in a way that takes account of public views and values, towards research outcomes that are aligned with social needs and increased confidence and trust in science.

The range of biotechnology tools available to make genetic changes in living organisms is moving faster than the current regulatory system can accommodate. Appropriate regulation is important for ensuring that risks are well managed. We are committed to ensuring that research has routes to achieve its potential impact and welcome regulation that does not needlessly restrain research, innovation and application. A fit-for-purpose regulatory system needs to have safety at its heart, but at the same time be research evidence-based, proportionate and allow potential risks and potential benefits to be balanced.

**Q1. Which human diseases, across the world, could be addressed through GM insect technology? Are there any human disease risks in Europe, particularly the UK, for which GM insects are under development?**

1. Vector-borne diseases account for 17% of the estimated global burden of all infectious diseases<sup>108</sup> (humans and animals). Most of these are transmitted by insects and no effective large-scale control measures exist currently.
2. GM insect technology has potential to interrupt the spread of many such diseases by controlling the disease vector; it offers a targeted alternative to developing vaccines, which can be a particularly challenging route towards the prevention of some diseases<sup>109</sup>. According to the WHO, drawing on the experiences of other vaccine-preventable vector-borne disease, effective surveillance, prevention and outbreak response tools (vector control and vaccines) must continue to complement each other in reducing the burden of the disease<sup>110</sup>.

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<sup>108</sup> <http://www.who.int/campaigns/world-health-day/2014/vector-borne-diseases/en/>

<sup>109</sup> For example malaria: <http://www.who.int/malaria/areas/vaccine/en/>

<sup>110</sup> See <http://www.who.int/mediacentre/factsheets/fs387/en/> and an example at <http://www.denguevaccines.org/why-a-vaccine>

3. Notable examples (but not a complete list) of human diseases to which GM insect technology could be applied are given below (alphabetical order) with further details at **Annex 1** of this response:
  - **African trypanosomiasis (sleeping sickness):** Caused by trypanosome (protozoan) parasites; transmitted by tsetse flies.
  - **Chagas (American trypanosomiasis):** Caused by *Trypanosoma cruzi* (a protozoan) parasite; transmitted by the triatomine bug.
  - **Chikungunya:** caused by a virus; transmitted by mosquitoes.
  - **Dengue fever:** caused by a virus; transmitted by mosquitoes.
  - **Japanese encephalitis:** caused by a virus; transmitted by mosquitoes
  - **Leishmaniasis:** caused by protozoan parasites *Leishmania* species; transmitted by sandflies.
  - **Lymphatic filariasis:** caused by a filarial parasite; transmitted by mosquitoes.
  - **Malaria:** caused by *Plasmodium* (protozoan) parasites; transmitted by mosquitoes.
  - **West Nile Fever:** caused by a virus and found naturally in birds; transmitted as a zoonosis to humans by mosquitoes.
  - **Yellow fever:** caused by a virus; transmitted by mosquitoes.
4. The geographic range of many insect disease vectors has increased over recent decades, due to factors such as climate change and globalisation, so that some non-endemic diseases now pose an imminent threat to Europe. For example, there are currently five invasive *Aedes* mosquito species known to be established in Europe<sup>111</sup>, of which two species implicated in the recent outbreaks of chikungunya and Dengue fever in Europe; laboratory and field observations indicate that they have the potential to also transmit other pathogens of public health importance<sup>112</sup>. Insecticide resistance in disease vectors is also an increasing problem, for example as cited by the WHO for malaria-carrying mosquitoes, which if left unchecked, could lead to a substantial increase in malaria incidence and mortality<sup>113</sup>.
5. The most notable human disease risk in Europe for which GM insects are under development is Dengue fever. GM insect technology is already available for Dengue transmitting mosquitoes and works by producing and releasing sterile males. It was developed by the UK company Oxitec<sup>114</sup>, based upon fundamental research supported by BBSRC, The Wellcome Trust and the Gates Foundation<sup>115</sup>. Field trials have seen a >90% reduction in numbers of the target species in the Cayman Islands and a 96% reduction in Brazil, which researchers believe is enough to prevent endemic Dengue fever anywhere in the world<sup>116</sup>.

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<sup>111</sup> Namely *Aedes albopictus*, *Aedes aegypti*, *Aedes japonicus*, *Aedes atropalpus* and *Aedes koreicus*.

<sup>112</sup> <http://ecdc.europa.eu/en/healthtopics/vectors/world-health-day-2014/documents/public-health-importance-mosquitoes.pdf>

<sup>113</sup> [http://www.who.int/malaria/areas/vector\\_control/insecticide\\_resistance/en/](http://www.who.int/malaria/areas/vector_control/insecticide_resistance/en/)

<sup>114</sup> <http://www.oxitec.com/>

<sup>115</sup> <http://www.pirbright.ac.uk/FrontStories/2014/Innovatoroftheyearfinal.aspx>

<sup>116</sup> <http://www.bbsrc.ac.uk/news/people-skills-training/2014/140414-f-innovators-pt1-alphey/>



**Q2. What are the possible livestock and agricultural crop applications of GM insects across the world? Of current livestock disease risks and agricultural insect pests that could be addressed through GM Insects, which should be the highest priority for Europe?**

6. Since many economically important crop and livestock pathogens are transmitted by insects, and insects are important herbivores, the range of potential applications of GM insects for pest and disease control is wide. Failure to control diseases can have a significant economic impact, one of the issues that led to the Government Chief Scientific Adviser and the Defra Chief Scientific Adviser publishing a report in 2014 on building our national science capability in animal and plant health<sup>117</sup>.

Some current key threats to livestock (including aquaculture) and horses

- **Bluetongue:** a viral disease of cattle and sheep; transmitted by biting midges.
- **Equine infectious anaemia:** a viral disease; transmitted by large biting flies.
- **Infectious salmon anaemia:** a viral disease; transmitted by sea lice.

Other potential threats (in no particular priority order)

- **African horse sickness:** a viral disease; transmitted by biting midges.
  - **Bovine ephemeral fever:** a viral disease of cattle; transmitted by mosquitoes.
  - **Epizootic haemorrhagic disease:** a viral disease of cattle and sheep; transmitted by midges.
  - **Equine encephalosis:** a viral disease; transmitted by midges.
  - **Lumpy skin disease:** a viral disease of horses; biting insects implicated in transmission.
  - **Rift Valley fever:** Caused by a virus; can be transmitted to humans as a zoonosis by blood-feeding insects.
  - **Schmallenberg disease:** a viral disease of cattle and sheep; transmitted by biting midges.
  - **Sheep pox virus; goat pox virus:** viral diseases; indirect transmission by insects.
7. Even individual incidents of insect-borne diseases can have significant economic impact; for example, BBSRC-funded research at the Pirbright Institute<sup>118</sup> has prevented Bluetongue disease becoming endemic in UK sheep and cattle, which is estimated to have saved the British economy £480M in 2008 alone<sup>119</sup>. While this did not require GM insects, future outbreaks of other insect-borne diseases will require a range of potential solutions at our disposal (see our response to **Question 3**), and have the potential to prevent significant economic loss.
8. Insect pests and disease vectors affecting **agriculture** are numerous and include moths, aphids, whitefly, thrips, leafhoppers, and borers<sup>120</sup>. Some aphid species, for example,

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<sup>117</sup> <https://www.gov.uk/government/publications/animal-and-plant-health-in-the-uk-building-our-science-capability>

<sup>118</sup> [http://www.pirbright.ac.uk/Disease/BT\\_aw.aspx](http://www.pirbright.ac.uk/Disease/BT_aw.aspx)

<sup>119</sup> DTZ, The economic and social impact of the Institute for Animal Health's work on Bluetongue disease (BTV-8) – <http://www.pirbright.ac.uk/ecosoc/docs/Blue-Tongue-case-study.pdf>

<sup>120</sup> <http://www.ecpa.eu/page/insects-animals>

are capable colonising over 400 different plant species and transmitting over 100 plant viruses, which causes major agricultural losses<sup>121</sup>.

9. There is no specific priority list of insect pests or vectors for pathogens for the Research Councils: it is important that research is targeted at a range of insect pests and vectors.
10. Some examples of agricultural pests and insect-borne crop diseases around the world are listed below. Not all of these are necessarily targets for current GM insect technology, and there may be technical difficulties to overcome for vector species such as aphids, which reproduce by parthenogenesis.
  - **Diamondback moth:** the biggest global pest of brassica crops and one of the world's significant agricultural pests, costing farmers billions of dollars every year<sup>122</sup>.
  - **Desert Locusts:** found in Africa, the Middle East and Asia. When swarming, locusts can travel 5-130km or more a day<sup>123</sup> and feed on nearly all crops, consuming roughly their own weight in fresh food per day<sup>124</sup>. Agriculture is threatened when they transition from a solitary phase to a swarming phase, triggered by crowding.
  - **Corn root worm:** one of the most devastating pests in North America, affecting maize. The US Department of Agriculture has previously estimated that the damage caused by the pest and costs associated with controlling it typically totals \$1 billion annually<sup>125</sup>.
  - **Colorado potato beetle:** attacks potato foliage and has developed resistance to all major insecticide classes. It is distributed throughout North America and has also invaded areas of Europe and Asia.
  - **Rice gall midge:** is a serious insect pest of rain-fed and irrigated rice in Africa and Asia. In India, crop losses of 10-100% have been recorded<sup>126</sup>.
  - **Black coffee twig borer:** leads to the loss of coffee berries. The disease has also been identified in about 50 plant species, particularly mangoes, jackfruit, eggplant, guavas, tomatoes, avocados, bitter balls and cocoa.
  - **Green peach aphid (GPA):** this is the most significant aphid pest of peach trees. It is also a vector for the transport of plant viruses such as potato virus Y and potato leafroll virus.

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<sup>121</sup> <http://www.cabi.org/isc/datasheet/35642>

<sup>122</sup> <http://www.oxitec.com/agriculture/our-products/diamond-back-moth/>

<sup>123</sup> <http://www.fao.org/ag/locusts/oldsite/LOCFAQ.htm#q7>

<sup>124</sup> <http://www.fao.org/ag/locusts/en/info/info/faq/>

<sup>125</sup> <http://www.monsanto.com/products/pages/corn-rootworm-background.aspx>

<sup>126</sup> <http://www.bulletinofinsectology.org/pdfarticles/vol61-2008-277-281lingaraj.pdf>

- **Spotted Wing Drosophila (SWD):** this is a major threat to soft fruit, stone fruit, tomatoes, vines and other crops and could cause serious losses if not controlled. SWD originated in Asia and has been identified in the UK since September 2012<sup>127</sup>.
- **Whitefly:** infests all types of brassicas, leading to losses, with kale and Brussels sprouts particularly affected in the UK<sup>128</sup>. Whitefly are also hosts of Begomoviruses and can transmit them into plants.
- **Asian long-horned beetles:** can result in the death of severely infested trees. Adult beetles feed on leaves, twigs and other plant matter, whilst larvae can cause damage by tunnelling into the wood.
- **Mediterranean fruit fly:** now spreading worldwide, a pest of fruit crops.
- **Barley yellow dwarf virus (BYDV):** Transmitted by green aphid and bird cherry aphid vectors into barley, wheat, oats and maize. BYDV is the most widely distributed viral disease of cereals.
- **Plum pox virus:** Transmitted by infected rootstocks, budwood and aphids from infected hosts into stone fruit species. The yield of affected trees may be reduced by 20 to 30%<sup>129</sup>.
- **Potato leafroll virus (PLRV):** Transmitted by aphid vectors into potatoes. In affected plants, losses in yields of over 50% are common<sup>130</sup>.
- **Potato potyvirus Y (PVY):** Transmitted by aphid vectors into potatoes.
- **Turnip yellows virus (TuYV):** Transmitted largely by the peach-potato aphid and infects oilseed rape. Research has indicated that TuYV could decrease yields of oilseed rape by up to 26%<sup>131</sup>.

**Q3. Are there likely to be opportunities provided by GM insects that cannot be provided by other approaches, such as biological control methods? How could GM insect approaches be complementary to existing Integrated Pest Management (IPM) programmes?**

11. As stated above, GM insects are not a panacea; there will be situations in which GM insects offer the best approach, situations where other approaches are more appropriate ('low' and 'high' tech), and situations requiring a combined or integrated approach.

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<sup>127</sup> [http://www.hdc.org.uk/sites/default/files/14\\_14%20Spotted%20wing%20drosophila%20\(SWD\)%20-%20Code%20of%20practice%20for%20packhouses.pdf](http://www.hdc.org.uk/sites/default/files/14_14%20Spotted%20wing%20drosophila%20(SWD)%20-%20Code%20of%20practice%20for%20packhouses.pdf)

<sup>128</sup> <http://horticulture.ahdb.org.uk/project/brassicas-improving-control-whitefly>

<sup>129</sup> [www.fera.co.uk/plantClinic/documents/factsheets/plumpox.pdf](http://www.fera.co.uk/plantClinic/documents/factsheets/plumpox.pdf)

<sup>130</sup> <http://jbaseedpotatoes.co.uk/info/potato-pests-and-diseases/leaf-roll-potato-virus/>

<sup>131</sup> <http://www.cereals.ahdb.org.uk/media/269200/rr69.pdf>

12. Opportunities provided by GM insects where other methods may be less effective include:

- **A targeted alternative to non-GM radiation insect sterilisation techniques:** Radiation sterilisation of male mosquitoes damages them and affects relative competitiveness with non-sterilised males to the extent that the method is currently deemed to be ineffective<sup>132</sup>. The GM approach produces sterile males that are otherwise viable and competitive within a population.
- **A more targeted alternative to non-specific chemical insecticides:** There are concerns about the impacts of insecticides on non-target species, environmental persistence and resistance in target species. The rationale for GM approaches is that they target single insect pest or vector species, leaving beneficial insects unharmed and reducing the amount of chemicals needed.
- **Enhancing bio-control:** Biological control approaches<sup>133</sup> are sometimes described as being slow to achieve results and may not achieve significant reduction of pest populations. GM approaches (particularly sterile males) can exploit insects' natural propensity to find one another so that pest populations inaccessible to traditional control methods could be suppressed<sup>134</sup>.

13. Research is underway for transferring Oxitec's GM technology to agricultural pests<sup>135</sup>; there may also be scope to also extend it to insect vectors of livestock or zoonotic diseases, for example in midges to prevent the spread of particular exotic variants of Bluetongue virus across Europe.

**Q4. How appropriate are current EU and UK GMOs regulatory frameworks in addressing the issues raised by GM Insects? Are there lessons to be learnt from the regulation of GM insects in other countries such as Brazil?**

14. The Research Councils recognise that appropriate regulation is an important way to ensure that risks are well managed. We are committed to ensuring that the research we fund has routes to achieve its potential impact and we welcome regulation that does not needlessly restrain research, innovation and application. A fit-for-purpose regulatory system needs to have the safety of human health and the environment at its heart, but at the same time be evidence-based, proportionate and allow for balancing of potential risks and potential benefits.

15. As Research Councils, we do not have first-hand practical experience of the EU GM regulatory framework but, as written, Directive 2001/18/EC on the deliberate release of genetically modified organisms<sup>136</sup> should in principle provide an adequate framework for GM insects. The Directive makes provision for evidence-based risk assessment for

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<sup>132</sup> <http://www.oxitec.com/health/florida-keys-project/>

<sup>133</sup> <http://www.journals.elsevier.com/biological-control/>

<sup>134</sup> <http://www.parliament.uk/documents/post/postpn360-gm-insects.pdf>

<sup>135</sup> <http://www.oxitec.com/agriculture/>

<sup>136</sup> <http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32001L0018>

potential harm to human health and the environment from the release of a GMO and can mandate post-release monitoring. Member States are also able to prohibit use of particular GMOs on their territories, although this might prove problematic in the case of highly mobile GM insects that will not respect national borders. Some commentators consider it a shortcoming of the current Directive that there is little or no scope to consider or balance ‘benefit’ of a GMO as part of the regulatory process, which focuses only on risk.

16. On a wider regulatory point, the range of biotechnology tools available to make genetic changes in living organisms is moving faster than current regulatory systems can accommodate, e.g., the range of new so called ‘gene editing’ technologies. There is a case worthy of further discussion that regulatory systems should be based on the specific trait (or phenotype) of the organism concerned and not on the method of its production<sup>137</sup>.

**Q5. Do the World Health Organisation (WHO) guidelines on the release of mosquitoes provide the basis of an effective regulatory framework? How should issues regarding the emergence of resistance be considered?**

17. We cannot comment on the WHO guidelines, as they are outside our frame of technical specialisation and expertise as Research Councils.

**Q6. Do the European Food Safety Authority (EFSA) guidelines on the environmental risk assessment of GM Insects for commercial use sufficiently address the different risks from population suppression and population replacement approaches? How should the ecological risks and human benefits that might arise from the application of gene drive techniques to population replacement approaches be assessed?**

18. We cannot comment on the EFSA guidelines, as they are outside our frame of technical specialisation and expertise as Research Councils.

**Q7. How is research into the development of GM insects currently funded? Are there opportunities to attract more private investment into this area?**

19. Research on GM insects is funded through public (e.g., the Research Councils) and private routes (e.g., the Wellcome Trust<sup>138</sup>, as well as industry). Various aspects of such research are within the respective remits of BBSRC, MRC and NERC; research grant applications are accepted via the Councils’ normal routes for funding, such as open Responsive Mode calls. Grant applications that have elements of GM insect work will be assessed in open competition with applications from other research areas; funding success is based primarily on the quality (excellence) of the research proposed.
20. The Research Councils fund basic research to understand vector biology, vector-host-pathogen interactions and development of novel tools and technologies that underpin

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<sup>137</sup> For example as BBSRC states in the case of plants and crops:

<http://www.bbsrc.ac.uk/news/policy/2014/141028-pr-position-statement-on-crop-breeding-techniques/>

<sup>138</sup> [http://malaria.wellcome.ac.uk/doc\\_WTD023971.html](http://malaria.wellcome.ac.uk/doc_WTD023971.html)

development of intervention strategies for emerging and resurgent threats. **Annex 3** provides a high-level summary of current investments from the three Councils that are relevant to GM insects. Points to note include:

- **BBSRC** total spend on research related to GM insects over the five financial years 2010/11 to 2014/15 was £10.5M, but the majority of this is research that uses GM insects as model organisms to explore fundamental biology questions such as understanding genetics or cellular processes. BBSRC's total spend on agricultural research in this period was over £500M.
- **MRC** has spent £0.5M on two projects relating to the development of GM insects between the FYs 2010/11 and 2014/15. Both awards were for research on mosquitoes and malaria control, investigating how fertility can be manipulated to control field mosquito populations and determining the optimal strategy for a field trial of GM mosquitoes (total awards value ~£1.3M). MRC investment in research using GM insects as models in other targeted research, for example to interrogate cellular processes, in between FYs 2010/11 and 2014/15 was £37.3M.
- **NERC** has funded one training grant NERC that relates to GM insects and supports a wider portfolio of underpinning research on insects (~22 awards between FYs 2010/11 and 2014/15, of total £5.7M). NERC's underpinning research is of importance in understanding or predicting how GM insects would survive and function in the natural environment.

21. The Research Councils, often in partnership with Innovate UK<sup>139</sup>, also provide a variety of programmes that could lever private investment for GM insects R&D. Such programmes seek to invest at every stage of the development pipeline and enhance the potential for the UK's world-leading public research base to link directly to industrial challenges. This enhances the international competitiveness of UK industry, attracts inward investment and supports job creation in the manufacturing and production sectors.

- Research Council programmes were instrumental in supporting the founding research for Oxitec Ltd<sup>140</sup>. For example, BBSRC investments<sup>141</sup> supported research on the genetic modification of insects to control populations as an alternative to chemical controls<sup>142</sup>. This research has gone from academic proof-of-principle to commercialisation via a spin-out company, successful multi-country trials and pilot operational use for the control of Dengue-carrying mosquitoes.

22. The Research Councils, with Innovate UK, also support research into agricultural pests via the UK Agri-tech Catalyst<sup>143</sup>. The three rounds of Catalyst research funding to date included projects investigating novel methods of insect pest control. None of these

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<sup>139</sup> <https://www.gov.uk/government/organisations/innovate-uk>

<sup>140</sup> <http://www.oxitec.com/>

<sup>141</sup> £2.3M between 2004 and present

<sup>142</sup> <http://www.oxitec.com/agriculture/>

<sup>143</sup> <https://www.gov.uk/government/publications/agri-tech-catalyst>

involve GM insects, but continuing support for this programme is certainly a major opportunity to attract private investment into this research area.

**Q8. Given the possible public health benefits of GM insects, should the Government be funding their commercialisation? Would this result in a conflict of interest with regard to regulation of releases? If so, how might this be managed?**

23. We refer to the Government's response to this question.

**Q9. How could the UK benefit economically from both developing GM Insect technology and its use within the UK?**

24. UK technical know-how and expertise in GM insect technology is exploitable on the global stage, e.g. through licensing, consultancy, new companies, etc., which would benefit our economy through revenue and inward investment – for example the UK company Oxitec's innovation portfolio resulted recently in its sale to Intrexon Corporation for \$160M<sup>144</sup>.

25. GM insect technology developed in the UK could contribute to the development of our national capability in plant and animal health<sup>145</sup>, and our bioeconomy<sup>146</sup>. UK agriculture faces a combination of challenges: increasing resistance to insecticide chemistry in pests, a lack of novel crop protection chemicals, drug resistance in livestock diseases (many transmitted by insects), increased globalisation introducing exotic pests, and extending geographical ranges of insect-borne pathogens. If the burden of insect-borne diseases increases in the UK due to these factors, the use of GM insects could become part of the range of measures to protect against significant losses in production in the future.

**Q10. How can the gap between regulatory approaches and public concerns over GMOs be addressed? Is there a role for 'responsible innovation' approaches? What are the critical factors in effective public engagement from lab to final release?**

26. The Research Councils are supportive of a responsible innovation approach. We do not prescribe exactly how responsible innovation should be undertaken but provide guidance. EPSRC, for example, has developed a framework for responsible innovation<sup>147</sup> and responsible innovation has been an integral part of BBSRC, EPSRC and MRC joint research funding calls in synthetic biology<sup>148</sup>, from project inception through the full project life cycle.

27. We believe that public engagement should aim to inform research so that it advances in a way that takes account of public views and values; this is likely to lead to outcomes

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<sup>144</sup> <http://www.oxitec.com/news-and-views/>

<sup>145</sup> [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/388571/14-1293-animal-plant-health-capability.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/388571/14-1293-animal-plant-health-capability.pdf)

<sup>146</sup> <https://connect.innovateuk.org/web/synthetic-biology-special-interest-group>

<sup>147</sup> <https://www.epsrc.ac.uk/research/framework/area/>

<sup>148</sup> <http://www.bbsrc.ac.uk/funding/opportunities/2014/joint-synthetic-biology-call2/>

aligned with social needs and increased confidence and trust in science. Critical factors in this public engagement approach would include:

- A willingness to engage meaningfully with public groups; to listen to and take account of public hopes, concerns and values
- The early and on-going engagement of the public in the process of research and its application
- The inclusion of the viewpoints from a breadth of stakeholders including industry, policy, civil society organisations and others alongside public engagement

**Q11. If there are any crucial issues not captured under the questions we pose, please highlight what they are and explain their salience.**

28. **Non-insect pests and disease vectors:** The Committee may wish to note that other arthropods could also be of relevance in considering disease control, particularly ticks. Ticks transmit a number of diseases to humans and livestock including Lyme disease, tick-borne encephalitis and Crimean-Congo haemorrhagic fever. The incidence of tick-borne diseases is increasing across the northern hemisphere<sup>149</sup>; for example, the incidence of Lyme disease in the UK has risen dramatically over the last 15 years<sup>150</sup>. The European Academies Science Advisory Council has highlighted that research on arthropod vector populations including ticks is a neglected area<sup>151</sup>.

*18 September 2015*

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<sup>149</sup> <http://www.sazu.si/files/file-138.pdf>

<sup>150</sup> <https://www.gov.uk/government/publications/lyme-borreliosis-epidemiology/lyme-borreliosis-epidemiology-and-surveillance>

<sup>151</sup> <http://www.sazu.si/files/file-138.pdf>



## ANNEX 1

### QUESTION 1: INSECT-BORNE HUMAN DISEASES

The most deadly vector-borne disease, malaria, caused an estimated 584,000 deaths in 2014<sup>152</sup>. However, the world's fastest growing vector-borne disease is Dengue fever, with a 30-fold increase in disease incidence over the last 50 years<sup>153</sup>. Mosquito-borne Dengue is now found in 100 countries, putting more than 2.5 billion people –over 40% of the world's population – at risk. Dengue has recently been reported in China, Portugal and the state of Florida, USA<sup>154</sup>.

**Dengue fever:** Dengue fever is transmitted through bites of *Aedes* mosquitoes and widely spread in Asia, the Pacific, the Americas and the Caribbean, and Africa. No specific treatment or vaccine exists for Dengue. Dengue prevention and control solely depends on effective vector control<sup>155</sup>.

**Chikungunya:** Chikungunya has been identified in over 60 countries in Asia, Africa, Europe and the Americas. The two mosquito species transmitting this disease can also transmit other mosquito-borne viruses, including Dengue fever. Around 1.8 million cases of this viral disease were reported between 2005 and 2007<sup>156</sup>. There is no specific antiviral drug treatment and no commercial vaccine<sup>157</sup>.

**Malaria:** Malaria is caused by genus *Plasmodium* parasites. The best available treatment, particularly for *P. falciparum* malaria, is artemisinin-based combination therapy (ACT). Resistance to antimalarial medicines is recurring problem with resistance reported in five countries<sup>158</sup>. There are currently no licensed vaccines against malaria or any other human parasite<sup>159</sup>; vector control is the principle means of control<sup>160</sup>.

**West Nile Fever:** Birds are the reservoir hosts of WNV virus. In Europe, Africa, Middle East and Asia, mortality in birds associated with WNV infection is rare, but WNV is highly pathogenic for birds in the Americas. WNV virus is transmitted to people and other mammals mainly through mosquito bites as a zoonosis. The virus can cause severe disease and death in horses, but equine vaccines are available. No vaccine is available currently for humans<sup>161</sup>.

**Chagas (American trypanosomiasis):** Vector-borne transmission occurs in the Americas. The insect vector is a triatomine bug that carries the parasite *Trypanosoma cruzi* which causes the disease. About 6 million to 7 million people are estimated to be infected worldwide,

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<sup>152</sup> <http://www.who.int/mediacentre/factsheets/fs094/en/>

<sup>153</sup> <http://www.who.int/campaigns/world-health-day/2014/vector-borne-diseases/en/>

<sup>154</sup> <http://www.who.int/mediacentre/news/releases/2014/small-bite-big-threat/en/>

<sup>155</sup> [http://ecdc.europa.eu/en/publications/Publications/emerging-vector-borne-diseases\\_annual-epidemiological-report-2014.pdf](http://ecdc.europa.eu/en/publications/Publications/emerging-vector-borne-diseases_annual-epidemiological-report-2014.pdf); <http://www.who.int/mediacentre/factsheets/fs117/en/>

<sup>156</sup> [http://www.who.int/Denguecontrol/arbo-viral/other\\_arboviral\\_chikungunya/en/](http://www.who.int/Denguecontrol/arbo-viral/other_arboviral_chikungunya/en/)

<sup>157</sup> <http://www.who.int/mediacentre/factsheets/fs327/en/>

<sup>158</sup> [http://www.who.int/malaria/areas/drug\\_resistance/overview/en/](http://www.who.int/malaria/areas/drug_resistance/overview/en/)

<sup>159</sup> One research vaccine against *P. falciparum*, known as RTS, S/AS01, is most advanced

<sup>160</sup> <http://www.who.int/mediacentre/factsheets/fs094/en/>

<sup>161</sup> <http://www.who.int/mediacentre/factsheets/fs354/en/>

mostly in Latin America. Vector control is the most useful method to prevent Chagas disease in Latin America.

## ANNEX 2

### QUESTION 2: INSECT-BORNE ANIMAL DISEASES – FURTHER INFORMATION

**Bluetongue virus (midges: Cattle/sheep)**<sup>162</sup>: The bluetongue virus (BTV) species contain 24 recognised serotypes and spread via *Culicoides* spp. BTV activity can be found on all continents except Antarctica, although different serotypes and strains cause markedly variable disease. Infection ranges from subclinical in the vast majority of infected animals, to fatal in a proportion of infected sheep, goats, deer and some wild ruminants. There is no specific treatment, but vaccines are available against some serotypes.

**Equine infectious anaemia virus (large biting flies: horses)**<sup>163</sup>: Equine infectious anaemia (EIA) occurs world-wide. The infection, formerly known as swamp fever, is limited to equids and characterised by recurrent febrile episodes, anaemia, rapid loss of weight and oedema. EIA is transmitted by large horseflies, which are active from May to September. There is no specific treatment and no vaccine available.

**Infectious salmon anaemia (sea lice: Salmon)**<sup>164</sup>: Infectious salmon anaemia (ISA) is one of the most important viral diseases of farmed Atlantic salmon. Sea lice (*Lepeophtheirus salmonis* and *Caligus* sp.) may be mechanical vectors; these parasites could also increase the susceptibility of fish by increasing stress. There is no specific treatment available.

**Schmallenberg virus (midges: Cattle/sheep)**<sup>165</sup>: This is a new viral disease that had not been detected previously before Europe. SBV is spread by members of the *Culicoides* midge family, which also brought Bluetongue virus serotype 8 (BTV-8) to the UK. They are more effective at transmitting SBV than BTV-8, which has resulted in the rapid spread of the virus across large distances. The virus causes fever, reduced milk production, and foetal deformity in pregnant animals. There is no specific treatment, but a vaccine is available.

**African horse sickness (midges: horses)**<sup>166</sup>: The usual mode of transmission is *Culicoides* spp. of midges. The disease causes fever, cardiac and respiratory problems and is often fatal. AHS is endemic in the central tropical regions of Africa and spreads regularly to Southern Africa and occasionally to Northern Africa. There is no specific treatment, but a vaccine is available.

**Equine encephalosis (midges: horses)**<sup>167</sup>: The causative virus is related to African Horse Sickness Virus (AHSV) and Blue Tongue Virus (BTV) and it originates from southern Africa. It

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<sup>162</sup>

[http://www.oie.int/fileadmin/Home/eng/Animal\\_Health\\_in\\_the\\_World/docs/pdf/Disease\\_cards/BLUETONGUE.pdf](http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/BLUETONGUE.pdf)

<sup>163</sup> [http://www.oie.int/fileadmin/Home/eng/Health\\_standards/tahm/2.05.06\\_EIA.pdf](http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.05.06_EIA.pdf);  
<https://www.gov.uk/guidance/equine-infectious-anaemia-swamp-fever>

<sup>164</sup> [http://www.oie.int/fileadmin/Home/eng/Health\\_standards/aahm/current/2.3.05\\_ISA.pdf](http://www.oie.int/fileadmin/Home/eng/Health_standards/aahm/current/2.3.05_ISA.pdf);  
[http://www.cfsph.iastate.edu/Factsheets/pdfs/infectious\\_salmon\\_anemia.pdf](http://www.cfsph.iastate.edu/Factsheets/pdfs/infectious_salmon_anemia.pdf)

<sup>165</sup> [http://www.signetfbc.co.uk/wp-content/uploads/2014/11/leaflet\\_on\\_schmallenberg.pdf](http://www.signetfbc.co.uk/wp-content/uploads/2014/11/leaflet_on_schmallenberg.pdf)

<sup>166</sup>

[http://www.oie.int/fileadmin/Home/eng/Animal\\_Health\\_in\\_the\\_World/docs/pdf/Disease\\_cards/AFRICAN\\_HORSE\\_SICKNESS.pdf](http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/AFRICAN_HORSE_SICKNESS.pdf)

<sup>167</sup> [https://www.aht.org.uk/skins/Default/pdfs/equine\\_vol5\\_1\\_focus.pdf](https://www.aht.org.uk/skins/Default/pdfs/equine_vol5_1_focus.pdf)

is transmitted by *Culicoides* midges, similar to AHS and BT. The virus appears to infect all equidae, but clinical signs are only seen in horses. There is no specific treatment and no vaccine available.

**Epizootic haemorrhagic disease (midges: sheep/cattle)**<sup>168</sup>: This is an infectious noncontagious viral disease of domestic and wild ruminants, primarily white-tailed deer, and cattle. Sheep and goats might also be susceptible, but usually do not develop overt disease. There is no specific treatment and no vaccine available.

**Lumpy skin disease (arthropods: cattle)**<sup>169</sup>: This is a viral disease of cattle, thought to be spread by insects such as mosquitoes and biting flies. It produces a chronic debility comparable to that caused by foot-and-mouth disease (FMD). In the past the disease was restricted to sub-Saharan Africa but it has been reported recently in Russia and Greece. There is no specific treatment, but a vaccine is available.

**Bovine Ephemeral Fever (biting insects: cattle)**<sup>170</sup>: This viral disease causes serious economic losses through deaths, loss of condition, decreased milk production, lowered fertility in bulls, occasional abortions, delays in marketing and restrictions on the export of live cattle. The transmitting insects have not been definitely identified, but mosquitoes and sandflies are implicated. There is no specific treatment, but vaccines are available.

**Sheep pox virus/goat pox (insects: sheep/goats)**<sup>171</sup>: This is an emerging viral threat with cases reported in Greece. Indirect transmission by insects has been established. The disease causes sudden onset of fever, stiffness, lameness and nasal and ocular discharges and it is often fatal. No specific treatment is available and vaccines have not been wholly effective.

**Rift Valley fever:** Rift Valley fever (RVF) is a viral zoonosis that primarily affects animals but also has the capacity to infect humans. The disease results in significant economic losses due to death and abortion among RVF-infected livestock. Among animals, the virus is spread primarily by the bite of infected mosquitoes, mainly the *Aedes* species. Current vaccines for livestock are ineffective.

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<sup>168</sup> [http://www.oie.int/fileadmin/Home/eng/Health\\_standards/tahm/2.01.04b\\_EHD.pdf](http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.01.04b_EHD.pdf)

<sup>169</sup>

[http://www.oie.int/fileadmin/Home/eng/Animal\\_Health\\_in\\_the\\_World/docs/pdf/Disease\\_cards/LUMPY\\_SKIN\\_DISEASE\\_FINAL.pdf](http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/LUMPY_SKIN_DISEASE_FINAL.pdf)

<sup>170</sup> <https://www.daf.qld.gov.au/animal-industries/welfare-and-ethics/animal-welfare/natural-disasters/animal-disease-issues-after-flooding/infectious-diseases/bovine-ephemeral-fever>

<sup>171</sup>

[http://www.oie.int/fileadmin/Home/eng/Animal\\_Health\\_in\\_the\\_World/docs/pdf/Disease\\_cards/SHEEP\\_GOAT\\_POX.pdf](http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/SHEEP_GOAT_POX.pdf); <http://www.discontools.eu/Diseases/Detail/59>

### ANNEX 3

#### RESEARCH COUNCIL INVESTMENTS IN GM INSECT & RELATED RESEARCH

##### BBSRC

|  | Annual Spend £M |            |            |            |            |
|--|-----------------|------------|------------|------------|------------|
|  | 2010/11         | 2011/12    | 2012/13    | 2013/14    | 2014/15    |
| Development of GM insects                    | 0.6             | 0.5        | 0.5        | 0.8        | 1.0        |
| Develops/uses GM insects as a model organism | 1.7             | 1.5        | 1.2        | 0.9        | 1.8        |
| <b>GM insects Total</b>                      | <b>2.3</b>      | <b>2.0</b> | <b>1.7</b> | <b>1.7</b> | <b>2.8</b> |

- BBSRC investment in plant and animal health research in FY 2012/13: £55.5M (£38.1M animal health; £17.4M plant health)

##### MRC

|  | Annual Spend £M |            |             |            |            |
|--|-----------------|------------|-------------|------------|------------|
|  | 2010/11         | 2011/12    | 2012/13     | 2013/14    | 2014/15    |
| Development of GM insects                    | 0.20            | 0.05       | 0.08        | 0.095      | 0.07       |
| Develops/uses GM insects as a model organism | 7.8             | 8.1        | 6.8         | 7.1        | 7.5        |
| <b>GM insects Total</b>                      | <b>8.0</b>      | <b>8.5</b> | <b>6.88</b> | <b>7.2</b> | <b>7.6</b> |

##### NERC

- NERC has funded one training grant award relating to GM insects of value £75K, between FYs 2010/11 and 2014/15.
- NERC support a wider portfolio of research on insects that should be considered underpinning GM insect research (approximately 22 awards in the timeframe requested at £5.7M) and which is of importance in understanding or predicting how GM insects would survive and function in the natural environment, including:
  - Tracking insects in the field
  - Adaptations to climate change
  - Genetic control of mosquitoes
  - Immune function v life history trade-offs and also in respect to environmental change
  - Kin-selected conflict with respect to evolutionary impacts on lifespan
  - Natural sexual selection in wild insect populations
  - Cross generational selection for behavioural traits
  - Understating density-dependant disease resistance

Biotechnology and Biological Sciences Research Council (BBSRC)—Research Council UK,  
Professor Tim Dafforn, Department for Business, Innovation and Skills (BIS), and Innovate UK  
– Oral evidence (QQ 1-15)

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*Evidence Session No. 1*

*Heard in Public*

*Questions 1 - 15*

TUESDAY 13 OCTOBER 2015

Members present

Earl of Selborne (Chairman)  
Lord Cameron of Dillington  
Lord Fox  
Lord Hennessy of Nympsfield  
Lord Hunt of Chesterton  
Lord Kakkar  
Lord Krebs (co-opted)  
Baroness Manningham-Buller  
Lord Maxton  
Duke of Montrose  
Baroness Morgan of Huyton  
Baroness Neville-Jones  
Lord Patel (co-opted)  
Lord Peston  
Viscount Ridley  
Lord Vallance of Tummel

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Lord Taverne

**Examination of Witnesses**

**Dr Paul Burrows**, Executive Director, Biotechnology and Biological Sciences Research Council (BBSRC), **Professor Tim Dafforn**, Chief Scientific Adviser, Department for Business, Innovation and Skills (BIS), and **Ian Meikle**, Head of Agriculture and Food, Innovate UK

**Q1 The Chairman:** Welcome. We are very pleased that you have been able to join us at this, our first evidence session on this inquiry. Thank you very much for joining us. Would you like to introduce yourselves for the record first?

**Dr Burrows:** I am Paul Burrows. I am Executive Director of Corporate Policy and Strategy with BBSRC.

**Professor Dafforn:** I am Tim Dafforn, Chief Scientific Adviser at BIS.

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**Ian Meikle:** *I am Ian Meikle, Head of Agriculture and Food at Innovate UK, the UK's innovation agency.*

**The Chairman:** Thank you very much. Would any of you like to make an initial statement before we go into our questioning?

**Ian Meikle:** Would it be useful if I just gave a little background to Innovate UK, so we are talking about a business context and so on? Would that be good?

**The Chairman:** Yes, please do so.

**Ian Meikle:** Innovate UK is the Government's innovation agency. We translate the research that comes out of our academic institutions to public benefit and for growth within the UK economy. We have been working for about the last eight years. We have invested £1.5 billion in UK companies. That is co-invested with the companies, because they have also invested £1.5 billion, so between us we have co-invested £3 billion in innovation in UK firms. For every pound we invest, we return about £6 to the UK economy, and every company we work with on average creates seven new jobs. In summary, we help the UK stay productive, help the UK remain competitive through innovation and prepare us for future growth. This is very much part of our agenda, helping pull through the academic research.

**Q2 The Chairman:** Thank you very much. If there are no other introductory remarks, let me start with perhaps the first question. First, I must remember to declare my interests in this first session. I have to declare that I am a fellow of the Royal Society, a fellow of the Royal Society of Biology, a farmer and horticulturalist and vice-patron of the Royal Entomological Society. If I could ask rather a general question to start, could you tell us how research and development of GM insect technologies is currently funded in the United Kingdom? Do you consider that there is a reasonable balance between funding for the basic research and translation, and particularly field trials? We would be interested in hearing, if the technology has moved to that stage, whether you feel funding would be in place for that stage of the technology development.

**Dr Burrows:** There are several opportunities for funding of GM insects in the university, academic and general business systems in the UK. There are the research councils, of course. It depends very much on where the research is in its development and its application. There are the research councils; BBSRC, MRC and NERC are primarily the important ones there. We have Innovate UK, and I will let Ian say a little more about Innovate UK's approach to the funding of GM insects. It could also potentially be funded, of course, by European funding or by other government department funding, although I am not personally aware of any funding coming from other government departments at the moment. That is more or less on the public side of things.

On the private side of things, there are of course big trusts and foundations. The Wellcome Trust, I notice, in its submission has said that it has funded GM insects to the tune of just short of £1 million in recent times. There are then large international foundations such as the Bill & Melinda Gates Foundation. That is broadly the funding environment in the UK.

Overall, the research councils, over a five-year period ending in 2014-2015, have invested around £50 million in GM insect research, although it is important to draw a distinction. There is the use of GM insects as a research tool in laboratories, which is where the vast

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majority of research goes: for example, genetic modification of drosophila, the fruit fly, which is a very useful model organism in biological research. It is used in genetics, in understanding cellular development and many other aspects. These are the research tool applications. There is no indication that those would ever be deliberately released; that is not the purpose of the research. It is the fundamental science that is interesting there. That is against the smaller proportion of funding that so far has been invested in GM insect research that would fit more in the interests of this inquiry. In that period, it is about £3.8 million from BBSRC and MRC together.

**The Chairman:** Innovate UK, would you like to tell us something about your funding?

**Ian Meikle:** Yes, certainly. Our funding follows on from that. As I said in the introduction, we translate that academic research to business benefit and support businesses that are doing research and development in this space. Our funding in the broader biocontrol space has been about £3.2 million thus far, and about £1 million of that £3.2 million is in this GM insect space that we are talking about today. It is all to one company, which we will be talking about a little more; Oxitec is the one we funded. We find that there are not that many companies in this space. We will continue that conversation later. Oxitec is the only one that we have been funding, because it appears to be the only one in this space at the moment.

**The Chairman:** In the written evidence, we have had a number of observations made about the difficulty of getting funding of field trials, for example—this, of course, up until now would have been overseas, but also within Europe and Spain—reliance on high-net-worth individuals and rather precarious funding lines; concern about the lack of clarity on regulation; and other inhibitions on investment. Would you like to comment on that?

**Professor Dafforn:** Certainly, that is an issue in this area. To allow you to do these sorts of large-scale trials, any company or academic getting involved in this needs to understand whether the regulatory environment is correct for that sort of trial. Partly because the insect research itself has moved quite quickly, in that it is regulated under regulations that are more related to the use of GM plants, there is some confusion, and it can make it challenging to provide funding and to generate these trials in the UK.

**Dr Burrows:** To answer your question about the field trials for GM insects, my personal impression is that it is still very early days for those. There are precedents of research councils funding trials for GM crops and environment trials. That is not for the commercial development of those crops, but to gather further data to test the performance of those crops in the field environment. There have been a couple of examples in recent years of GM wheat at Rothamsted and a GM camelina at Rothamsted with modified oil content. There are other examples as well of where we have done that. Where there is a proper programme of research—and funding a field trial is part of that—then the research councils will do that, but, for GM insects, it is still very, very early days.

**Q3 Viscount Ridley:** I am sure this will come up later, but, just to follow on from what Mr Meikle said about there being only one company in this space in the UK, do we know of other people who have wanted to start companies in this area and have failed to find funding because of the political and regulatory risk, or indeed of other projects that are stymied because of this?



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**Ian Meikle:** It is probably worth saying it is one company that we know of. There may be others but our research does not reveal others, and I do not know whether anybody else has found any others. We do not know that others have been stymied, as it were. One of the things that Paul and I have been discussing—there is a very good link between BBSRC and Innovate UK in this space, and broadly between the research councils and us—is that we could start talking to some of those universities that receive funding. Oxford University and a number of others have received funding. A great starting place would be to speak to those universities about which companies are interested in the research that they are doing. That would be a good starting place in the academic arena.

**Lord Peston:** You may be coming to this, but part of the Lord Chairman’s question was to ask you whether we are spending enough, and you have not answered that yet. The numbers seem very low to me, if the subject is as important as we are being led to believe. You may say that, essentially as officials, it is not your job to say whether we are spending enough. I hope you will not say that. Unless I have misread them, the numbers seem ridiculously low, considering the potential benefit.

**Ian Meikle:** Which numbers have you seen?

**Lord Peston:** For example, BBSRC spends £2.8 million, it says here. If you look at what we fritter £2.8 million away on in other parts of the public sector, this seems absurd to me. I am ignorant, so I am just asking you the question.

**Dr Burrows:** Let me deal with the research council side of things, first of all. We have not to date necessarily prioritised funding for GM insect research. The amount that we spend is a product of the number of grants that academics come forward to us with, and then how many of those get through the peer-review system. We have a very encouraging system: we have open doors; we have responsive mode. The academic community is free to come forward with applications to do research on GM insects. The fact is, at the moment, we are not seeing many of those, and that is why the spend is relatively small. If they want to come forward, they are very welcome to do so, and we have the mechanisms by which they can do that.

**Q4 Lord Hunt of Chesterton:** You have touched on this, Mr Dafforn, and I had some briefings; some of us were not at the previous meeting. The use of the word “GM” is very problematic, and other words have been used. The House of Commons had a committee on this, and the conclusion was that we need to change the words. Now, when you change the words, you are into a different regulatory regime. The word that was mentioned was “vaccine”, as opposed to “GM insects”. “Vaccine insects” sounds highly obviously attractive. Is this being considered?

**Professor Dafforn:** I cannot say it is being considered, but I think people are very aware of this. The phrase has ended up as being quite emotive among the public. It describes directly what is happening. It is a genetic manipulation or genetic modification of an organism of some biology.

**Lord Hunt of Chesterton:** But that is the process, not the end product. The end product is a vaccine, for example.

**Professor Dafforn:** Absolutely, yes. There has been discussion—this is quite important—about the product, actually using the product, its phenotypes and what it does as being the

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important part of what you are making. As you say, a vaccine can be genetically modified and it is a vaccine, which is what is important. We have not found the right phrase for this sort of technology yet. It has been called RIDL, which really describes what it does, but it is not easy to explain that, necessarily. You are right; nomenclature can be quite important.

**Q5 Baroness Morgan of Huyton:** Dr Burrows, in your experience of the academic community, do you think it is influenced at all by what it may consider to be the difficulty of the regulatory environment? What is the point of doing research if it will not be able to go anywhere?

**Dr Burrows:** I think, once it is at the very basic stage and they are just investigating cellular mechanisms, for example, not so much. Anecdotally, though, we hear from the research community that it has found it increasingly difficult, particularly in the GM crops space, to get commercial investment in their research. At one point, I believe that that was quite a significant part of what helps them along the process and into the Innovate UK space, because companies have, perhaps understandably, stood back from the uncertainty that they see in the GM regulatory regime within the European market. There are examples of some really fantastic research going on in UK universities, and it may well find its application first in North America, rather than in the UK.

**Q6 Lord Kakkar:** Occasionally, research councils decide to have strategic initiatives to drive research interests. Has that happened in this particular area for the research councils or would they consider doing it in the future?

**Dr Burrows:** Not in the case of GM insects. You are absolutely right. We do prioritise. We do have initiatives, particularly where we see the need to encourage research in a particular area or build a research community. We have not done that with GM insects. There is no reason in the future why perhaps we should not, but we need to wait to see the outcome of the spending review. It is unlikely that we would have a specific initiative in GM insects. It is likely that, if we were to do that, it would be framed in a much broader sense of alternative control mechanisms for agricultural diseases or something, so it would keep the options open. There is no reason why, technically, we should not prioritise this type of research in the future, along with all the other priorities that we have and our future budgets, if it was considered to be a priority.

**Lord Kakkar:** I should declare my interest as UK business ambassador for healthcare and life sciences.

**Viscount Ridley:** Could I also declare my interest as a fellow of the Academy of Medical Sciences and the owner of a farm?

**The Chairman:** Is there anyone else who would like to do so?

**Lord Hunt of Chesterton:** I am a fellow of the Royal Society.

**Baroness Morgan of Huyton:** I am a member of King's College council.

**Lord Patel:** This is supplementary to the question that Lord Kakkar asked. Before that, I am a fellow of the Academy of Medical Sciences and a fellow of the Royal Society of Edinburgh. It is not about whether you are financing research into insect gene editing; it is about whether you are financing research into the science of gene editing, which is what we are

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talking about when we talk about insect modification. It is whether you are funding the science, not specifically about insects.

**Dr Burrows:** Gene editing in insects is an application of those gene editing technologies, which, incidentally, BBSRC published a position statement on last year, recognising that these sorts of biotechnologies are moving incredibly quickly. The gene editing technologies are moving, at the moment, more quickly than the regulatory framework can keep up with. I understand the Commission is about to publish an opinion on whether the gene editing technologies are part of the current regulatory process. Similar conversations have been had in other regulatory authorities around the world.

It comes back to the point that Tim made earlier. At the moment in Europe, we have a regulatory framework that regulates the process by which the modified organism was created. From a scientific perspective, the logical process is to regulate the end point—the characteristic or the trait of the organism at the end.

**Lord Patel:** My question relates to whether you are funding the science, not the regulation.

**Dr Burrows:** Yes, we will be funding the underpinning science, absolutely.

**Q7 Lord Hunt of Chesterton:** The UK is said to be a global research leader in the field of GM insects—a comment about that would be useful—and yet there is only one British company active in this area. How can this be accounted for? Apropos of this, is the research leading to significant IPR? Secondly, is the UK research at the moment very fundamental, or is there in fact a good deal of applied research that does not lead into companies?

**Professor Dafforn:** Coming back to Paul's comment that you can break GM insect research into two sections, one is this specific application we are talking about with Oxitec, which is for crops or for protecting against things like dengue. Then, on the other side, you have far more fundamental research, which there is much more being put into at the moment and has generated significant insights into healthcare. At the moment, we have a balance between those two going on.

On the question about the UK leading in this area, scientifically we lead or are close to leading in insect molecular biology, which covers both of these: the fundamental and what Oxitec do. You have to remember that we have one company that leads; it is the only company in the world as well. It leads not just the UK; it leads the world. It is one company. One might have to wonder about whether this is an industry, if it is only one company, so you have picked a very specific example. There is no reason why we cannot have more examples in other areas, as and when people have an idea about how to use this technology.

**Q8 Baroness Neville-Jones:** May I declare an interest as a member of the Engineering and Physical Sciences Research Council? I would like to pursue a little the implications of what has happened with Oxitec, which, as we all know, was taken over by an American firm, Intrexon Corporation. I would be interested in the comments of the panel on the implications of that. Presumably, the takeover would not have taken place if it had not been regarded as a worthwhile asset, so there must be something of value there. It is very curious that you should have a valuable company that seems to stand alone in the field.

I would be interested in two aspects. First, what do you make of the takeover and what do you think the future will be? Will there go on being continuing investment, or is this a way

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of wrapping up that kind of activity? Secondly, where do you see the real problem as being? Is it in the regulatory environment, or is it other factors that inhibit more companies getting going?

**Ian Meikle:** It is important to point out that Oxitec has been doing research since 1995, when it was still part of Oxford University. It spun out of Oxford University in 2002, moved into its own premises in 2005 and started on business funding through us in 2010, so this has been a 20-year journey. It has not sold any products in that time. It is still in its R&D phase. It has been developing IP, to talk to the comment there. Having visited Oxitec, as we do all the companies we fund, it has to raise funds to be able to do that. It does not have sales that it is generating off the back of it, so it continually has to raise funds, and it is generally philanthropic individuals, who have a social conscience but also want to make some money as well, who have been investing thus far.

The journey that companies take is that they are generally trying to grow a business, and then they will need a significant injection of investment at some stage. That is either an IPO, where they float on the stock market, or a private investment. Oxitec has got to that stage. After 20 years, it needs that large scale of investment. The company that has taken it over is not planning to re-headquarter it. It is not planning to relocate it. It will still be based on UK soil. It is planning to grow its footprint because of this investment on UK soil. The headquarters will also remain in the UK, as we understand it as such.

We could see this as inward investment, really. In many ways, we could look at it in the way that we have Nissan up in the north-east. It is a foreign company, but it is based there because of the academic and engineering environment we have in that area. It creates jobs; it creates investment; it creates taxes for the UK economy. In some ways, when we work with UKTI, we think of inward investment as not such a bad thing. We have to be careful that we do not think of it as a bad thing. I think you are right: if they purchased it and took of it offshore, that would be another matter and one that we should be concerned about.

**Baroness Neville-Jones:** Which they would be able to do, as owners.

**Ian Meikle:** Yes, if they own it.

**Lord Vallance of Tummel:** As a matter of interest, do you know whether Oxitec approached Intrexon because it was looking for a parent and capital, or was it Intrexon that approached Oxitec?

**Ian Meikle:** I am not sure whether I can report that. I had a conversation with them around that. I cannot remember the order of it, but I believe you are seeing Oxitec in a couple of weeks, so they will be able to give you a better insight. What I remember of the conversation was that one of the questions was dealing with US versus UK investors. One of their comments was, “Actually, investors did not get us, be they UK or US”. It was a particular individual in this organisation that “got them”, to put it colloquially.

We have talked about philanthropic individuals investing thus far. It was somebody with a particular insight in this organisation that bought Oxitec. It was not because they were US or whatever; it was because of the insight of that person who saw this match come together.

**Professor Dafforn:** It is worth adding as well that it is not just a financial transaction that you are looking at there. Intrexon has a significant amount of technology in the synthetic biology arena, which will enable its company to grow and enable Oxitec to grow. Without that, it

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may have foundered, so it is one of those really classical joinings of two companies with two separate technologies, which together can really have some distinct benefit.

**Dr Burrows:** The bigger piece here, of course, is that the challenge for all of us, while it is a sign of success, seeing this inward investment and the recognition of these globally competitive companies coming out of our science base, is retaining the value in the UK, in terms of them paying their taxes, creating jobs and so on. It is a rather big, philosophical point, but I think the best way we can do that is to maintain the excellence of our science base, our infrastructure investment and our skills, so that those other companies coming in and buying our small biotech companies recognise that they are already embedded in a really permissive, high-tech environment and there is no incentive to move them on.

**Q9 Duke of Montrose:** I declare an interest as a livestock farmer and as president of the National Sheep Association. This whole framework we are operating in is a European one, with European regulation. Do we know how other countries are approaching the question of GM insect research, or are we the only one taking a big interest in it?

**Professor Dafforn:** The only knowledge we have is that there have been attempts to have a trial in Spain, and the negotiations had been rather protracted. Probably our colleagues in Defra are better placed to describe how that has gone.

**Duke of Montrose:** Germany is not interested in GM insects.

**Professor Dafforn:** Not to our knowledge.

**Ian Meikle:** Oxitec has been doing trials in Brazil. It points out that, when it talks to other countries to sell its technology, the fact that we are not trying it in our own back yard can be a bit of a tricky conversation if it is talking to prospective customers.

**Q10 Lord Fox:** I will declare my interests as an employee of GKN and shareholder in Smiths Group, neither of which, I think, are active in this particular area. You talked about retaining value in the UK, and, in another conversation, we talked about the need, when companies get to a certain point, for the injection of money. The other way of retaining value in the country is for there to be a source of that investment and capital. Is there any evidence that the landscape for biotech companies at that level is better in the USA, for example, than compared to the UK? Are there other countries that we would look up to when it comes to that level of biotech support and development?

**Professor Dafforn:** Anecdotally, certainly in certain sections of the US—one would think of California—there are significant amounts of extra capital there: a lot of private capital and rich individuals who are able to invest heavily. I am part of a group working on synthetic biology. We did a UKTI trade mission to California and it was very clear that the investment environment was good in California, not across the whole of the States, and one must remember that. It is quite patchy.

If you need to look at the long piece, the knowledge base since the Lambert review, more than 10 years ago, has been moving slowly towards more applied research. This is a super tanker you have to move gently. We are seeing really good feed-through from the research councils and Innovate in encouraging academics to see their work not just as pure research but also with an eye to market. In many ways, you are now seeing, with Oxitec and other companies coming through, that we are getting that sign of growth, which is a really good

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sign: companies moving into the £80 million to £200 million requirement for investment. Even more encouraging is that our own financial institutions are beginning to see that happen. Neil Woodford has just put together a fund, which is half a billion, to put into high-tech, late-stage, research-based companies. We are seeing the products and companies are beginning to change the overall fiscal environment in the UK for developing new tech, which can only be a good thing.

**Lord Fox:** Is there anything you can do to encourage that?

**Professor Dafforn:** I think the best way of encouraging it is to see good science coming through as good products with a good market. That is happening. Funding the research base, not cutting off the research base in terms of funding, is key to that flow-through. All the mechanisms we have with Innovate and the research councils seem to work well at the moment in ensuring those products and ideas come through and then letting the environment, which is the financial environment, pick them up, because, if they see a good bet—if they see a good company—they will invest.

**Q11 Baroness Neville-Jones:** Can any of you comment on the following? Oxitec in a submission, when it was talking about the funding of biotech SMEs in the UK, said that the advantage and benefit of its activity “can be substantially eroded for an SME as they lose the research and development tax credit on all grant-related activity regardless of the level of grant funding”. You say the real answer is good science, but what about the fiscal regime; what about the tax context?

**Ian Meikle:** Basically, the tax incentive and grants are both within the state aid regulations, so they cannot take both; otherwise they would be getting too much public funding.

**Baroness Neville-Jones:** This is a European regulation.

**Ian Meikle:** Yes, exactly. There is a choice for companies of whether they take the tax credits or come for our grant. As a rule of thumb, companies need to go to their tax advisers to understand this, but if the funding level is above about 40%—and, again, you would need to get proper advice on that—then it is probably beneficial to come to us for grant funding. Of course, there are other benefits as well of coming to us for grant funding, because they can meet other collaborators, people that they might want to work with. It is also a tick in the box for when they go to investors later that we have endorsed that. We go through a process of competitive funding. We have assessors who are knowledgeable in the field, so there are opportunities there.

I do not think we should look at it as stopping them from doing something. They are both under state aid. We try to support companies to the maximum that we can, but we cannot go beyond the state aid rules, and companies have to make a decision as to whether they go for the tax credits or for the grants option. That is a choice they have to make themselves.

**Q12 Lord Kakkar:** I must declare a further interest as professor of surgery at UCL, an institution that may be involved in this area of research. The regulatory framework for genetically modified organisms in the UK is driven principally, as we have discussed so far, by EU directive, and has been referred to in some of the evidence we have received as serving to prohibit innovation. I wanted to explore what your views were on the balance between regulation and innovation being struck currently, whether it is fit for purpose and how we

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**Dr Burrows:** Broadly speaking, the regulatory framework for genetically modified organisms in Europe, as it is drafted, is a reasonable framework. It allows for evidence-based risk assessment, post-release monitoring and scientific advice through the process. The regulation itself is, broadly speaking, okay. There are some caveats, which I will mention in a moment. It is the way, essentially, it is applied across the 28 European states. It is not applied as an evidence-based risk assessment for harm to human health and the environment. In my view, there is too much politics and other things that are brought to the table, so it does not work, and undoubtedly that impacts on innovation within Europe and the willingness of other global companies to invest in the European market.

I have mentioned two of the main issues with the regulatory framework already. The biotechnology is moving more quickly than the framework can keep up with at the moment. We need a trade-based process, rather than a method-based process. Most significantly, it does not really permit risk and benefit to be taken into account in the decision-making process, which is of course common with medicines. Where you have a serious disease, I think the public's appetite for risk is a bit higher than if the disease is less serious. The same principles apply to the risk-benefit ratio in weighing up, and nowhere is that brought into higher contrast than in the area of GM insects. If there is a major public good in the release of a GM insect to suppress malaria in an area, then how is that weighed up with the risk of doing the release of the GM insects? That is a really gritty philosophical question.

**Chair:** Do either of you want to comment further on the regulatory aspect?

**Professor Dafforn:** I think Paul has put it perfectly.

**Lord Kakkar:** It is very interesting to hear you say that part of the problem is the way that this regulation is drafted, that there is no mobility to look at benefits in doing a proper risk-benefit analysis. You also mentioned a view that there is a lot of political interference, that the ability to apply a framework independently, based upon scientific advice rather than political interference, does not appear to exist at the European level. Would that be an appropriate interpretation?

**Dr Burrows:** I think it would, because, in the way the voting mechanisms are set up around the directive, one can get a positive scientific opinion on an evidence-based risk assessment to human health and the environment, and yet the voting procedures in committee continue to delay the approval. In fact, I am sure the Committee is aware that the Commission has just changed the rules in many respects, in that one would still have Europe-wide marketing approval for a genetically modified product, and yet the member states can individually opt out if they wish to. That has not yet been tested in committee. Whether that would help the member states give a positive opinion by qualified majority in committee, knowing that they could then step out afterwards, or whether the objections are more fundamental and ideological than that remains to be tested.

**Lord Kakkar:** To follow up on that point, do you think there is now increasing confusion around the area of regulation, as those new mechanisms and opportunities for member states to opt out individually are about to be tested? Would it be right to conclude that the area of this confused regulation at European level now is one of the greatest roadblocks to adoption of this technology in our part of the world?

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**Dr Burrows:** I do not know if there is greater confusion; there is certainly greater complexity in the process than when it was first envisaged and, anecdotally, it must be correct that the uncertainty of the regulatory process in Europe for the deliberate release of GM technologies generally is impacting investment in Europe. It is difficult to believe otherwise.

**Baroness Neville-Jones:** Do I understand correctly that what you are saying is that the regulatory regime is not really suitable and the solution at European level is to allow people to opt out of it?

**Dr Burrows:** Please bear in mind that Defra is the competent authority here. I have some past experience.

**Baroness Neville-Jones:** You have said that there is both drafting and practice, but there is a shortcoming in the approach because it does not allow benefit. Even within its own terms, what you seem to be saying is that we have a bad regime or an inappropriate regime and, instead of reforming the regime, we allow people to opt out of it.

**Dr Burrows:** In my opinion, the regulatory regime, as it is drafted, is an adequate framework; it is just not being applied properly. When I say an adequate framework, it could perhaps be better if it was permitted to take risk and benefit into account—if it was a trait-based system rather than a process-based system. We have to recognise that we live in the real world, and the prospect of throwing the European regulatory regime up in the air and renegotiating it fills a number of individuals with horror, because there is a distinct possibility that we will end up with something worse than we have at the moment.

I personally agree with the line that Defra has taken in its evidence, that the priority at the moment is to try to get the regime, as it is currently drafted, working properly.

**Lord Hunt of Chesterton:** May I take you up on this point and try to elaborate? There is concern about risk. That is the point. My wife is a landscape architect and she is always saying, “How do we know this is not going to affect the lesser spotted this or that?”, and quite reasonably. I know that in France, because I go there a lot, they are very, very concerned about what effect any of these kinds of technologies will have on wildlife and ecology. My question really is: are we doing enough research on these risks? I speak to people in the lab and they grumble about these things. They want to focus on the pure and then they want it to be released. There does not seem to be half the amount of research on the potential risks in the environment for all sorts of ecologies, and that is the focus of our European colleagues.

I have the feeling that in Britain that is not considered a very gutsy thing to do. You want to do your pure stuff; you will get your money; off you go and here is a product, whereas the Europeans are all doing this incredibly detailed ecological risk stuff. Is that a ridiculous way of putting it?

**Professor Dafforn:** You may be casting the scientists in a slightly negative role. I think there is a distinct drive, particularly among the younger scientists, for a new way of doing research. There is a responsible innovation proposal or framework, to which we now adhere when we are doing research, where we look at that side of things. The idea that we just go forward, generate new insects and new varieties and think, “To hell with the consequences” is not what is going on. Again, you get tied up with the regulatory situation, because you can consider how an insect might affect an ecosystem but, in some ways, you need to test it. If you have a regulatory framework making that difficult, then people will stop doing the



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research in the first place. Given we have only one company, which is Oxitec, one might say that could be an inhibitor, but it is very hard to tell when people do not do something.

**Ian Meikle:** Also, in the Oxitec experience, the technology they are using is self-limiting. It dies out. They are also using marker dye as well, so you know which insects have been released, so it is a failsafe technology. It is important that we are seeing that responsible innovation coming through from the company that is taking part at the moment. You are right; we need to be wary of that and ensure all companies that take part are similarly responsible.

**Lord Kakkar:** Do you think that, rather than having a wholesale redrafting of these directives and regulations, a recommendation for this may be to further solidify the role of independent scientific advice in this particular area of European activity?

**Dr Burrows:** I think we have a good regime of independent scientific advice at the moment; it is just that, in many instances, that advice is not necessarily listened to. If one could build into a regulatory framework more of a requirement that that advice was listened to, to harden that part of the regulations, then perhaps that could help.

**The Chairman:** As the GM insect debate warms up, as it might well as people become more aware of the scientific opportunities and threats, I suspect that some of the concern will relate to the possibility that resistance, for example, to gene drive mechanisms might occur. The BBSRC have said, Dr Burrows, that you are in response mode. You wait for people to come and, if the application is appropriate and of high scientific quality, then you will fund it. Are you convinced that these concerns, which probably have not yet been identified but will almost certainly be coming up over the hill, are likely to be met by this response mode?

**Dr Burrows:** The example here of how we address the concern of various publics about new technologies is exemplified by the way we have gone about looking at synthetic biology.

**Professor Dafforn:** Your concern is correct, and, again, we come back to the change in the way that scientists behave. I have been leading on syn-bio, synthetic biology, which includes things like gene drives, as being a new area of science that might provide opportunities but also will provide some risks. In the development of that area of science within the UK, probably for the first time ever, the scientists have been involved from day one, looking at the negatives that might come out of this, engaging with non-scientists—so the various publics that are around—to discuss what the science is, what the opportunities are, what the risks are. From day one, we have been engaging with regulatory experts as well and the people who are defining the regulations for syn-bio, the idea being that you need these conversations to define where the risks might be, to understand where risks are real and where risks are non-real, where there may be mitigation strategies that can be put in place, whether it is regulation or whether it is the science itself. One would expect, with gene drives, that this should happen as well. It does seem to be a pathway that scientists are generally engaging in now. It is a new pathway and it is central to the way we do research at the moment.

**Q13 Lord Krebs:** I should declare interests as a member of the department of zoology at Oxford, where Oxitec started, a fellow of the Royal Society, a fellow of the Academy of Medical Sciences and an advisor to the Wellcome Trust. I want to follow up on Lord Kakkar's question and Dr Burrows's response about the role of scientific experts in the risk

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assessment. Could you just clarify for us, Dr Burrows, who actually carries out the risk assessment in the European context?

**Dr Burrows:** In the European context, it is EFSA. As to the individual member states, I can speak particularly for the UK, because I know the Committee has the Advisory Committee on Releases to the Environment and the Advisory Committee on Novel Foods and Processes, so the individual competent authorities take their own expert advice as well. I had some experience in a previous life of working very closer with ACRE, the Advisory Committee on Releases to the Environment, which is the main committee that advises Ministers on releases of genetically modified organisms. ACRE gave its advice to Ministers. Ministers, of course, do not have to take that advice, but the way it was couched at that time—I am talking about 10 years ago now—was that, if Ministers did not want to take that advice, they had to have a very good reason for not doing so. As a statutory committee, my impression—please bear in mind that I am only giving my impression; I have not been in this field for some time now—is that that requirement to have a very good reason not to do so is softer in the European system than it necessarily was in the UK at that time. While you get positive scientific opinions, the applications and the dossiers still do not progress through the system as they are intended to do in the drafting of the legislation.

**Lord Krebs:** If I may ask another question of Dr Burrows apropos the point that Lord Hunt of Chesterton made a few minutes ago on the ecological research related to the environmental risks, while it is probably too early to look at ecological research in relation to GM insects given the early stage of that work, if we think of GM crops, am I not right in saying that the UK has sponsored quite a significant amount of ecological research in this area? I am thinking of the work carried out by Professor Michael Crawley at Imperial College and the very large farm-scale trials of GM crops that looked at the ecological consequences for two or three different crop varieties.

**Dr Burrows:** Yes, that is correct. Historically, BBSRC and NERC have had joint initiatives looking at horizontal gene transfer, for example, in the natural environment. There is a history of the research councils funding those types of research. The farm-scale evaluations that you referred to are, of course, government-funded, with a combination of government and industry funding. They were at the time, and I believe still so, the largest ecological trials of their type of herbicide-tolerant crops in the world, and we really were ahead of the thinking at that time.

**Q14 Lord Hennessy of Nympsfield:** May I declare I am a fellow of the British Academy and a professor of contemporary British history at Queen Mary University of London? Genetically modified history is in its infancy, but it is better to over-declare than under-declare. My question builds on Lord Hunt's question a moment ago about perceptions. Ipsos MORI's *Public Attitudes to Science* of 2014 is full of good things, but there is one very striking statistic in there that is relevant to today. Scientists in university labs are trusted by 90% of the people to tell the truth, where it goes down to 60% if you are in industry. What are the roots of all this? Does it go back to Rachel Carson's *Silent Spring* nearly 55 years ago now? It seems to me that there is a great problem that, if commerce is involved in the private sector, a whiff of *Dr Strangelove* comes into it and quite often it is the same people. What can you do about that? You have touched a little on it in the new pathway you have been describing, but it seems to me that it is a deep-set secular problem of probably 50 years' duration. Do you have cunning plans, please, to put it right?

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**Ian Meikle:** It is about benefits. Some of this technology we are looking at is applicable both in health—things like transfer of malaria—and in agriculture. If the consumer sees benefit, then they are more likely to understand it and take it on. For instance, if we are using GM insects to tackle malaria, you and I may have a benefit of not catching malaria as well as the health service of not having to treat malaria. We can clearly see the benefit for us as individuals.

The problem with the GM debate, which links with what you are saying about big business and GM working together, is that the benefits were generally seen to be for the producer and not so much for the consumer. As we are developing this, if we can build on the syn-bio approach, as long as we can build in the benefits to consumers, that is where we need to start getting. The benefits to consumers are things like: potentially we could reduce or take to zero the amount of pesticide residues on some of our crops. That is the sort of thing that is being pulled through. People are looking for more sustainable practices, so a lot of Marks & Spencer's advertising, for instance, is based on its green approach to the products that it produces. Of course, there is cost. If our crops get decimated by pests and disease, the price can go up.

That is a start of what the benefits might be for the consumer. They can be quite long-term. For instance, costs might be a 10-year horizon. What we have to do is really start from the benefit for the consumer, because that is the way you sell a product and that is the way you sell an idea. You have to start from the why and what it means for me.

**Professor Dafforn:** I should make one other comment, which is that a figure of 90% is incredibly high for any profession. Aspiring to 90% would be excellent, but somehow academics have ended up at 90% and that might be part of the problem. Inherently, you are looking at a different being in industrial science, or a perceived different being, because industrial scientists—and I run a small biotech firm myself—are not just looking at purity of science, which I think the public really gets; we are looking at purity of science and the need to make some money, because that is what a company is about. That is an inherent difference. You cannot get over that difference. If the public are unhappy with that—60% is not bad—I do not know that you can change it too much. It is a real struggle.

**Lord Peston:** I am a bit fed up that I do not have any interests to declare. I suppose the reason is, whenever I am asked to do anything, I always automatically say no, and so on. Do we not have an example here? In asking the question, "Why do the public appear to mistrust industrial science?", is the correct answer not that they are right to? If we look back at the history—let us take the tobacco companies as the classic example—long before Richard Doll did his work and published it, they had done all the research and had suppressed it. That creates what economists call an external diseconomy, namely that that also reflects badly on the honest people and so on. Therefore, one ought to be supportive of the honest people; the trouble is that, with somewhat dishonest people around, what can you do? Do you have any views on that?

**Dr Burrows:** I hesitate to tackle this question, knowing the expertise that is sitting behind me at the moment. I am sure in the next session these are exactly the sorts of questions that it would be good to explore. I would question the premise that people naturally distrust industrial science in its entirety. It is highly contextualised. Your smartphone is industrial science; your tablet computer is industrial science.

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There seem to be particular areas of science that raise the hackles in a way—a visceral concern—particularly where it seems that we are interfering with nature. People value naturalness in many respects. They are particularly concerned about where there are interventions in what seem to be complex ecosystems, unanticipated events and unanticipated side effects. I found the Sciencewise submission to this Committee very illuminating, in the way that it has systematically gone about having a conversation with the public about being transparent and honest in the reasons for having that conversation. If the public, in plural terms, think you are trying to force something down their throats or sell something to them, rather than having a proper dialogue in listening mode, you are immediately at a disadvantage in beginning those kinds of conversations. In answer to your question, what can be done about this is open, honest, transparent conversation.

**Q15 Lord Patel:** We had several comments made about the state of the science, about the state of the regulatory framework, whether it is needed or not and at what stage we should give thought to the regulatory framework. My question is related to all these areas. The US National Academy of Sciences has set up a group to look at the state of science, of things like gene editing using CRISPR, even synthetic editing using endonucleases, to inform them of whether there is a need to look at the regulatory framework as it is now and what it ought to be, recognising that GM insect modification could be used in benefitting the treatment of diseases and of course improving crops, but it could also be used for quite dangerously harmful effects. Do you think we should set up such a group to look at the science and the regulatory framework?

**Professor Dafforn:** Our American cousins are often very good at looking ahead. They are perhaps slightly more ahead in the gene drive technology. It is a revolutionary new technology.

**Lord Patel:** The technology is no different from gene editing, where we are way ahead.

**Professor Dafforn:** Yes, okay. The other thing is, as a scientist engaging in discussions about new technology as it comes forward and getting people to look at it more closely, if it is a new technology that is disruptive like this, this is valuable. This is something we should do. It is not for me as a scientist to initiate those larger-scale conversations regarding committees, but it may be something that is worth looking at, certainly.

**Lord Fox:** It goes back to where you said you wondered if this was an industry, as I think one of you put it. This was really my question: is the problem regulatory, in that it is too hard to make this an industry, which seems to be what you have said, or is it actually the application, in that the main application for which you could get regulatory approval is one in public health, which tends not to be in developed countries? I wondered if that was one aspect.

**Ian Meikle:** I can start to answer that question. We still have pests and diseases. The amount of chemicals we can use to tackle those is being diminished by regulation, so companies are starting to look at other approaches. When we look at the radar, we are looking at two big disruptive technologies coming through. One is precision agriculture; that is using things such as satellites, drone technology and sensors on the back of tractors to figure out exactly where your problem is, and then using very precise methods to use some of those chemistries in much smaller amounts. The other space we are looking at that is very disruptive coming through—and both are growing at about 15% or 20%—is the biocontrol space, of which this GM insect technology is part, but it is part of a slightly bigger sphere that

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includes insects that prey on other insects, the use of waxes and funguses to kill insects that are destroying grain stores and those sorts of things. There is this broader biocontrol sphere that is coming through.

It is the only company in this GM insect space. There is a bigger biocontrol sector that is starting to emerge, and it would be surprising if, given the success of Oxitec thus far, it does remain to be the only player there.

**Dr Burrows:** Building on that, is this an industry or not? With the exception of Oxitec, we are still at a very, very early stage. With GM insects in particular, it would be my view that the unhelpful regulatory environment we have around GM generally in Europe has not really impacted yet that excitement of the initial research. Also, if we look at the major initial applications of GM insects, they are probably outside the UK in other markets anyway.

**Lord Patel:** I am not so sure that is a correct comment. First, the reason I think we are not investing and we do not have such a strong science base in GM insects is that we have not funded the science specifically for GM insects. The science itself is as common to humans as it is to non-human organisms. If we do not fund it, we will not get biotech companies developing, because they normally develop from scientific institutions, as happened in Oxitec from Cambridge. We might be wrong in thinking that it is outside this country that it will be useful. Brazil is not the only country that has crops destroyed by insects and therefore requires genetic modification.

**Ian Meikle:** You are correct. In this country, the soft fruit industry—strawberries, raspberries—had got to a point whereby it reduced the pesticide residues on those crops down to zero. It now having to use them again, because of a pest called spotted-wing fruit fly; there is probably a Latin name for that that I do not know, I am afraid. This technology could be used in the UK, and one of the frustrations for Oxitec is that to be able to do trials in this country would be within the UK jurisdiction, as it understands it to be, but to release it as a commercial opportunity would need EU clearance. What it would quite like is to just be able to do the trials in this country.

Building on your comment about going from a responsive mode to being targeted, that is something where we would look for the results of this inquiry, certainly in the Innovate UK space, and we always work in partnership with the research councils. If the results of this inquiry are positive, we could certainly do something that was more targeted to draw through more.

**Lord Peston:** I do not know whether you saw the evidence we took before the House rose, when we started this inquiry. Have you read that?

**The Chairman:** It was a private seminar.

**Lord Peston:** Just let me put the point to you. It may well be that our scientists and our country make the great contribution, but what really impressed me was that the real beneficiaries will be in the poorest countries in the world, and therefore we should place this, surely, within the aid context. We will save the lives of an enormous number of very poor people who deserve not to die if we make good progress in this area, notwithstanding the risks, let me add. That seems surely a context in which we ought to place the whole of this inquiry.

**Lord Fox:** That is the point to which I alluded at the end of my question as well.

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**The Chairman:** I had better make clear that that was not on the public record, because we were having a private seminar.

**Baroness Neville-Jones:** I want to come back to the question you asked right at the beginning about field trials. Just a moment ago, you said that what Oxitec would really like to do is at least have the field trials in this country. What is stopping that?

**Ian Meikle:** Its understanding of the regulations is that it is a UK decision as to whether we can have field trials in this country. I am not sure what the mechanism is; I am not an expert in that.

**Dr Burrows:** They could make the application.

**Baroness Neville-Jones:** What is holding them back, do you think, then?

**Dr Burrows:** That would be based on the advice from the Advisory Committee on Releases to the Environment to Ministers, and Defra is the competent authority, but there is nothing stopping Oxitec technically putting a dossier together and applying to do field trials in the UK.

**The Chairman:** We have run out of time on this session. We are most grateful to the three of you for a very informative session. We clearly have a lot more work to do, and we will have some further interesting sessions. Thank you very much for having got us off to a very good start.

## **Rothamsted Research – Written evidence (GM10007)**

### **Q. Which human diseases, across the world, could be addressed through GM insect technology?**

A. Potentially any transmitted by an insect (or tick). The most common insect vectors of human disease are mosquitoes (malaria, yellow fever, dengue fever, encephalitis, west Nile, Chikungunya) but others' vectors include sand-flies (leishmaniasis), tsetse flies (sleeping sickness), assassin bugs (Chagas disease), ticks (Lyme disease, typhus) and plague (fleas). However, so far the main area of work for control of human disease vectors by GM has been in mosquitoes (*Anopheles* and *Aedes* spp.) where the work has got as far as field trials and where we have already seen successes.

### **Q. Are there any human disease risks in Europe, particularly the UK, for which GM insects are under development?**

A. Although mosquito species in the UK and Europe are largely not vectors of human disease, there are occasional reports of malaria, dengue and West Nile in some European countries. This could become much more common if climate changes include warmer, wetter conditions needed for mosquitoes to breed. Probably the most important human disease/vector system in the UK is Lyme disease/ticks and as far as I know there is no GM work in this area. Although the Scottish biting midge doesn't vector disease it is a severe nuisance pest and could be target for GM control.

### **Q. What are the possible livestock and agricultural crop applications of GM insects across the world? Are there any potential applications of relevance to UK agriculture?**

A. The possible applications of GM insects across the world is enormous as in theory any insect causing nuisance damage or vectoring disease to livestock and any insect damaging crops either directly or indirectly (via transmission of plant pathogens) could be controlled this way. There are many possible applications to UK. For livestock 'blue tongue', a disease of ruminants that is vectored by *Culicoides* midges, would be a good target. For UK crop pests there would need to be a lot more work on generating GM insects as the technology doesn't currently extend to many species. Preliminary work on the diamond back moth looks promising and other Lepidoptera could follow. The main vectors of crop viruses, aphids, would be more difficult as their largely asexual reproduction would make it more difficult to get traits into populations. One area where there is potential, is to engineer 'beneficials' in protected environments so that they are resistant to insecticides, allowing control of pest species without losing natural control in IPM programmes.

### **Q. What could GM insects do that other approaches, such as biological control methods, can't?**

A. GM insects offer the potential to eradicate a species in a particular area, which biological control can't do. The need to completely eradicate is particular important for disease vectors

where even small numbers can do a great deal of damage. Biological control only works when a reduction in number is enough to have an effect.

**Q. Do the current EU and UK GMOs regulatory frameworks work for GM insects?**

A. No it does not cover the newer techniques of generating GM insects (such as TALENS and CRISPR) which are a more site-directed approach. There should be consideration of whether this genome editing is really GM and what regulation is/isn't needed.

**Q. Are there lessons to be learnt from the regulation of GM insects in other countries such as Brazil?**

A. Yes – all use of GM should be looked at to see what the consequences were for both the desired effect and potentially other effects that weren't anticipated. For example do other species move into the vacant niche? Do other species suffer because of lack of food supply?

**Q. How is research into the development of GM insects currently funded, and how can we attract more private funding?**

A. Work on the development of GM insects is state-funded especially in the US. However, there is private funding, e.g. Oxitec in the UK. Permission to do field/glasshouse trials would encourage company investment.

**Q. Given the possible public health benefits of GM insects, should the Government be funding their commercialisation?**

A. Where there is a 'public benefit' such as for use in disease-endemic countries or to control a specific outbreak of a disease that needs to be brought under control, the Government should be involved. But where the technique is being developed for commercial use in pest control it should be left to market forces (i.e. in the same way as commercial development of new insecticides is). However the technology to make GM insects also has considerable application in the laboratory as a research tool to answer scientific questions which should be subject to public funding.

**Q. How could the UK benefit economically from both developing GM insect technology and its use within the UK?**

A. Developing the technology would benefit UK insect research broadly. It could place the UK in the forefront of this area of research, attracting more talent and potential inward investment in instances that GM solutions are developed. The use of GM technology could potential protect yields and thus financial returns for UK farmers by reducing the risk of yield losses and environmental damage. It could also help to eradicate invasive pests as you describe especially those resistant to pesticides (e.g. the *Tuta absoluta*).

**Q. How can the gap between regulatory approaches and public concerns over GMOs be addressed?**



A. In general the use of GM insects will only be acceptable to the public if:

- They can see a real benefit so only commercial releases that have a positive impact should be allowed.
- We are very open about potential risks and encourage a realistic risk/benefit analysis, not a precautionary principal.
- The gains should be primarily for the public good, this should be easy where there is potential to control life-threatening disease.

A public education campaign needs to accompany the development of the technology before it is adopted.

We could potentially merge bullet point two and the final sentence and put it further up followed by the current bullet point 1. The suggested sentence could be that public consultation based on openness about potential risks, which ultimately will encourage a realistic cost/benefit analysis would contribute towards responsible innovation in eth area of GM insects.

*17 September 2015*

## The Royal Entomological Society (RES) – Written evidence (GMI0021)

- 1) The Royal Entomological Society (RES) aims to improve and disseminate knowledge about insect science. The RES has an international fellowship and membership composed of entomologists that conduct research on insects across a wide range of scientific fields. Insect scientists have more experience and knowledge about moving, manipulating and managing insect populations than researchers from any other discipline. The RES is therefore ideally placed to gather evidence for a response to the inquiry on *genetically modified insects* of the House of Lords Science and Technology Select Committee. This response has been formulated in consultations by the RES President, Professor John A. Pickett CBE, FRS, with RES Fellows and the Editors of the RES scientific journal *Insect Molecular Biology*, each of whom conduct research at the forefront of insect genetics and are international authorities on the subject.
- 2) The RES would like to make it clear to the Committee that genetics-based insect control technologies first emerged 50 years ago and that in the intervening half century there has been continuous interest and progress in creating insect genetic technologies and genetics-based insect control programmes. The RES therefore welcomes the Committee's inquiry on GM insects and recognises that placing genetically modified insects in that continuum of research and development could be very helpful in contextualizing the problem and ultimately make it clear that the answers are largely available already if connections between the existing scientific evidence can be made. The RES response to the ten questions posed by the Committee are outlined below and followed by some background on the science of genetically modified insects.

### **Q1. Which human diseases, across the world, could be addressed through GM insect technology? Are there any human disease risks in Europe, particularly the UK, for which GM insects are under development?**

- 3) In the near future, this is likely to be restricted to those insect vectors where transgenic technology is reasonably well-developed. This includes *Aedes aegypti*, *Aedes albopictus*, *Anopheles gambiae* and *Anopheles stephensi*. This means that the principal global targets might be malaria, dengue and perhaps other arboviruses. Transgenic technology is now progressing with *Culex quinquefasciatus* but lags some way behind. In the EU, transmission of chikungunya by *Aedes* sp. has been evidenced (e.g. in Italy) and may become an increasing problem as the climate warms and the vector species move further north. At present, the risks specific to the UK (at least in terms of human disease) are not large. Oxitec Ltd has some *Aedes* sp. development efforts ongoing.

### **Q2. What are the possible livestock and agricultural crop applications of GM insects across the world? Of current livestock disease risks and agricultural insect pests that could be addressed through GM Insects, which should be the highest priority for Europe?**

- 4) There are ongoing efforts to develop and use genetics-based insect control strategies against agricultural and livestock pests and all of these efforts could benefit from the use of genetic modification technologies. The biggest threat may be blue tongue virus transmitted by biting midges. However, no GM midges have yet been developed and so any interventions would be limited to some extent by the available transgenic technologies. Here is an authoritative source of information <http://www-naweb.iaea.org/nafa/ipc/sterile-insect-technique.html>

**Q3. Are there likely to be opportunities provided by GM insects that cannot be provided by other approaches, such as biological control methods? How could GM insect approaches be complementary to existing Integrated Pest Management (IPM) programmes?**

- 5) Classical biological control requires the identification of appropriate agents – often these are found by scouting for parasites, pathogens, parasitoids in the home range of the pest, in the case of an invasive species. In the event that no suitable agents can be found or used, genetics-based approaches could be an alternative. This question is tied up with the robustness and flexibility of available transgenic technologies. In principle, very subtle and targeted changes could be introduced via GM strategies whereas biological control could suffer from major ecological difficulties perhaps related to invasive potential and off-target interactions. Of course, classical biological control has risks that are different in some cases from those associated with genetics-based strategies and those risk scenarios could favour genetics-based strategies. Genetics-based approaches such as the Sterile Insect Technique can be effective when pest densities are low and consequently can be highly complementary to chemical-based approaches that are effective at high pest densities. In fact, Sterile Inset Technique programmes are often deployed following chemistry-based programmes.

**Q4. How appropriate are current EU and UK GMOs regulatory frameworks in addressing the issues raised by GM Insects? Are there lessons to be learnt from the regulation of GM insects in other countries such as Brazil?**

- 6) The regulatory frameworks are more than adequate and perhaps stifling in some aspects. It is clear, for example, that the HSE were prepared to largely overlook genetically modified *Drosophila* for many years (perhaps some form of model organism bypass) but took a great interest in GM mosquitoes for reasons that are unclear. The whole approach to GM insect regulation has been clouded and hampered somewhat by the historical 'Monsanto' fiasco surrounding GM crops. It is true that these issues were handled poorly but perhaps it is time to release the brake a little to allow more innovation. This is perhaps what has happened in Brazil (where releases of GM *Aedes aegypti* have either happened or are imminent). It is becoming apparent that those countries at the sharp end of dealing with vector-borne disease are far more ready to embrace technologies such as GM than are affluent western societies.
- 7) The US National Academy of Science is currently investigating and reporting on this topic <http://nas-sites.org/gene-drives/>. The US also seems to be in the process of

reevaluating the roles of various agencies in dealing with genetically modified insects.  
<http://news.sciencemag.org/biology/2015/07/u-s-review-agricultural-biotech-regulations>

**Q5. Do the World Health Organisation (WHO) guidelines on the release of GM mosquitoes provide the basis of an effective regulatory framework? How should issues regarding the emergence of resistance be considered?**

- 8) The guidance that emerged does provide an adequate regulatory framework but national regulatory agencies will adapt their existing frameworks to current needs and cannot be expected to simply adopt WHO's framework. The term 'resistance' in this question is not entirely clear but we take it to mean problems over the breakdown of a transgenic intervention. This would have to be anticipated, perhaps due to instability of a transgene construct at the population level or perhaps silencing of a transgene cassette. Both have been seen in the laboratory and would undoubtedly happen in nature given the scale of such operations. However, there are few inherent risks in such breakdowns, apart from the loss of disease control. Such breakdowns could be identified by sampling and repeat interventions with the same or different transgenes made.
- 9) A thorough understanding of how various genotypes might evolve and change over time will need to be part of any evaluation process. Resistance and resistance management will be an integral part of any implementation plan. It seems these concerns could be addressed as current concerns for resistance are addressed.

**Q6. Do the European Food Safety Authority (EFSA) guidelines on the environmental risk assessment of GM Insects for commercial use sufficiently address the different risks from population suppression and population replacement approaches? How should the ecological risks and human benefits that might arise from the application of gene drive techniques to population replacement approaches be assessed?**

- 10) Yes they do. In fact they are probably overbearing and inhibitory to innovation. It may be the case that the risks of transgenic technology lie far more in making them work to combat disease than in ecological risks or health and safety risks. Webber et al. suggest that classical biological control provides a relevant framework from which to begin assessing gene drive programmes and other genetics-based programmes. Classical biological control introduces a novel, usually non-native, genotype (in the form of a parasitoid, for example) into a new environment and depends upon it performing as planned to affect the pest population. Our abilities to predict outcomes in this case will be no better and are likely worse than our abilities to predict outcomes from the introduction of novel genotypes produced in the laboratory involving small modifications of a genome using genetic technologies on a native species. Nonetheless, the framework for assessing these programmes should be very similar. (Webber, B.L, Raghu, S. and Edwards, R. (2015) Opinion: Is CRISPR-based gene drive a biocontrol silver bullet or global conservation threat? PNAS Early Edition [www.pnas.org/cgi/doi/10.1073/pnas.1514258112](http://www.pnas.org/cgi/doi/10.1073/pnas.1514258112)).

**Q7. How is research into the development of GM insects currently funded? Are there opportunities to attract more private investment into this area?**

11) Essentially all research and development of insect genetic technologies is done in academic laboratories funded by traditional sources – governments, foundations etc. Funding is a major difficulty. The EU and Wellcome Trust have put limited funding into this area but the UK research councils are reluctant in the extreme. The inquiry might, for example, look at how many vector biology projects are currently supported by the MRC. Currently, this may be zero. Perhaps worse, this seems to be a political stance with the MRC openly stating that they are unconvinced of the merits of GM approaches. This stance is stifling innovation, research and development in all sectors, and investment by the private sector in particular. We need much more funding and innovation in this area. There will be opportunities when a path to commercialisation is clear. Currently, there is much uncertainty about whether and how using insect genetic technologies will be implemented.

**Q8. Given the possible public health benefits of GM insects, should the Government be funding their commercialisation? Would this result in a conflict of interest with regard to regulation of releases? If so, how might this be managed?**

12) In the current economic climate, we do not envisage much interest in commercial development of transgenic technologies for tropical disease control. There has never been money in tropical diseases, except in relation to military or tourism interests. This ‘conflict’ arises in the US on a regular basis. For example, the US Department of Agriculture’s Agriculture Research Service has a research and development mission while the US Department of Agriculture’s Animal Plant Health Inspection Service has a regulatory mission. The Services are administratively distinct and firewalls are in place to allow autonomy. Governments and organisations deal with this problem all the time. US federal agencies have an office of the Inspector General responsible for monitoring and auditing an organization to prevent fraud, mismanagement etc. Again, structural solutions are needed to insure autonomy.

**Q9. How could the UK benefit economically from both developing GM Insect technology and its use within the UK?**

13) Any commercial developments would almost certainly involve crop protection (aphids, beetles?) and perhaps bluetongue control (biting midges) but this would require seedcorn investment to develop technologies for the target species. If these were successful, they would presumably be widely marketable.

**Q10. How can the gap between regulatory approaches and public concerns over GMOs be addressed? Is there a role for ‘responsible innovation’ approaches? What are the critical factors in effective public engagement from lab to final release?**

14) By consultation and persuasion but also by the willingness of the UK government to allow new technologies to develop and prosper without unreasonable hindrance. Transparency is key to any efforts to move technology out of the laboratory. Oxitec’s

lack of transparency is perhaps an example of how it should not be done. Having a good solution to an important problem is an important driver of success as well.

## Background

- 15) Beginning in the middle of the 20<sup>th</sup> century, there emerged within the area of applied entomology an interest in using our growing knowledge of insect genetics as leverage in efforts to control insects of significance to human health and agriculture. The successful development and implementation of the Sterile Insect Technique to control the New World Screwworm was a powerful example of how genetic technology, in this case random mutagenesis, could be used with great effect against devastating pests.
- 16) The Sterile Insect Technique relies on the mass production of the target pest species followed by mutagenesis using radiation and then release of those insects into the environment. The mutagenized insects act as ‘smart bombs’, seeking out individuals in the pest population and upon finding and mating with those individuals, preventing them from reproducing. The net effect is that insect geneticists have used the genes of the pest species as a highly specific and effective means to reduce population levels.
- 17) The continuing effectiveness of this highly specific and environmentally-friendly insect pest control method - there are many current examples of this technology being used worldwide - has provided the inspiration for continued research efforts into other ways by which genes and genetics could be used.
- 18) The Sterile Insect Technique relies on a very simple but powerful genetic technology – mutagenesis – to alter or manipulate the genomes of insects. Today insect scientists have a much wider array of genetic technologies that allow them to make more planned and precise changes to the genomes of insects. These technologies include the ability to introduce genes into genomes to create what are commonly referred to as ‘transgenic’ insects and, more recently, the ability to make very precise alterations and modifications to genomes using ‘gene editing’ technologies.
- 19) The Sterile Insect Technique was the first genetics-based insect control strategy and in the intervening half century since its conception there has been no dearth of other ideas for additional genetics-based insect strategies. What have been lacking are suitable technologies for accomplishing the necessary genetic manipulations. While contemporary insect genetic technologies are diverse and powerful and are beginning to be applied to important insect systems, they remain challenging to deploy in most insect species.
- 20) Genetics-based insect control strategies have important similarities to Classical Biological Control strategies and the widespread acceptance and use of this approach to controlling insects could provide a useful framework from which to consider genetics-based strategies moving through the research and development pipeline. Webber et al. (2015) have recently articulated this view (Webber, B.L, Raghu, S. and

Edwards, R. (2015) Opinion: Is CRISPR-based gene drive a biocontrol silver bullet or global conservation threat? PNAS Early Edition ([www.pnas.org/cgi/doi/10.1073/pnas.1514258112](http://www.pnas.org/cgi/doi/10.1073/pnas.1514258112)).

- 21) In the last three years a ‘gene editing’ technology has become widely available that allows great precision and control of genetic modifications. It also can be used to easily create ‘gene drive’ systems, genetic systems that severely skew inheritance patterns in favour of chromosomes containing the ‘gene drive’ elements. Consequently, ‘gene drive’ systems can, under the right conditions, spread through a targeted population with great rapidity. This technology has tremendous potential as a pest control tool because ‘gene drive’ systems can be designed to have effects on the phenotype of the host insect that will lead to the demise of the target population (and just the target population). Chemical-based insect control programmes aim to eliminate an insect species from an area but inflict enormous collateral damage. ‘Gene drive’ technology could be seen as a magic bullet of sorts for pest control – specific, effective, inexpensive, flexible. The potential to serve as an effective tool is enormous and there should be great enthusiasm within the insect science community and elsewhere for efforts to explore this technology and to find ways by which it can be used that comply with our current standards of safety. We do not want genetics-based insect control technologies and gene drive to be the next DDT – a magic bullet that had a severe uncontrolled down side.
- 22) While the public’s awareness of insect genetic technologies is almost always in the context of direct applications to pest insects, it is critical to understand that the most substantive applications will be in the laboratory to ask questions about insect biology. The significance of these insect genetic technologies to the study of insects cannot be overstated and the benefits that will emerge from the basic knowledge of insect biology as a result of using these technologies will be felt by the public in the form of food security and public health.

*18 September 2015*

## Sciencewise – Written evidence (GMI0005)

### *Introduction*

1. This response to the Science and Technology Committee’s inquiry has been developed by Sciencewise. Sciencewise is the UK’s national centre for public dialogue in policy making involving science and technology issues. It is funded by the Department for Business, Innovation and Skills (BIS). We welcome the opportunity to provide evidence to the Committee. Our submission draws on our extensive experience of engaging the public in some of the most challenging and controversial policies involving science and technology, including genetic modification (GM).
2. Our submission focuses solely on Question 10 of the Committee’s call for evidence which directly concerns Sciencewise’s public engagement expertise.

**Q10. How can the gap between regulatory approaches and public concerns over GMOs be addressed? Is there a role for ‘responsible innovation’ approaches? What are the critical factors in effective public engagement from lab to final release?**

***Context: Genetic modification is an area of high public concern and GM insect technologies are likely to be of particular public interest***

3. History has shown that genetic modification is an area of high public interest. Possibly more so than any other area of new science and technology over the last 20 years, it has captured public anxieties around the direction of scientific development. It is politically charged, with strong and active public interest groups.
4. Sciencewise has comprehensively reviewed the results of previous exercises in public and stakeholder engagement in the United Kingdom on issues related to GM and its application.<sup>172</sup> There is not a simple picture of public opinion regarding GM, and public concerns are often conditional on the intended use of technologies and their governance. Public concerns around GM fall into the follow categories:
  - Safety: The starting point for many people’s concerns regarding GM is that the technology is perceived as unsafe, or seen to create risks, either for individuals or the environment.
  - Novelty: Concerns around safety and risk relate to the fact that GM is relatively new and untested at scale.
  - Sustainability, uncertainty and ignorance: There are public concerns that new interventions in complex ecosystems challenge scientific understanding, and may have unknown and unintended consequences.

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<sup>172</sup> Stilgoe, J, Stirling, Andrew, Jackson, R, Warburton, D, Acland, A and Lansdell, S (2011) *Talking about GM: approaches to public and stakeholder engagement*. Other. Sciencewise-ERC subgroup, UK, <http://www.sciencewise-erc.org.uk/cms/assets/Uploads/Talking-about-GM.pdf>.



- Socioeconomic concerns: GM technology is not just seen as an intervention into the food chain or the environment. Public dialogue exercises bring to the surface a recognition that GM technologies also present economic issues. This includes questions about intellectual property, patenting and the livelihoods of developing country farmers.
  - Governance and regulation: The public lacks confidence in the ability of scientists, companies and governments to understand and appropriately regulate the myriad possible implications of GM technology.
5. GM insect technologies are likely to trigger concerns in all of the above categories, and public interest groups have already raised concerns around safety, risk, transparency and regulatory oversight.<sup>173</sup> This makes investing in appropriately designed engagement essential to ensure public concerns are mitigated as part of the policy process.

***Bridging the gap between regulatory approaches and public concerns: What would good public engagement around GM insect technologies look like?***

6. Sciencewise’s experience engaging the public in a range of policy areas involving science and technology suggests a number of critical success factors for public engagement around GM insect technologies.

**Clarity and transparency around the purpose of engagement**

7. Government needs to be clear about its objectives at the outset of any public engagement exercise. In particular, it should be clear if the primary purpose of engagement is simply to *inform* the public about decisions with little room for influence over policy, or whether it is to seek the public’s views as an *input into decision making*. Different public engagement methods achieve different outcomes and appropriate methods are identified once the purpose of the engagement is clear.
8. In the case of GM insect technologies, Sciencewise recommends stakeholder and public engagement as an *early input* to the policy process, and where there is still considerable room for *public influence* over decisions. This ensures likely public concerns can be addressed as part of regulatory and communications approaches, reducing the chance of public ‘backlash’ against uninformed or poorly communicated decisions.

**Selecting an appropriate method of engagement**

9. Sciencewise’s expertise is in public dialogue. This is a particular type of public engagement which brings together members of the public, policy makers, scientists and other expert stakeholders to deliberate and come to conclusions on public policy issues. Well-designed public dialogue allows public participants (usually representative of the public at large) to move relatively quickly from little or no knowledge of, or opinions on, a topic to understanding the key issues of even complex scientific and technological developments and come to a view. Public dialogue enables the public to take on new

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<sup>173</sup> For example, see “Is the world ready for GM animals?” BBC, 23 February, 2015, <http://www.bbc.co.uk/news/science-environment-31604233>.

information, have time to discuss and reflect, and develop their own thinking. In this way, public views are allowed to develop and shift. This presents policy-makers with a rich picture of plural and conditional responses. Policy-makers have found this type of exercise particularly effective in:

- getting beyond vested interests and enabling debate with members of the public without polarisation and acrimony
- providing useful insights and information on detailed policy issues, from public comments and from their questions
- fully understanding the considered and informed views of the public, why they are held and how strongly

10. GM insect technologies are an appropriate topic for public dialogue. This is both because of their complexity, which requires a deep approach to public engagement in order to elicit informed views, and because they are controversial and likely to evoke a strong and polarised response from stakeholders. Sciencewise is unaware of any deliberative public engagement work done on GM insect technologies to date.<sup>174</sup>

11. Other public engagement methods include providing information to the public, convening open meetings and online and written consultations. Public engagement via these methods tends to engage stakeholders and members of the public with an existing interest or knowledge of the topic. Policy-makers also find this approach useful as it:

- opens up the process to wide public scrutiny and comment
- enables those with particular interests to formally present their views
- allows for free and wide access to the process
- can reach large numbers of people (depending on the topic and the methods used).

12. Sciencewise’s experience suggests that public dialogue and other engagement methods usefully complement one another, allowing for robust representation of diverse public perspectives. For example, Sciencewise led a process of public engagement around the ethical, social and regulatory issues involved in mitochondria replacement to support advice provided by the Human Fertilisation and Embryology Authority. This process included deliberative workshops, public meetings, focus groups, an opinion poll and a consultation website, with the various methodological strands used to add depth to and triangulate results.<sup>175</sup>

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<sup>174</sup> Survey evidence on public views on the release of GM Mosquitoes from the United States shows support depended on how the issue is presented, including discussion of risks and use of the terms “genetically engineered,” “genetically modified” or “transgenic” rather than “sterile.” For a summary of the results, see <http://www.news.ncsu.edu/2012/08/wms-cobb-mosquitoes/>.

<sup>175</sup> For more information on the Sciencewise public dialogue on mitochondria replacement, see <http://www.sciencewise-erc.org.uk/cms/mitochondria-replacement/>.

### **Case study: Public dialogue on Synthetic Biology**

#### *Background*

Synthetic biology is an emerging area of science and technology, using developments in engineering and bioscience to create new biological parts or to redesign existing ones to carry out new and useful tasks. Synthetic biology has the potential to deliver groundbreaking applications, but raises issues of societal concern including bio-security and social justice issues. Sciencewise led a process of public engagement on Synthetic biology from July 2009 to April 2011.

#### *Dialogue activities*

Public engagement combined stakeholder consultation with deliberative dialogue. *Phase 1* included a series of in-depth telephone interviews with 41 stakeholders to understand some of the technical, social and economic drivers shaping synthetic biology in the UK. This was used to frame and inform the content for the public dialogue. *Phase 2* comprised 12 deliberative workshops that brought 160 members of the public together three times in four locations (London, Llandudno, Newcastle-upon-Tyne and Edinburgh) along with scientists, social scientists and representatives from the Research Councils. These were designed to get to the heart of participants' aspirations and concerns around synthetic biology as well as to explore how different views and values come into play when considering potential applications of the research.

#### *Key messages from the public*

Findings from the dialogue showed there was conditional support for synthetic biology: while there was great enthusiasm for the possibilities of the science, there were also fears about control; who benefits; health or environmental impacts; misuse; and regulation.

Five central questions emerged for synthetic biology:

- What is the purpose?
- Why do you want to do it?
- What are you going to gain from it?
- What else is it going to do?
- How do you know you are right?<sup>176</sup>

Results of the dialogue have been widely used by research councils and policy makers.

### **Overcoming distrust**

13. Public engagement around contentious issues such as GM often starts from a position of mutual suspicion between those involved. This could include the suspicion that engagement is designed to 'sell' a particular technology (by manipulating or limiting information that is provided), suspicion of bias on behalf of the commissioning body, or

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<sup>176</sup> For more information on the process and outcome of the Synthetic Biology public dialogue, see <http://www.sciencewise-erc.org.uk/cms/assets/Uploads/Publications/SWSyn-Bio-FINAL03-2012.pdf>.

the suspicion that engagement is designed to ‘rubber stamp’ decisions that have already been made.

14. These suspicions can be tackled through a carefully designed and transparent engagement process. Techniques to consider include (among other things): direct involvement by policy makers in the design and delivery of engagement activities, representing a diverse range of perspectives in engagement activities, use of independent facilitators, maximising transparency by publishing information provided and the results of the engagement process, and a clear response by the policy-making body to the conclusions of the public engagement.

### **Selecting the scope of engagement and framing issues appropriately**

15. Carefully selecting the scope of engagement is crucial to ensuring a robust public engagement process. In the case of GM technologies, public interests and concerns include regulatory issues around safety and risk, but also extend to wider issues including financial control, social and economic impacts, and the distribution of risks and benefits. Discussion of alternative solutions that may be ‘more natural’ has also been an important part of the public debate around GM. A focus simply on regulation without discussion of these wider factors may therefore miss the most salient aspects for the public, leading to later unexpected controversy or opposition.
16. Framing issues appropriately is also crucial when presenting information about new technologies to the public. An important part of this is clearly presenting the purpose of the new technology or the problem that needs to be addressed. In order to ensure issues are presented to the public without bias, Sciencewise invariably recommends the use of an expert stakeholder group that represents a diverse spectrum of views to test and validate public communications materials as they are developed. Involvement of stakeholders in this manner is also likely to lead to greater trust in the process and buy-in to the outcomes of the dialogue.

### **Responsible innovation**

17. Responsible Innovation approaches are relevant to GE insect technologies. Responsible Innovation promotes opportunities for science and innovation that are socially desirable and undertaken in the public interest. It also recognises that innovation is often ambiguous in terms of purposes and motivations and unpredictable in terms of impacts, beneficial or otherwise.
18. Responsible Innovation ensures public interest aspects of innovation can be explored in an open, inclusive and timely way. The Engineering and Physical Sciences Research Council has developed a framework for responsible innovation that can be usefully drawn upon in funding and governance decisions around GE insect technologies. This framework suggests decisions should:
  - Anticipate – describing and analysing the impacts, intended or otherwise, (for example economic, social, environmental) that might arise. This does not seek to

predict but rather to support an exploration of possible impacts and implications that may otherwise remain uncovered and little discussed.

- Reflect – reflecting on the purposes of, motivations for and potential implications of the research, and the associated uncertainties, areas of ignorance, assumptions, framings, questions, dilemmas and social transformations these may bring.
- Engage – opening up such visions, impacts and questioning to broader deliberation, dialogue, engagement and debate in an inclusive way.
- Act – using these processes to influence the direction and trajectory of the research and innovation process itself.

19. Since the development and implementation of GE insect technologies impinge on societal, economic and cultural practices (including agriculture) it is essential that innovation acknowledges and responds to these. This requires appropriate dialogue with interested parties and publics, and a multidisciplinary approach to research prioritisation and development.

### **Managing risks**

20. Any future engagement process has the potential to receive significant media attention and thus raise the public profile of GM and related issues. Negative press coverage could represent a threat to the engagement, or even harm the credibility of the policy-making process. The risk of negative coverage is likely to be enhanced should the engagement lack a clear and widely understood purpose, not be planned or commissioned transparently, or not command the confidence of a broad enough range of stakeholders. Sciencewise-ERC is able to discuss more tailored advice to public bodies looking to include public and stakeholder engagement in developing their policy on issues related GM and its application.

### **Conclusion**

21. GM insect technologies are likely to be an issue of high public interest and concern. Sciencewise's experience engaging the public on controversial science and technology issues suggests well-designed public engagement can play an important role both prior to and during the regulatory process, ensuring the public's views are considered, helping ensure that innovation trajectories carry wide support, and potentially avoiding later controversy or opposition. The Committee may wish to consider promoting deliberative public dialogue, in combination with other public engagement methods, as a mechanism through which regulators start a conversation with the public on GM insect technologies.

*16 September 2015*

**Sciencewise, the British Ecological Society (BES), and Dr Sarah Hartley, University of Nottingham – Oral evidence (QQ 16-25)**

*Evidence Session No. 2*

*Heard in Public*

*Questions 16 - 25*

TUESDAY 13 OCTOBER 2015

Members present

Earl of Selborne (Chairman)  
Lord Cameron of Dillington  
Lord Fox  
Lord Hennessy of Nympsfield  
Lord Hunt of Chesterton  
Lord Kakkar  
Lord Krebs (co-opted)  
Baroness Manningham-Buller  
Lord Maxton  
Duke of Montrose  
Baroness Morgan of Huyton  
Baroness Neville-Jones  
Lord Patel (co-opted)  
Lord Peston  
Viscount Ridley  
Lord Vallance of Tummel

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Lord Taverne

**Examination of Witnesses**

**Sir Roland Jackson**, Executive Chair, Sciencewise, **Professor Sue Hartley**, President Elect, British Ecological Society, and **Dr Sarah Hartley**, School of Biosciences, University of Nottingham

**Q16 The Chairman:** Could I welcome you to this next session? Thank you for joining us. We are being broadcast, just for the record. Would you like to introduce yourselves for the record? If anyone would like to make an introductory statement, please feel free to do so.

**Professor Sue Hartley:** I am Professor Sue Hartley. I am president elect of the British Ecological Society. I am also a professor of ecology at the University of York. Between 1999

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and 2006, I was a member of the Advisory Committee on Releases to the Environment, and I chaired their working group on post-market environmental monitoring. I was also an ad hoc expert on the GMO panel of the European Food Safety Authority between 2004 and 2009.

**Dr Sarah Hartley:** I am Sarah Hartley. I am a research fellow in the School of Biosciences at the University of Nottingham.

**Sir Roland Jackson:** I am Roland Jackson. I am executive chair of Sciencewise, which is a programme funded by the Department for Business, Innovation and Skills, so I speak here on behalf of the experience and expertise of Sciencewise. I should say that I am not a civil servant, and I certainly do not speak on behalf of the Government. I should add that I am also a member of the management board of the Industrial Biotechnology Catalyst, which to my knowledge has not funded work directly on GM insects but does fund other GM research and translation activities. I am a member of the Nuffield Council on Bioethics and—I think this relevant to this inquiry—I am the chair of the council’s current project on naturalness, understanding how the concept of naturalness is used in public and ethical discourse about biotechnologies in particular.

**The Chairman:** We will later be taking evidence from the Nuffield Council on Bioethics, so that will add to today. If none of you wants to make an initial statement, shall we go straight into our questions?

**Q17 Lord Krebs:** I would like to start with a very general question for all three of you, which is to give us your insight into what level of public awareness, understanding or concern there is in relation to GM insect technology, as opposed to GM crops. We know there has been a lot of investigation of public opinion and so on, including the Government’s own GM Nation? debate a few years ago, in relation to crops, but has there been anything similar in relation to insects?

**Sir Roland Jackson:** As far as I know, the simple answer is not very much. It certainly has not appeared, for example, unlike GM crops issues, in the Public Attitudes to Science survey or generally. There has been quite a bit of media comment and reporting about it, but no significant structured public information and engagement in that sense, or dialogue in terms of listening to what people think about the issues. There is one exception, which is in your evidence given by the Pirbright Institute, which ran an event, to which it gives a link in the evidence. About 70 people attended. They know who the audience was, but they do not report it in the report of the event. Looking at it, it was a self-selected and quite knowledgeable audience, but interestingly it raised quite a lot of the generic questions around biotechnology that you would expect in any biotechnology, not just GM insects.

**Professor Sue Hartley:** Just to reinforce that, there has been far, far less engagement so far on GM insects, but I think that is beginning to start now. The Pirbright Institute meeting was held at Charles Darwin House and partially funded by the British Ecological Society. So far, it is probably fair to say that things have been a little ad hoc and quite localised compared with the much more comprehensive efforts on GM crops, but I think it is rising up the agenda and we are starting to see articles on BBC News webpages and so on, so I am sure that more is going to happen.

**Dr Sarah Hartley:** In the last five years, media articles have been increasing on GM insects, but for the most part those articles deal with the scientific aspects of GM insects, and there is very little debate around the governance issues or the issues we might think the public will

Sciencewise, the British Ecological Society (BES), and Dr Sarah Hartley, University of Nottingham – Oral evidence (QQ 16-25)

be concerned about. That really has not changed. We have seen localised public engagement exercises within the regulatory processes, where specific applications are made for releases. We have seen one in New York State, with the release of the GM diamondback moth. That is an Oxitec and Cornell project. We have seen some debate on GM insects in the development of the EFSA guidance in 2013; a public consultation was held then and there was certainly some discussion about insects in that. These are localised pressure points where public concern has the opportunity to emerge.

**Lord Krebs:** Would you mind, Lord Chairman, if I just ask a follow-up question to Sir Roland Jackson in particular, although others may wish to comment?

I notice in your written submission you talk quite a lot about dialogue as a method of eliciting public responses and public views. I just wondered whether that is the approach you would advocate in relation to GM insects and we are going to start on developing an approach to public understanding, and, if so, how you go from the rather small scale of a dialogue, or even the event at Pirbright, which involved 70 people, to thinking about the view of the nation as a whole. How do you link the small to the large?

**Sir Roland Jackson:** It depends very much what you are trying to do, because any process of public engagement should follow the purpose of that engagement. If you are trying to inform a wide public about the underlying science, different perspectives on GM insects, then that requires one type of engagement. If, as a government department, as a regulator, as a scientific institution, as a funder, you want to listen and understand what issues the public brings to choices about research and development for GM insects, that is completely different. Those sorts of things, where you are feeding public discourse into policy and funding decisions, can be done, amongst other techniques, through these deliberative approaches; they are particularly suited to that. As I say, it very much depends on your purpose.

**Q18 Lord Hunt of Chesterton:** At a previous session, we noted that there is concern about using the name “GM insects”. The House of Commons inquiry felt that there might be a different title. In some countries, there is a different usage; they look at the output and the net result, rather than the scientific process involved in it. GM has all this history behind it. Is that a useful part of the public debate? Do you think we could focus on the product, that these are vaccines, cures or help the development of plants, rather than using this very scientific word, which people do not understand and gives them all the shakes?

**Professor Sue Hartley:** There are number of facets to our terminology, and I agree with you that it can be very damaging to the public debate if people get too fixated on terminologies and technologies, but we have certain regulatory and legal requirements that require, at the moment, things to be acknowledged as genetically modified if they are, and that has quite a strict definition. That said, my personal opinion is that moving away from the technology and thinking more about what the technology is designed to deliver, its aims, its benefits, its risks, its impacts and the need for that technology, is probably quite helpful.

Thinking about things as GM and therefore bad, and non-GM and therefore good, might not make a lot of sense when you are talking about impacts that could be delivered in either way. If you take what we are thinking about today and apply it to sterile insects, for example, they can be produced in an entirely non-GM way. Certainly some countries have a different approach to regulation. In Canada, for example, they look at the novelty of a trait,



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rather than how it is produced. We are where we are in terms of UK regulation and EU regulation, which is our jurisdiction, so we have that to deal with, but if we can engage in a bigger discussion about what these technologies do rather than exactly what they are called, that might be quite helpful.

I know we are talking about insects today, but as techniques develop it is now very easy to do lots of different sorts of modifications to plant genetics, for example, so the terminology is getting ever more sophisticated and confusing.

**Lord Hunt of Chesterton:** In terms of organisations—I should not call them “campaigning organisations”—that are concerned with the public dimension, which as I understand it is your interest, and Sir Roland’s and Dr Sue’s, do you feel there is going to be some public debate about this that will help the Government perhaps to change its view or develop a different terminology, or are you just going to accept the current framework and make the best of it? The framework is wrong, is it not? It is misleading to people and it is causing all these difficulties.

**Professor Sue Hartley:** I am not sure it is entirely fair to say that the framework is wrong. We have to do a lot more to engage the public in that framework, and my colleagues will comment here, because that is really their area of expertise. One thing that has driven the debate on genetic modification is that the public have not been sufficiently engaged at an early enough stage.

**Lord Hunt of Chesterton:** “Framework” was the wrong word. “Terminology” is the word I was looking for.

**Lord Fox:** Slightly following on from that, I have engaged in a little non-scientific public engagement on this, since I knew that we would be discussing it. The public, whilst not having a knowledge of gene drive versus self-limiting, do have a received understanding of the introduction of non-native species and non-native organisms into an ecology. Generally, they understand these as the law of unintended consequences. The words “grey squirrel”, “cane toad” and “Japanese knotweed” crop up spontaneously quite quickly. I wondered, in your sense, whether in fact we have to take that wider cultural understanding about the introduction of new creatures into environments if we are going to explain and indeed get assent from the public.

**Sir Roland Jackson:** I would say absolutely. This is summarised in our evidence. Looking at a range of public dialogues and other engagement activities around GM crops in particular, because there has not been much around GM insects, it is quite clear that there is no evidence of overwhelming intrinsic opposition to GM. Public concerns are very much conditional, including along the lines that you have mentioned. Clearly, safety and how that is assessed—I am sure we will come to regulation of it—is a starting point. So is this question of novelty. The technology is being sold to us as novel; that is exciting and people find it exciting. It is also slightly worrying, and when scientists turn around in the same breath and say, “Yes, it is novel, but of course we know how to manage it and regulate it”, there is a slight mismatch there.

People worry about sustainability, uncertainty and ignorance. They ask, “Do scientists really understand the ecological complexity of these things?”. People are not stupid. They know you have unintended consequences. People ask about the wider socioeconomic issues. They know that the introduction of a technology is not just about the science; it is about how

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it affects social structures, how it affects cultures, how it affects jobs and economies, so decisions have to be taken on broader grounds. People worry about governance and regulation. As we heard in the session earlier, there is a sense that these fields are moving very, very quickly, and if you look at the Public Attitudes to Science survey, the majority of people agree with the statement that it is moving too quickly for government to be able to regulate properly. There are legitimate concerns that go beyond the science and the risk assessment, and we need those discussions earlier on about GM insects before we get into any discussions about regulating a particular example. It would be safe and sensible, and a risk-management strategy, to do so.

**Q19 Lord Maxton:** First, can I just say, like Lord Peston, that I have no interest to declare whatsoever? Unlike Lord Peston, I have never been asked either. My question is a simple one. The link to the public knowledge of what is a very complex science, both yours and crops, is of course the public media. Are you happy with the way in which your science and the science of insect biology, et cetera, are covered, and crop is covered, by the British media?

**Professor Sue Hartley:** Shall I start? Yes—the media.

**Lord Maxton:** The *Sun* headlines.

**Professor Sue Hartley:** I would make a couple of general points first. It is important to recognise that the public can engage very effectively, even though they may not understand the science fully, because there are still the wider cultural, socioeconomic and value criteria that the public can engage with. As we heard a moment ago, they recognise the bigger picture, so that is a good thing. The other thing that is quite good is that, funnily enough, I think a climate of scepticism is actually quite healthy. As scientists, being challenged is a very good thing. As tempting as it is to say that the media have not been helpful, there is a responsibility on scientists to communicate clearly and effectively, and they often do not. We cannot blame it all on the media. Also, the pieces I have seen on the BBC about GM insects have been very accurate and balanced, so I think things are improving, and it is important for the science that they improve, but it is also important that we have that healthy debate and extensive public engagement.

**Q20 Lord Cameron of Dillington:** I have to declare an interest as a farmer, a Lawes trustee at Rothamsted, chairman of the advisory board of the Centre for Ecology & Hydrology and chairman of the strategic advisory board of the Global Food Security programme, which is a government-research co-ordination programme.

The danger of asking the second question of the session is that your question has been asked before by almost everybody, so perhaps I can put my question in a different way. There has undoubtedly been a big brouhaha about GM crops and polarised opinion, but from our research on the Global Food Security programme, when you ask people about genetic modification in the health industry, of antibiotic clusters and so on, the basic summing-up of the answer is, “Get on with it. Why are you waiting? Get it to us as soon as possible for the benefit of human health.” Now it seems to me that with insects you have both sides, have you not? You have agriculture and health. I just wonder what lessons can be learnt from perhaps both sides of that debate and how we can make certain that both sides get acceptable to the public.

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**The Chairman:** I wonder if Dr Hartley would like to address that, because, particularly in your written evidence, you refer to some of the wider issues than just the scientific evidence.

**Dr Sarah Hartley:** To bring in an answer to one of the previous questions, where we have seen public reaction to insects there is also a sense of powerlessness at the moment, because the debate is so framed by the science. The only opportunities that the public have to engage on GM insects have been in scientific terms, and they have not been allowed to debate these broader issues—what we sometimes term governance or political issues. The science-based regulatory framework certainly privileges some at the cost of others, and it privileges those with scientific expertise at the cost of these other political issues. Certainly when we look at the kinds of documents that the public are asked to comment on within these scientific processes, they simply do not have the expertise to be able to contribute meaningfully to the risk-assessment stage of the regulatory process.

The panel talked earlier about the difference between health and agriculture. Certainly we suspect that within Europe the agricultural applications of the insects will come through first. In the Brazil case, the public were on board. There was practically no public opposition to the GM mosquito in the fight against dengue in Brazil. There was certainly great political will at every level—both at the state and the federal level—for the GM mosquito. That kind of political will and the engagement of publics in actively fighting dengue in their communities on a regular basis put them in touch with the problem that they were facing.

In an agricultural context, it is going to be much harder, not just on the back of the GM crops crisis but in general. The problem is not so clear to the public, and this comes back to your earlier point. We can talk about the term “genetic modification”, but if we talk, as Professor Hartley said, about the problem at hand and bring the public into finding solutions to that problem, GM insects may be part of that solution. However, we will have to approach agriculture in a different way from health.

**Professor Sue Hartley:** To follow up very briefly on that, that is absolutely right, and the key thing for the public is who benefits and the need for this technology. With agriculture, people fail to see why we need to do this kind of tinkering: the crops are in the fields, the food is in the shops. For medical needs, people can see that this is appropriate, can benefit them and will lead to some real advances that might not have been possible by other techniques. I think back to when I was on ACRE and our agendas were first made public. We had on the agenda an application for a small field trial for GM wheat and several applications for GM vaccines. The postbag absolutely bulged with public objections to the GM wheat field trial. No one made a comment on the GM vaccines, although, from a risk-assessment point of view, they were much more problematic.

**Q21 Lord Vallance of Tummel:** Who is responsible for orchestrating this public debate? Where does the initiative lie? At the moment, it seems to be up in the air. Who should be doing it and how should it be done? A linked question is: where do the NGOs sit in all this? Are they helpful, or are they demonisers?

**Baroness Morgan of Huyton:** Which NGOs are engaged? Is it the NGOs that are involved in the ecology space, or is it NGOs that are currently involved, for example, in providing mosquito nets in sub-Saharan Africa? How widely do we draw partners into the debate?

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**The Chairman:** Let us have an answer to that. I should just note that of the written evidence we have had, we do not have a lot of evidence at all from the NGOs, which is in itself quite interesting. Would you like to respond?

**Sir Roland Jackson:** Who leads or orchestrates any public debate or dialogue or whatever depends on who wants to listen and what the purpose of that listening would be. That gets us to questions of how the regulatory system works, which you dealt with in your previous session. The regulatory system is very much couched, rightly, around questions of risk to human health and the environment, and a science-based assessment of those. We have had a call in a lot of the evidence mentioned this morning to assess benefits against risks during that process. My response would be that benefit is not the opposite of risk. The opposite of benefit is disbenefit or disadvantage. Questions of benefits encompass a much wider range of issues than the question of science-defined risk. If you are to have a system that looks at benefits as well as risk, you have to look at wider disbenefits—things like impacts on employment, ways of farming or landscapes, which are not dealt with in a risk assessment.

Then it becomes a question of how you get that sort of discourse, and what sort of institutions would listen to that sort of discourse. There are several possible loci for that. It could be government looking to frame decisions about choices for allocation of funding or policies around funding. It could be research councils or Innovate UK looking at how they prioritise particular activities and allocate particular funding. It could be a regulator, like ACRE, although I am not sure if it would be possible, under its current constitution, to look at those broader issues. However, if regulators are looking at those issues, they would need very different expertise on them from that they currently have. They need much wider social science and other people to take account of these broader issues. The simple answer is that it depends, and it depends on who is listening.

**Lord Vallance of Tummel:** I am asking something very specific; I am talking about GM insects, which is our agenda today. Who is responsible for starting off the debate? You have given us three could-bes. In whose in-tray does it sit?

**Dr Sarah Hartley:** It will depend on whether it is a health or agricultural application, first, but certainly Defra would be a key agent in establishing public dialogue outside a science-based regulatory framework. ACRE does not have the remit to consider those broader issues, and certainly within the European regulatory framework we do not have an opportunity to discuss those issues. That is why the reform of the regulatory system in Europe has taken place: to allow member states to reject GM crops on an individual basis outside the scientific system that EFSA manages.

We have learnt from GM crops that there is a need to discuss those political issues. Defra would be an obvious first choice. It would depend on the purpose of the engagement: whether it was to steer the direction of research towards social needs and to increase the potential social impact of the research, or whether it was to test public perceptions and bring the public on board, in which case you may want to engage BIS if it is more industry-focused. It would depend.

**The Chairman:** I would be disappointed if our final report does not clearly identify who should be owning this problem. I think that is one of our issues.

**Lord Patel:** My comment is in relation to the answer that Dr Hartley gave to Lord Fox's question. You felt that the discussion on GM insect modification for agriculture would be

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much more difficult than for health. When we think about and discuss the harm and benefits, we have to put it in the context of what harm the current technology might be doing regarding increasing crop production, for instance insecticides. The science now clearly shows that some of the insecticides used for improving crop production are doing a great deal of harm to non-human organisms and humans, and bees might be one of the examples from the recent science that came out of Berkeley University. The debate must include the harm and benefits of the current methodology and science compared with insect modification.

**Dr Sarah Hartley:** I might even go one step further and expand that out and say that perhaps we need to look at the problem of agriculture more generally and crop protection. If you look at the potential solutions that we have, right now we have a very insecticide-heavy solution to that problem. We are suggesting, with GM insects, that we may have a better solution to the problem of crop protection.

**Professor Sue Hartley:** That is very true. This is a really important point, and it goes back to our earlier discussion about the terminology and “GM good” and “GM bad”. We have to set this against the wider context of what else we are doing to the environment. There may be some applications of GM that have environmental benefit. Equally, in comparison with what we are doing at the moment, there may be some that make things worse, and this is why this case-by-case assessment of impacts is so important. At the moment, we are probably not paying sufficient attention to the other modifications that we make to our environment.

Going back to the NGO engagement, this is where there might be a very interesting debate to be had. I held a workshop at the University of York on potential new applications of GM crops that were of benefit to agriculture in the global south—to developing economies and areas where farming is really struggling. Friends of the Earth were joint organisers of that workshop, because they felt that maybe now is the time to get away from this polarisation and to look at what the technology can deliver and whether that is beneficial or not—and, indeed, beneficial to whom? I think that is a huge concern to the public and where GM crops may have lost their way a little, in that the beneficiaries were thought to be multinational companies rather than farmers in India, for example.

**Q22 Baroness Morgan of Huyton:** That leads in quite nicely to my question, in a sense, which is: to what extent do you think public concern is about industry, and particularly big industry, more than the technologies themselves? Building on the previous conversation, is one of the lessons that we should be taking that we have to pitch the conversation at a higher level? I was quite disturbed, Dr Hartley, when you said, “This bit could be Defra and this bit could be the DoH”. Is there not a case for a much bigger, higher level conversation? Arguably, we have had that as a country around the use of stem-cell technology. Of course, there are detailed scientific conversations happening as well, but the public has engaged at a higher level, I think. Is that possible with this technology, and could it mitigate some of the concerns there are about industry?

**Sir Roland Jackson:** One of the issues is: why privilege one particular technology and one very specific aspect of the technology? The message from all the public dialogues around these contentious issues is: start with the problem that is of public interest. You may well find that GM technologies offer one solution or a set of solutions to that, but look at them in context. Lord Cameron mentioned the Global Food Security programme. I ought to state another interest in that I am chairing the oversight group for the public panel for the Global

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Food Security programme, which is a standing public panel that helps the programme look at some of these wider issues. It is interesting that when the debate is framed around broader questions of food security, questions about GM arise perfectly naturally but in the context of everything else. It does not make it any easier to say who the owner is, but that is a sensible way to have the discussion.

**Dr Sarah Hartley:** Often when we talk about public debate, we see this homogenous public at one side, whom we want to somehow engage with, but there are other ways of doing that. We can pluralise the kind of expertise that we have in some of the committees and governing bodies that we have, and at the research councils; Sir Roland will talk about that at some point. Certainly the WHO guidelines have been very clear about engaging stakeholders and publics at the research project level, and this is where responsible innovation can help us. There are lots of opportunities throughout the innovation process—from the conception of the research right through to the kind of high-level public debates we are talking about—where we can engage with that homogenous, disinterested public. Also, there are lots of pressure groups, civil society groups, that have expertise that those projects would benefit from, understanding the kinds of concerns that are out there from experts who are not necessarily scientists in that field.

**Q23 Baroness Manningham-Buller:** I declare an interest as chair of the Wellcome Trust. In your answer to Lord Cameron, Professor Hartley, you said how much easier in this country it was to address health benefit as opposed to an agricultural benefit. Of course, that distinction between the health benefit and the agricultural benefit is absolutely not there in much of the third world. Can I have any of your observations on the difference between how we engage the public as to what we need in this country and in our compassionate response to the needs of the third world? There are going to be different attitudes. By the way, we have already covered the question I was scheduled to ask. I am more interested in this.

**Professor Sue Hartley:** That is very true. The important thing is to come back to what we have said all along. If we focus on the problem, we can then identify the most appropriate technology to address that problem, which may or may not be GM, depending on a whole suite of things such as the receiving environment that we want to operate in, what kind of agriculture we are talking about, what kind of crop, what kind of disease and so on. What was interesting and what emerged very clearly when I held this workshop at York—which involved GeneWatch, a large number of pressure groups and some of the cutting-edge researchers who were doing things like working on improved photosynthesis in rice—was that once you focused on the problem and the technology became a little secondary, people moved together much more. I think the public are able to recognise very clearly the issues in the global south. We only have to watch how much they donate for mosquito nets during Comic Relief and other charity events. They want to see these problems solved. That can be a starting point for engagement.

My colleagues know more about how best to develop that engagement than I, but I would say that one key factor is identifying an honest broker. That, I think, is what the public want to see. We have had issues before where there has been an appearance of vested interests in charge of the process, whether those are multinationals or scientists who do not want to discuss things openly and transparently, whatever the interests are. Everyone brings their

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values to a conversation, and it is about how to identify the best, most open and transparent way to have a conversation in which all voices are heard.

**Lord Fox:** In an earlier answer, Sir Roland, you put a question in the mouth of the public: do scientists understand the complexity of this? I suspect the answer to that is touched on by some of the discussions we had in the previous session, instigated by, I think, Lord Hunt, over whether sufficient research is going into ecology, but also whether the advent of gene drive versus self-limiting also opens up a whole new level of understanding that we require in other issues. Where are we in the level of understanding? How sincerely can we answer that question when the public ask it?

**Sir Roland Jackson:** I am not competent to answer that one.

**Lord Fox:** I am looking at all three of you.

**Professor Sue Hartley:** Thanks, Roland. I guess the overarching question is whether we understand enough about the ecological consequences of these technologies, and I guess the question is whether the public understand it and whether we, as ecological scientists, understand it. Of course, there is always the issue of just how much prior knowledge is sufficient before you do anything, which is a vexed issue in itself.

It is fair to say that we do know some things about the ecological consequences of GM insects and the different ways of producing them. We have done a lot of lab work, we have done a lot of modelling work, and we are good at modelling population consequences in this country. However, we have not done a lot of field trials. We can learn a little from where field trials have been conducted, but it is fair to say that we have rather more theoretical research than practical research at the moment. What might hold us back is that although we have a good knowledge of the ecological processes that are going to be at work—things like competition and impacts on food chains and food webs—it really is quite hard to generalise, partly of course because the technology is only one of the factors that is affecting outcomes. The nature of the species concerned, its lifestyle, its lifespan, its ecological environment—things that it feeds on and feed on it and so on—are all going to have an impact. There are a lot of indirect effects, and predicting those is a little more challenging than we might like. However, I would say that we have some good knowledge as a basis and more fieldwork would be helpful.

**Lord Fox:** Looking at Dr Hartley, how much of that answer is going to affect people's reaction—public perception—to this technology? How convincing does it have to be? How much does the ecological outcome really affect the acceptance of this technology?

**Dr Sarah Hartley:** It is definitely a factor, but I do not think it is the most important factor in public concern. The way this technology is governed will be more important.

**Q24 Lord Peston:** My question follows from what Lord Vallance asked some time ago about public debate. I am not persuaded, let me say, about this. Public debate legitimises the activities of the vast group of people who are anti-science and anti-technology. If you can conduct a thought experiment, there was a patent clerk sitting in an office in Switzerland over 100 years ago who was about to publish a paper on special relativity. If there had been public debate of the sort that you appear to think is a valuable thing, they would rather he had been shot, because the ultimate result of that was the atomic bomb and so on. In other words, we must not use this as a paradigm case that legitimises one of the greatest glories of our civilisation, which is natural science. Equally, we are rich because of technology. We are

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not rich, despite all talk of the Chancellor, from working harder; we are rich, because overwhelmingly we have made technological progress over the last 100 years. I am deeply troubled by your comment that this particular case is especially worthy of public debate. I am not saying that we should suppress public debate, but legitimising the anti-scientists is not something I would want to be a party to in any way—and I hope you would not either.

**Sir Roland Jackson:** I have a couple of things to say. I am not sure we have specifically said that we think there should be a massive debate about GM insects. We have probably said the opposite: that it should be done in context. I would also seriously challenge the view that the public is anti-science. It is absolutely the reverse. If you look at the Public Attitudes to Science survey work, the vast majority of the public, 85% to 90%, think that science has done wonderful things for us and is wonderfully beneficial. Eighty per cent would like the Government to fund basic research, even if it has no conceivable or obvious outcome. There is huge public support for science and research. There are issues around the application of specific technologies, not all technologies. Because technologies interfere in social and cultural systems and employment, they are bound to be political. How political they are and the ways in which they are political depends on the technology. It so happens that GM is one of those technologies. It digs into people's ideas of naturalness. It has all these questions about motivations and purposes, balancing risks and benefits. It is just one of these things that by its very nature is social and political. You have to debate that, and you have to debate it before you start regulating it.

**Lord Hunt of Chesterton:** Can I put to you, in a way, the comment that comes from Lord Vallance? In the last 40 years, there have been two enormous scientific government outreach programmes. One was on AIDS, which was an enormous programme, which was accepted. The second one was climate change. Lord Vallance asked who was responsible. A very remarkable thing happened. A government department, Defra, went around the country having huge numbers of meetings. East Anglia was going to be underwater practically by now, the way it was being put. It was rather extreme, perhaps, but it was a huge programme, run by government, and you had all sorts of other organisations coming to these meetings up and down the country. Everybody accepted that we were dealing with a massive problem. It seems to me that there are precedents of a government department grabbing an issue and then working through it all over the country.

First, is this question of insects and plants on the same scale that requires that kind of national debate, or is it, if I may say so, a sort of series of functional debates, with the applications, but broadly co-ordinated? It seems to me that it would be quite interesting to know how big a scale this should be, and whether these previous examples are useful analogues?

**Dr Sarah Hartley:** At this stage, with GM insects, what is needed is an engagement perhaps even with expert publics to start with on where we might want to channel this technology. What are the kinds of problems that we encounter within the UK, in the agricultural or health systems, where this technology might play a role? That is where the concept of responsible innovation comes into play: this interaction between external stakeholders and the research community. There is a technology that has ability and potential, and then we have these societal problems. We need to marry those two together. This, I think, will help us in the future to deal with potential public concern, because the benefits will then be



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clearer. At this stage in the technology's development, that would be more beneficial than a more open public debate.

**Professor Sue Hartley:** That is exactly right, and one of the lessons from GM crops is having those debates early on and being realistic, open and transparent about what the technology can do and what it cannot do. That is something that we sometimes neglect to talk about.

**Baroness Neville-Jones:** It seems to me that this discussion reveals that intelligent and meaningful public involvement in the context of disruptive technologies is really quite important, otherwise things can go off the rails quite easily. It also seems to me that it should be embedded in what has come to be known as responsible research and innovation. Can you think of an example—bearing in mind the whole question of scale—of where that kind of engagement was really intelligently conducted? Is there a good possible paradigm example of where it has been done well that would help us and that could act as a model?

**Sir Roland Jackson:** There are a couple I can think of, one at the very early stage and one at a later stage. The discussions about synthetic biology were mentioned in the session before, and it was very positive that the two research councils—BBSRC and EPSRC at that point—commissioned that public dialogue, and the two chief executives wrote an open letter afterwards to the participants saying what they would do in consequence. A lot of those things have been followed through. I think it is still too early to tell whether sustained engagement is continuing in the right way, but it started right.

Much more at the applications end is the whole raft of consultations, including public dialogues and other surveys, that happened around the debates on mitochondrial replacement, on which, of course, both Houses of Parliament voted. That, again, is an example of a wide variety of engagement methods and scientific analysis and evidence being brought to bear and a judgment made in Parliament, as the ultimate body, as to the right thing to do. Both of those, in very different ways, are good examples.

**Baroness Neville-Jones:** That is very helpful. How much does it matter in all this that the scientists to whom people would turn have to say, “I do not know the answer to that question”? One thing that seems to emerge is being able to answer the questions, but there must be instances where you do not know the answer. How much does that matter, and how do you engage the public in acceptance of that being a perfectly legitimate position to be in and one that should not stop further research being done?

**Professor Sue Hartley:** That is a really good question. It is what I was alluding to a moment ago when we talked about what the technology can and cannot do. When people overhype technology or sound a lot more certain than they really are, it leads to a lot of problems. It is far better to be open and honest from the start about what you can say with confidence, what you can say with a bit less confidence and what you are genuinely uncertain about. You can then follow that up by saying, “Because of this uncertainty, there are certain things we should not do until we have more evidence, and this is how we might approach getting that evidence, and then there are other things we can say we are fairly convinced about and we think we should be able to move forward”. There is the IPCC approach of saying, “We are 95% confident about this; we are 50% confident about that”. It is probably a little harder to do with some of this ecological data, but we can try to do that. The key message is open, honest and transparent communication about what is known and what is not yet known.

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**Baroness Neville-Jones:** Will that help move towards things like field trials, when one goes from the laboratory to the real world?

**Professor Sue Hartley:** In the end, we have to gather evidence from the real world. That is the only way some of these questions will be answered. We have to identify the point at which we feel we know enough to safely move to real-world field trials, and fortunately in some areas of the world they have already started to do that, so we can build on that experience.

**Q25 Lord Patel:** I have a quick question, because we have had a lot of background discussion about this. The US National Academy of Sciences set up a group to look at the state of the science related to gene modification, including all the different technologies of gene drive, gene editing and chemical—or synthetic, as some people call it—modification of genes, and what regulatory framework ought to underpin this science. Do you think we should have a similar group? If we were to, the Royal Society and the Academy of Medical Sciences would be the kinds of academies involved.

**Professor Sue Hartley:** That is very sensible, and the Royal Society has done this sort of thing before. It would be an approach. One thing to bear in mind is that the UK and the US are quite contrasting in rather more ways than we probably have time to discuss right now, but that might underpin exactly how that was driven forward here.

**The Chairman:** I take that as a yes, I think.

**Sir Roland Jackson:** My response would be that it is not just a science issue, and therefore having an activity like that very publicly led, for example, by the Royal Society, might not be ideal. A broader partnership might be sensible to bring in a genuine diversity of voices. As you will know, the Nuffield Council on Bioethics has just started a piece of work involving quite a multidisciplinary group on genome editing, which will produce a framework report.

**Lord Patel:** That is for humans, though.

**Sir Roland Jackson:** No. It will initially produce a framework report, and then the plan is to work up particular examples. I would expect human germline editing to be an early one, but you would have to ask the chair when he comes in front of you in a few weeks' time.

**The Chairman:** As I said earlier, we will have the opportunity to talk to the Nuffield Council on Bioethics later this month. We have run out of time. We could have spent a lot longer, and I must apologise to my colleagues who have been trying to come in unsuccessfully. However, we have covered a lot of ground, and I am absolutely clear that public engagement strategies is going to be a very important component of the inquiry and the subsequent report. Thank you for giving us a very strong lead as to how this should be conducted. Thank you very much to Professor Hartley, Dr Hartley and Sir Roland Jackson.

## Sciencewise – Supplementary written evidence (GMI0028)

### Where next for GM Insects?

*Author: Sir Roland Jackson*

Some brief reflections following my appearance on 13 October before the House of Lords Science and Technology Committee inquiry on GM Insects.

The first is the framing of this inquiry around GM insects specifically. In other words, as a technology (or technologies) at an early stage in search of solutions. The implicit agenda was the opportunity for UK leadership and commercial benefit, although the ‘industry’ is in its infancy. The only commercial company in the world currently deploying this technology, Oxitec, is of UK origin and has just been bought by a US company for some \$160m.

But perhaps that is exactly why we should be having discussions about the implications now, learning from the lessons of GM crop debates. Should we not be addressing questions of public interest and concern, and of public good priorities, before (most) choices are made and trajectories get fixed? However, it may be more constructive to have those discussions in the context of key challenges to human health or agriculture rather than a narrow focus on one particular set of technologies.

If this is considered a worthy aim – and it will be interesting to see where the Committee comes down on this – the question is how? What are the implications for shaping regulation and for governance processes within the innovation system?

Two things struck me sharply about the written evidence submitted. The first is that the deficit model and the championing of a science-based regulatory system as the sole arbiter of decisions about the deployment of technologies is alive and well in the business sector. As the Bioindustries Association put it: ‘...some technologies risk being politicised in response to perceived public concerns...’; and as Oxitec expressed itself on GM crops: ‘...which society has politicised in the EU...’. Is there really no recognition that the spread (or not) of a technology is a social process, with its impact on economies and cultures – such as visions of agriculture, and of ‘naturalness’ – on jobs and ways of life, in the UK and abroad? There will be winners and losers, benefits and disbenefits. How could this not, in the most general sense, be a political process, informed by the science but by no means determined by it? It is noticeable that the evidence from many public sector bodies, such as BBSRC and InnovateUK, acknowledged these dimensions. The public sector understands the issues even if it struggles at times to address them. The private sector seems woefully adrift.

The second is the repeated suggestion with respect to regulatory processes, made in evidence from different bodies, that benefits should be assessed as well as risks, because a risk-based model has ‘failed’. This argument is fundamentally flawed unless the whole regulatory system is to change. Benefit is not the opposite of risk, nor can it be assessed in the same manner as a science-based risk assessment of safety to human health and the environment. The opposite to benefit is disbenefit, or disadvantage, of which risks to human

health and the environment are but one aspect. If benefits are to be considered, then so must disbenefits, which go well beyond questions of risk.

The regulatory system cannot be expected to cope with this, nor should it. These broader political issues, which include policies for the risk assessment itself, are questions for wider stakeholders and society. They need to be embraced by the governance structures of our innovation system; by the relevant Government departments, InnovateUK, the Research Councils, other funders, and business organisations. That necessitates a greater diversity of expertise and voices around the points of power, as choices are made about priorities, directions and funding. As things stand, the business sector is privileged in terms of its access to, and membership of, governing bodies and funding panels. Civil society organisations and wider perspectives are demonstrably absent (see [here for an analysis for the Research Councils](#)) and tend to have to shout from the side-lines to be heard. That is not a state of affairs likely to reduce polarisation.

There are of course many other ways of bringing in these voices and expertise through stakeholder and public engagement, and particularly through the mode of deliberative dialogue that Sciencewise supports. In the temporary absence of a wholesale refashioning of our governance systems these should now be explored. It will be interesting to see if the Committee recommends that the relevant public sector bodies, and others, should actively consider now how they might engage wider expertise and public input into exploring the potential for GM insect technologies to contribute to particular pressing challenges. These might focus on human health and agriculture, in the context of other approaches to addressing the same challenges within those domains.

*15 October 2015*

This text was published on the Sciencewise blog on 15 October: <http://www.sciencewise-erc.org.uk/cms/where-next-for-gm-insects/>.

Dr Jack Stilgoe, University College London, Professor Paulo Paes de Andrade, Federal University of Pernambuco, Brazil, and Professor John Mumford, Imperial College London – Oral evidence (QQ 39-47)

**Dr Jack Stilgoe, University College London, Professor Paulo Paes de Andrade, Federal University of Pernambuco, Brazil, and Professor John Mumford, Imperial College London – Oral evidence (QQ 39-47)**

[Transcript to be found under Professor Paulo Paes de Andrade, Federal University of Pernambuco, Brazil](#)

Dr Jeremy Sweet, Sweet Environmental Consultants, Oxitec Limited, and Advisory Committee on Releases to the Environment (ACRE) – Oral evidence (QQ 26-38)

**Dr Jeremy Sweet, Sweet Environmental Consultants, Oxitec Limited, and Advisory Committee on Releases to the Environment (ACRE) – Oral evidence (QQ 26-38)**

[Transcript to be found under Advisory Committee on Releases to the Environment \(ACRE\)](#)

## Target Malaria – Written evidence (GMI0013)

*Professor Austin Burt, Professor John Mumford, Ms Delphine Thizy and Dr Tony Nolan (Imperial College London), Professor Charles Godfray (University of Oxford), and Dr Mark Benedict contributed to this submission on behalf of Target Malaria.*

### **Possible applications of genetically modified mosquitoes for malaria control**

1. Malaria is a disease that causes an immense burden, affecting over 200 million people each year in the developing world. It is a disease that feeds the vicious cycle of poverty and deprivation through the social and economic toll it takes on communities. It affects not only today's generation but also future generations because of its dramatic impact on children. Beyond the human burden of the disease, the social and economic costs of malaria are estimated to reach over \$12 billion a year in Africa alone, hindering the capacity of poor countries to invest in development<sup>177</sup>.
2. Bringing an end to malaria will require ongoing support for existing methods of control, and the development and deployment of new methods. The international malaria campaign has reduced cases by half in the last decade, largely through sustained investment in conventional vector control. But progress has not been sufficient to bring an end to the disease and the high costs of maintaining current levels of intervention undermine the prospect for continued reduction in malaria cases<sup>178</sup>. Novel applications of biotechnology, such as genetically modified malaria mosquitoes, offer one potential avenue for developing more easily applicable methods of vector control that can be applied as the fight against malaria moves on to the more difficult vector control situations that remain.
3. The limitations of current approaches were well-illustrated in the latest data from the World Health Organisation (WHO), which noted that while at least three quarters of malaria deaths occur in children under 5, only about 1 in 5 African children with malaria received effective treatment for the disease, 15 million pregnant women did not receive a single dose of the recommended preventive drugs, and an estimated 278 million people in Africa still live in households without a single insecticide-treated bednet<sup>179</sup>.
4. The use of genetically modified mosquitoes offers a number of potential benefits that can address shortcomings of existing methods and help make those more efficient by offering a long-term, cost effective and sustainable method of reducing the incidence of malaria.

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<sup>177</sup> WHO on the occasion of World Malaria Day 2015:

<http://www.who.int/mediacentre/news/releases/2015/world-malaria-day-2015/en/>

<sup>178</sup> The current investment on malaria reduction is \$2.7 billion a year. The recent estimations from WHO Global Technical Strategy for Malaria call for an investment of \$6.4 billion per year by 2020 to eradicate the disease in 40% of countries by deploying existing methods at a larger scale.

[http://www.who.int/malaria/areas/global\\_technical\\_strategy/en/](http://www.who.int/malaria/areas/global_technical_strategy/en/)

<sup>179</sup> WHO on the occasion of World Malaria Day 2015:

<http://www.who.int/mediacentre/news/releases/2015/world-malaria-day-2015/en/>

5. Current methods require repeated interventions which raises logistical and cost issues.
  - Malaria is mainly a rural disease which spreads over vast areas, which creates major challenges in terms of reaching all households<sup>180</sup>.
  - The focus on methods based on individual protection, such as bednets, makes achieving full coverage difficult because of the cost to governments, individuals and families.
  - An additional obstacle for existing methods is the behaviour change required for their effectiveness. In the case of bednets for instance, they require intensive awareness raising to help communities understand how to use them effectively and replace them when they are damaged or the insecticide treatment is no longer effective. In other cases, such as in Sahelian countries, outdoor sleeping habits often hinder the use of bednets.
  - Malaria-carrying mosquitoes have historically been most active between dusk and dawn, and the female mosquito which bites humans and transmits the disease tends to rest indoors. For this reason, current methods focus on protection in the home and during the night but do not offer protection at other times or places. This is a concern as mosquito behaviour has been evolving to more frequent day biting outdoors, where bednets and indoor sprays are not effective.
  - Finally, resistance of both the mosquitoes and the parasite adds urgency to the need to develop new methods of malaria control. WHO reports that “insecticide resistance in malaria vectors has been reported in 53 of 65 reporting countries around the world since 2010. Of these, 41 have reported resistance to two or more insecticide classes, with the most commonly reported resistance is to pyrethroids, the most frequently used insecticide in malaria vector control”<sup>181</sup>. If the resistance to artemisinin-based combination therapies observed in Asia emerges in Africa, the recent trend of reduced mortality rates from the disease could be reversed.

### ***Potential benefits of genetically modified malaria mosquitoes***

6. The use of genetically modified mosquitoes would be part of an integrated approach to reducing the prevalence of malaria that combines several tools and techniques tailored to local conditions. The use of modified mosquitoes for malaria control is not in itself a ‘silver bullet’ but it offers the promise of important benefits and the potential to remedy some of the limitations of current methods.
7. Modified mosquito technology offers a long term solution: the modified mosquitoes pass on the modification to the next generations, providing long-lasting effectiveness without

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<sup>180</sup> WHO reports important gaps in coverage: “Despite impressive increases in malaria intervention coverage, it is estimated that, in 2013, 278 million of the 840 million people at risk of malaria in Sub-Saharan Africa lived in households without even a single ITN, 15 million of the 35 million pregnant women did not receive even a single dose of IPTp, and between 56 and 69 million children with malaria did not receive an ACT.”

[http://www.who.int/malaria/publications/world\\_malaria\\_report\\_2014/wmr-2014-key-points.pdf?ua=1](http://www.who.int/malaria/publications/world_malaria_report_2014/wmr-2014-key-points.pdf?ua=1)

<sup>181</sup> WHO World Malaria Report 2014 -

[http://www.who.int/malaria/publications/world\\_malaria\\_report\\_2014/wmr-2014-key-points.pdf?ua=1](http://www.who.int/malaria/publications/world_malaria_report_2014/wmr-2014-key-points.pdf?ua=1)



the intensity and frequency of application required by current methods. This is particularly valuable in remote and difficult to access places.

8. It improves access because the intervention spreads naturally through wild mosquito populations and benefits all communities and individuals, regardless of wealth, education, or access to services and without direct cost to them.
9. It should be cost-effective and easily deployable. Because the mosquitoes themselves spread the technology, it does not require extensive facilities, labour or equipment. Moreover, it would not require investment in human behaviour change because people do not need to change the way they work, live or sleep to obtain the protection provided by modified mosquitoes.
10. It limits harm to non-target species in the environment because it directly targets only the species of mosquitoes responsible for transmitting malaria, without affecting other species or the environment. While malaria mosquitoes cause great human suffering they make up an extremely small part of the biomass in the environment, and tend to live apart from many other species in small ephemeral water pools.
11. Modified mosquitoes would be complementary to existing malaria control methods: the modified mosquitoes would help reduce the burden of infection and transmission, making other control methods more effective. For example, using bednets or carrying out indoor spraying in an environment with much lower density of malaria mosquitoes would make those methods more effective. The same would be true for malaria vaccines.
12. If resistance to the gene drive mechanism arises, as has been observed with insecticides and malaria drugs, a recoded modified intervention could be deployed to bypass the resistance. This is different from chemical insecticides when resistance can render a whole class of compounds ineffective.
13. The benefits offered by genetic modification combine to offer a sustainable approach to malaria vector control, which could help address the challenge of funding ongoing efforts for malaria elimination globally.

#### **Regulating genetically modified mosquitoes**

14. While there are uncertainties associated with the development and deployment of any new technology, risks can be mitigated through effective regulatory frameworks. New genetically modified insects and the broader control systems in which they would be used will inevitably raise new issues as the various applications are further developed. An essential lesson is that these frameworks need to be adaptable to new technologies and that they should take into account the whole implementation systems, not just the component technologies.
15. One of the principal challenges is that most countries that have regulatory frameworks for genetically modified organisms use legislation initially developed for biotech crop

technologies. With the advent of new methods of modification, such as the use of gene drive, new questions need to be considered. While much of the basic biomolecular and genetic science involved is similar, the applications now being contemplated for insect control are different from the crop production systems in several ways.

16. Unlike the cultivation and harvesting of genetically modified crops and the passive spread of genetically modified pollen, in modified vector control applications the modified organisms would be actively disseminated in the wild and their mode of action may require sustained populations achieved either by repeated applications or by incorporation of gene drive mechanisms. Some of the questions raised by the regulation of modified insects are thus different from those posed by the regulation of biotech crops.
17. Much of the current regulatory guidance is focused on assessing risks, while paying little or no attention to the assessment of benefits. Vector control is very different from most other modified crop or animal applications because the target organism in its natural state is itself harmful to human health, and is often subject to control or eradication under public health regulations<sup>182</sup>. Likewise, agricultural pests are directly injurious to crops and thus harm the economy.
18. The choice of comparators for risk assessment needs careful consideration for vector control applications. Comparisons may need to be made at a population level, and over time, rather than at an individual organism level, to get a complete comparison of impacts. Where conventional control is widely adopted the whole control systems with and without conventional controls and genetically modified should be compared.
19. It is also worth noting that many countries - in particular those that could benefit most from the use of gene drive techniques to address diseases such as malaria - still do not have clearly defined processes in place to assess either plant or modified insect biotechnologies. Capacity building in this area should therefore be a priority, particularly in those countries most at risk from diseases that modified insects could help prevent.

#### ***WHO genetically modified mosquito guidance***

20. The WHO Guidance Framework for testing genetically modified mosquitoes addresses the staged testing of new modified vector control technologies from initial lab studies through to implementation decisions. It describes good practice in addressing technical and ethical issues and the general regulatory requirements in place across many national systems. It was not intended to be the basis for any national regulatory framework, but it reflects the practices that are expected across a range of countries with operating regulatory systems. Target Malaria works within this guidance in each country involved, as well as with national regulatory procedures.

#### ***EU EFSA Directive for the Deliberate Release of Genetically Modified Organisms (GMOs) (2001/18/EC)***

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<sup>182</sup> Pan American Health Organization (PAHO) (1997). The feasibility of eradicating *Aedes aegypti* in the Americas. Rev Panam Salud Publica [Internet].1:68–72

21. The EFSA guidance is specifically structured to interpret the European GMO Directive. It has not yet been applied to cases involving gene drive in insects, and therefore experience of regulators even in the EU and the UK is at an early stage. In addition, the EFSA guidance does not include consideration of benefits so it does not provide advice on how decisions to implement gene drive systems might be made. The EFSA guidance is helpful in that it provides extensive indications on what information applicants would be expected to provide to regulators, and how such information may be derived. There is a particular recognition of the important role of modelling in the guidance as a way to demonstrate expected outcomes.

### ***Other examples and available guidance***

22. Brazil has adopted a technically competent and pragmatic approach to modified mosquito technology. There is substantial public awareness of the threat from dengue, concern over the lack of effective mosquito and disease control measures, and reasonable knowledge of the sterile insect control concept due to earlier radiation-based sterile fruit fly management in the area where field releases of RIDL mosquitoes have been approved. Panama has followed the example of Brazil with field trials of the same technology.

23. The US National Academy of Sciences is currently conducting a study to assess the state of gene drive science and consider existing regulatory frameworks, guidance and other mechanisms that frame such research, with the goal of issuing general principles that will guide responsible practices in gene drive research<sup>183</sup>. Target Malaria supports this initiative as a positive way forward to provide guidance to researchers in the field, not only in terms of regulatory elements, but in terms of best practices and ethical guidelines.

### **Acceptability & stakeholder engagement**

24. Guidance for research and development of genetically modified insects should include stakeholder engagement as a key aspect of technology development, in particular where the technology is meant to serve a public health or public good role and acceptability is a paramount concern. This may be a requirement of the regulatory approval process but it may also be considered not as a regulatory requirement but as a best practice. Such an approach can ensure engagement takes place throughout the research process, rather than solely at the application stage because early and continuous dialogue with stakeholders is an important component of ensuring the technology meets actual needs and can be used.

25. Stakeholder engagement is an essential component of Target Malaria's work. Our teams include community engagement officers, advisors, and social scientists which carry out consultation with local communities and other stakeholder at each step of the project. The objective is to ensure that there is an adequate level of understanding amongst stakeholders for them to express any concerns or expectations that they may have, and

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<sup>183</sup> NAS Announcement <http://dels.nas.edu/Study-In-Progress/Gene-Drive-Research-Human/DELS-BLS-15-06>

## Target Malaria – Written evidence (GMI0013)

for the project to address or integrate in its design. This is particularly important for our project because we seek to develop a tool for public health in which broad public acceptance is needed.

*17 September 2015*

### **Target Malaria – Who we are**

Target Malaria is a not-for-profit research consortium that aims to develop and share technology for malaria control.

Target Malaria started as a university-based research program and has grown to include scientists, stakeholder engagement teams, risk assessment specialists and regulatory experts from Africa, North America and Europe.

Three of our teams are based in countries affected by malaria (in Burkina Faso, Mali and Uganda) and they work hand in hand with other researchers in Europe and North America through all aspects of the development of genetically modified mosquitoes.

Target Malaria is funded by a core grant from the Foundation for the National Institutes of Health (FNIH) through a programme of the Bill & Melinda Gates Foundation. Individual labs also receive funding from a variety of sources, including DEFRA, the European Commission, MRC, NIH, Ugandan Ministry of Health, Wellcome Trust, and UNCST.

Target Malaria partner institutions include:

- CDC Foundation, USA
- Fred Hutchinson Cancer Research Centre, USA
- Imperial College London, UK
- Institut de Recherche en Sciences de la Santé (IRSS), Burkina Faso
- Polo d'Innovazione di Genomica, Genetica e Biologia (Polo GGB), Italy
- Seattle Children's Research Institute, USA
- Uganda Virus Research Institute (UVRI), Uganda
- Malaria Research and Training Center, University of Science Techniques and Technologies Bamako, Mali
- University of Cambridge, UK
- University of Notre Dame, USA
- University of Oxford, UK
- University of Perugia, Italy
- University of Washington, USA

## **James Thackery, student at University of Sheffield – Written evidence (GMI0003)**

### **Credentials**

I am a PhD student at the University of Sheffield, working on food security and genetic modification in crops. I am well versed in both the scientific and social aspects of genetic modification, and I have experience in public engagement. I am happy to be related to for further information on this or related topics.

### **Executive Summary**

Genetically modified insects (GMIs) are a promising tool for use in disease control and food production; however, their use in the UK is limited. The UK health benefits are minimal, whilst abroad they are extensive. Crop yield benefits abroad will be considerable, but in the UK they would currently lead to further food waste. Finally, the UK has large public concern over the use of GM technology, making its implementation costly. Thus, I conclude that UK investment in development of GMI technology is worthwhile, but only for use abroad.

### **1. Which human diseases, across the world, could be addressed through GM insect technology? Are there any human disease risks in Europe, particularly the UK, for which GM insects are under development?**

There are many insect-borne diseases across the world that can be controlled with GMIs (see Table 1). Malaria and Dengue Fever are the most significant of these. Most of these diseases are contractible in Africa and Asia, not in the UK.

Insect-borne diseases contracted in the UK are predominantly tick-borne. Lyme disease is the most common, but the UK incidence is comparatively low. There are GM versions of the Sterile Insect Technique (SIT) for ticks under research which would see success in controlling tick-borne diseases across the globe, but none are currently being developed for large-scale use.

GMI use in the UK for disease control would not be worth investment for several reasons. Firstly, the medical value is too low, as Lyme disease is readily treatable with antibiotics. Secondly, there is a high cost for developing and implementing GMI policies and products. Finally, there is a high public concern about GM use; only 25% of surveyed Britons reported being unconcerned by GM use in 2012. As such, use of GMIs in the UK for medical purposes would not be cost effective.

**Table 1) Major diseases caused by insects**

| <b><u>Insect</u></b> | <b><u>Disease</u></b> | <b><u>Cases (worldwide)</u></b>                  | <b><u>Contractible in the UK</u></b> |
|----------------------|-----------------------|--|--------------------------------------|
| Mosquito             | Malaria               | 198 million in 2013 <sup>1</sup>                 |                                      |
|                      | Dengue Fever          | 390 million new infections annually <sup>1</sup> |                                      |
|                      | West Nile virus       | 141 cases in the US in 2015 so far <sup>2</sup>  |                                      |

|              |                         |   |                             |
|--------------|-------------------------|---|-----------------------------|
| Assassin bug | Chagas Disease          | 16-18 million infected <sup>1</sup>                 |                             |
| Sandfly      | Leishmaniasis           | 1.3 million new infections annually <sup>1</sup>    |                             |
| Tsetse fly   | Sleeping sickness       | 50-70,000 new infections annually <sup>1</sup>      |                             |
| Flea         | Plague                  | 1-2000 cases reported annually <sup>1</sup>         |                             |
| Tick         | Tick-borne encephalitis | 10-12 million cases reported annually <sup>1</sup>  |                             |
|              | Rickettsial infection   | Rare – millions depending on infection <sup>1</sup> | Yes – rare                  |
|              | Lyme disease            | 85,000 cases annually <sup>1,2</sup>                | Yes (2-3000 cases annually) |
|              | Babesiosis              | 1800 cases annually in the UK <sup>2</sup>          |                             |

( 1- WHO Reports, 2- CDC statistics)

**2. What are the possible livestock and agricultural crop applications of GM insects across the world? Of current livestock disease risks and agricultural insect pests that could be addressed through GM Insects, which should be the highest priority for Europe?**

Of livestock, only sheep and cattle farming would benefit from SIT GMI use. Trypanosomiasis (tsetse fly) and Bovine Babesiosis (tick) have large impacts on cattle and sheep farming, though they rarely affect Europe. Bluetongue disease (culicoid midge) can affect European livestock, but outbreaks are rare. As such, I conclude that European applications of SIT GMI for livestock safety would not be economical.

Of crops, all have pests and would benefit from SIT GMI use. It is estimated that 40% of crop yield is lost to insects, weeds, and diseases combined. Unfortunately, not every insect pest is amenable to the SIT technique. SIT can only be used on insects for which the adult male (released at large) does not itself damage the crop. Pests that don't lend themselves to SIT include: locusts, aphids, some beetles, and some cockroaches. However, combining other GM approaches with SIT might make those pests targetable. SIT GMIs would not be a panacea to crop insect pests, but there would be many applications.

Europe's main crops would benefit from the use of GMIs. Wheat pests that can be targeted include sawflies, wheat midges and hessian flies. Targetable maize pests include corn borers, cutworms and click beetles. Previous successful SIT trials have shown that GMIs would see large reductions in these crop pests, and thus, large crop yield increases.

However, it is worth considering the ultimate outcome of EU food increases. Any additional food produced would need trade policies to oversee its export, else we repeat the "butter mountains" and "wine lakes" of the 1980s. SIT GMIs for European crop use would not be a worthwhile investment until policies to deal with significant food production increases are made.

**3. Are there likely to be opportunities provided by GM insects that cannot be provided by other approaches, such as biological control methods? How could GM insect approaches be complementary to existing Integrated Pest Management (IPM) programmes?**

SIT GMIs have several advantages over biological controls (BCs):

- SIT becomes more powerful over time, as released males seek out the diminishing population of females. BC cannot achieve this effectively; it reduces the pest population but does not eliminate it.
- SIT provides direct control over the pest population. If there are extreme consequences of removing the pest population, they can be allowed to repopulate by stopping SIT GMI release. BC approaches lack this regulation, as reintroduction of pest insects would require elimination of their predators.
- The spread of SIT GMIs also have regulation advantages. If SIT GMIs spread across borders they will only last for a single generation, whereas BC insects may become a permanent feature of that environment.

Overall, these characteristics make GMI a uniquely effective and controllable technology.

GMI could also conceivably be introduced into IPM schemes at the BC level of dealing with pests. The IPM system would then rank preferable pest management approaches as follows:

- 1) Mechanical pest-management techniques
- 2) GMI or BC
- 3) Pesticides

This introduction of SIT GMIs into the IPM would achieve several things. Firstly, mechanical techniques would be retained as the primary pest-control method. Secondly, SIT GMIs could be used as a more effective option than BC, but BC could still be used if GMI regulations or public concern proved contentious. Finally, pesticide use would be a final resort, keeping environmental penalties low. This structure would allow use of SIT GMIs if they were necessary, desired and approved.

**9. How could the UK benefit economically from both developing GM Insect technology and its use within the UK?**

GM SIT is effective, and has high-value worldwide uses, making it a desirable and profitable product. Over time, the total worth of SIT GMIs will lessen as pest populations are brought under control, but that value is still considerable. The main value lies in the breadth of the pest issue; there are many insect pests for which SIT has yet to be developed, and there are opportunities to design novel GMI techniques to target pests that aren't amenable to SIT. Developing and patenting these GMIs promises to be profitable. Thus, it is my opinion that the encouragement of GMI development in the UK would be a valuable investment.

However, given the above arguments, I conclude that the actual use of GMIs in the UK would currently be uneconomical. There is limited medical and livestock value, the high crop value is stymied by a lack of policies to deal with the extra yield, and there would be high costs to gain public acceptance. To make UK use of GMIs economical, public concern over GMIs must be alleviated, and policies must be put in place to export additional produced food.

**10. How can the gap between regulatory approaches and public concerns over GMOs be addressed? Is there a role for ‘responsible innovation’ approaches? What are the critical factors in effective public engagement from lab to final release?**

To achieve public acceptance of GMIs for use anywhere in the world (even if they are not directly ‘affected’), a key factor is that the safety of GMI technology must be made clear. To achieve this, the technical material must be translated into non-specialist outputs (infographics, media sources, interactive software, and policy briefs). Additionally, experts in the field must be encouraged to speak publicly; outreach by experts has proved successful in increasing public awareness of other topics, such as climate change and the dangers of smoking. Finally, media sources should be encouraged to fairly represent scientific opinion on the technology. This would allow more widespread understanding on GMIs, which will dramatically improve public opinion.

To achieve acceptance by the members of public that live in the areas where GMIs will be used, that public should be part of the solution-making process. Techniques such as deliberative forums have proven effective at finding agreeable solutions in contentious topics. The bringing together of all stakeholders allows the public to understand all the facets of the issue. The public is then far more likely to find the solution equitable and acceptable, as they have been part of the decision-making process. Allowing the public to come to the decision of using GMIs themselves is much more effective for public acceptance than giving them a limited voice.

**Recommendations**

With these arguments in mind, I suggest some recommendations that could be put in place to facilitate a productive and profitable use of GMIs.

- The UK should aim to be a leading developer of GMI technology.
- GMIs should be developed for use for use abroad, but not in the UK at this time.
- Policies to deal with increased UK food production should be put in place before GMIs are used for UK crop-pest management.
- Public awareness campaigns and deliberative forums should be implemented to achieve public understanding and encouragement of use of GMIs around the world.

I suggest that these recommendations will allow the most economical and equitable use of this technology.

*28 August 2015*



## Wellcome Trust – Written evidence (GMI0025)

### Key messages

- Insect-borne diseases continue to pose a significant risk to human and animal health globally. Over half the world's population are at risk of debilitating infectious diseases such as malaria, dengue, chikungunya, West Nile fever and others. Diseases affecting livestock such as bluetongue and Schmallenberg have spread to various parts of Europe.
- Due to the burden posed by insect-borne diseases, all avenues of intervention to treat or prevent insect-borne diseases should be supported if found safe to do so, within a robust regulatory environment which maintains the confidence of the public.
- The Wellcome Trust believes that Genetically Modified Insects (GMIs) potentially offer a more targeted and less environmentally harmful approach to insect-borne disease control than non-GM techniques and insecticides.
- However, the most effective way to control a vector-borne disease is through a combination of approaches and we envisage GMIs will play a complementary role alongside existing Integrated Pest Management (IPM) programmes.
- The regulatory framework for GMI technologies needs to assess both the risks and benefits of the technology.
- Increased funding and alternative funding models are required for the continued development and application of such technologies, due to the lack of market forces to drive development.
- Effective public engagement to raise awareness of GMI technologies will be essential. This is particularly important given the lack of public confidence in GM crops due to poor public engagement prior to and upon their release. Engagement with communities in which GMIs are to be released for vector control is critical.

### Introduction

1. The Wellcome Trust is a global charitable foundation dedicated to improving health. This year, we are planning to invest £750 million in biomedical research and the medical humanities. Our breadth of support includes public engagement, education and the application of research to improve health.
2. As a funder of research addressing the burden of insect-borne diseases, including insect control strategies such as GMIs, we are pleased to respond to this consultation.

### Our interest in GMIs

3. Insect-borne diseases continue to pose a significant risk to human and animal health globally. Over half the world's population are at risk of debilitating infectious diseases such as malaria, dengue, chikungunya, West Nile fever and others. Dengue fever is the fastest growing vector-borne disease in the world, with a 30-fold increase of incidents over the last fifty years. About half of the world's population are now at risk to the

disease, with the most serious illnesses and deaths being amongst children in some Asian, African and Latin American countries<sup>184</sup>.

4. Although low- and middle-income countries (LMIC) have the greatest burden of insect-borne diseases, there is also a growing threat to Europe and the UK<sup>185,186</sup>. Invasive mosquitoes have become widely established across Europe, with subsequent transmission and outbreaks of dengue and chikungunya virus. Malaria has re-emerged in Greece, West Nile virus has emerged throughout parts of eastern Europe and the prevalence of tick-borne diseases, such as Lyme disease, continue to increase. In animal health, Bluetongue and Schmallenberg viruses have emerged in northern Europe proving it to be equally susceptible to transmission of vector-borne disease.
5. Changes in vector distribution are due to a number of factors: increased global travel creating new opportunities for invasive vectors and pathogens; climatic changes and changes in land use, infrastructure, and the environment. Such changes represent a significant risk to the UK. Lessons from the outbreaks of West Nile virus in North America and chikungunya in the Caribbean emphasise the need to assess future vector-borne disease risks and prepare contingencies for future outbreaks<sup>187,188</sup>.
6. The Wellcome Trust has supported a range of research into treatments, vaccines and vector-control techniques to control mosquito-borne diseases such as malaria, West Nile virus, chikungunya and dengue fever, however no successful vaccines have been developed to date. Given the increasing risk of vector-borne diseases – and because the most effective way to reduce transmission remains control of disease-carrying mosquitoes<sup>189</sup> – the Trust supports the development of safe and effective new technologies that have the ability to reduce the transmission of insect-borne disease to humans, livestock and agricultural crops, within robust and appropriate regulatory frameworks.
7. We have funded £846,000 towards the development of RIDL (Release of Insects carrying a Dominant Lethal), an innovative gene drive technique developed by Oxford based company Oxitec Ltd. Their approach uses advanced genetics to modify male insects to be 'sterile'. Oxitec has created RIDL strains of *Aedes aegypti*, the principal mosquito species responsible for spreading dengue fever. These genetically modified male mosquitoes, which do not bite or spread disease, are then released to mate with wild females. No viable offspring can result from these matings and as a result, the mosquito population is ultimately reduced below the threshold level that is required to transmit the disease.

### Advantages of GMIs over other approaches

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<sup>184</sup> <http://www.who.int/mediacentre/factsheets/fs387/en/>

<sup>185</sup> *Effect of climate change on vector-borne disease risk in the UK,*

[http://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(15\)70091-5/fulltext](http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(15)70091-5/fulltext)

<sup>186</sup> <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4491199/>

<sup>187</sup> [http://ecdc.europa.eu/en/healthtopics/vectors/vector-maps/Pages/VBORNET\\_maps.aspx](http://ecdc.europa.eu/en/healthtopics/vectors/vector-maps/Pages/VBORNET_maps.aspx)

<sup>188</sup> <http://researchbriefings.files.parliament.uk/documents/POST-PN-483/POST-PN-483.pdf>

<sup>189</sup> <http://www.nature.com/nature/journal/vaop/ncurrent/full/nature15535.html>

8. Releasing sterile insects has been used as an effective control method against agricultural pests for over 50 years. But it has not until now been applied to mosquitoes because of the limitations of conventional non-GM sterilisation techniques, such as radiation.
9. The Wellcome Trust believes that GMIs offer significant opportunities. *Aedes aegypti* are easier to manipulate in labs than other types of mosquito, which is a major reason why this technology has been able to develop. Therefore if the technique is successful, it may have the potential to reduce the transmission of more *Aedes aegypti* mosquito-borne diseases (not just dengue) making GMIs a powerful mechanism to improving health.
10. Secondly, GMIs can target specific diseases and species very precisely. Field trials by Oxitec have seen a >90% reduction in the population of the target species in the Cayman Islands and a 96% reduction in Brazil. Researchers believe that this level of effectiveness would be enough to prevent endemic dengue fever in any setting globally<sup>190</sup>. The approach leaves non-target insect species unharmed and reduces the amount of chemicals used, unlike non-specific chemical insecticides, which may have a significantly negative impact on the environment and local ecology.
11. However, it is important to note that the most effective way to control vector-borne diseases is through a combination of approaches (e.g., for malaria, a vaccine when available, plus vector control, bed nets and anti-malarials). We envisage GMIs will play a complementary role alongside existing Integrated Pest Management (IPM) programmes and we encourage this approach.

#### Regulation of GMIs

12. In Europe, the regulation of GMIs currently falls within the scope of the EU Directive for the Deliberate Release of Genetically Modified Organisms (GMOs) (2001/18/EC). This Directive rightly requires that all GMOs undergo an extensive risk assessment prior to any release into the environment. However, the Directive only approves organisms for release into the environment based on the risks of GMOs to human health and the environment as opposed to focusing on the purpose of the organism. Given the potential benefits of GMIs for both human and animal health, the Wellcome Trust encourages the development of a regulatory framework that assess both the risks and the benefits of GMI technologies, similar to legislative frameworks in the U.S, Australia, New Zealand and Brazil<sup>191</sup>.

#### Limitations, risk and resistance in GMIs

13. There are limitations to the current technologies used to develop GMIs for insect-borne disease control. For example, not all species of mosquito can be mass bred in laboratories and such approaches are only likely to work where there is only one main pathogen-carrying species<sup>192</sup>.

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<sup>190</sup> <http://www.bbsrc.ac.uk/news/people-skills-training/2014/140414-f-innovators-pt1-alphey/>

<sup>191</sup> <http://researchbriefings.files.parliament.uk/documents/POST-PN-483/POST-PN-483.pdf>

<sup>192</sup> <http://researchbriefings.files.parliament.uk/documents/POST-PN-483/POST-PN-483.pdf>

14. Another risk is the development of resistance in target vector populations. As might be expected in any intervention which drives down a population or exerts any other selective pressure, resistance would be expected to build up over time and should be monitored. Resistance would be expected to evolve both to the drive mechanism (e.g., mutations in the genomic region you were targeting making the drive mechanism ineffective) and towards any genetic trait you were modifying (e.g., the ability to resist a particular pathogen). In developing such technologies, it will be important to learn from the development of resistance in other pathogens. This could be done through mathematically modelling the expected speed and spread of resistance before planning and implementing any intervention, to make any successful interventions last as long as possible (e.g., by using them in combination or in a co-ordinated way).
15. Companies developing GMI technologies, such as Oxitec, are required to make in-depth assessments of the impact GMIs may have on the local ecology and food chains, based on controlled studies. Monitoring must be undertaken before, during and for years after release of GMIs to prove its safety and efficacy, including ensuring that the environmental impact is minimal. Further research and longer-term studies are required to ensure new GMIs have no adverse effect or unintended impacts on the environment and other organisms.

#### Funding the development of GMIs

16. GMI technologies have struggled to attract funding for development and commercialisation due to the uncertainty of return on investment. It seems that this is partly a result of target markets being in LMICs but also the uncertainty surrounding public acceptance and government approval of release of GMIs. Large amounts of capital are needed to establish and scale up GMI technology. Current funding for such technologies rests with charitable and public funders. Given the significant potential benefits to populations at risk of vector-borne diseases, we would welcome alternative financial incentives and business models to support development and commercialisation.

How could the UK benefit economically from both developing GMI technology and its use within the UK?

17. The UK currently spends millions per year in aid to countries with significant vector-borne disease burden and in research for interventions to prevent such diseases. Contributing to reducing this burden could help reduce aid spend. Further, development of such cutting edge technologies enhances the UK science base.
18. The use of GMIs to control vector-borne diseases in livestock, and the potential wider use of GMIs in agriculture in the UK is further reason to support development. The most important economic problems to be addressed using GMIs may well be crop pathogens and pests since current use of insecticide is much greater in agriculture than in human and animal vector-borne disease control. The additional economic benefits resulting

from agricultural use should also be taken into account when assessing the potential benefit of GMI technologies.

What are the critical factors in effective public engagement from lab to final release?

19. We believe that effective public engagement with communities in which GMIs are to be released for vector control is essential. The introduction of GM crops provides a salutary lesson about the dangers of not engaging effectively. Companies and academics proposing release of GMIs need to engage regulatory authorities, citizen groups and the Government from an early stage, ensuring dialogue with all groups in the community. We strongly believe that people need to understand both the risks and the benefits of GMI technologies so that they can come to an independent and well-informed view regarding such technologies.
20. Public engagement will be necessary both in the LMICs where most of these technologies will be deployed but also in the countries where these technologies are being developed, to help build up trust and ensure there is an environment conducive to research and investment in this technology.

*September 2015*

**Professor Christopher Whitty, London School of Hygiene and Tropical Medicine – Oral evidence (QQ 65-74)**

*Evidence Session No. 7*

*Heard in Public*

*Questions 65 - 74*

TUESDAY 3 NOVEMBER 2015

Members present

Earl of Selborne (Chairman)  
Lord Cameron on Dillington  
Lord Fox  
Lord Hennessy of Nympsfield  
Lord Hunt of Chesterton  
Lord Kakkar  
Lord Krebs (co-opted)  
Lord Maxton  
Baroness Morgan of Huyton  
Baroness Neville-Jones  
Lord Patel (co-opted)  
Lord Peston  
Viscount Ridley  
Lord Vallance of Tummel

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**Examination of Witness**

**Professor Christopher Whitty**, Professor of Public and International Health, London School of Hygiene & Tropical Medicine

**Q65 The Chairman:** Welcome, Professor Whitty. It is very good of you to join us today. I know it was at fairly short notice. You are on your own. We were hoping you would have some support from elsewhere, so thank you for that. We are being broadcast by the web camera. Would you like to introduce yourself for the record? If you want to make an introductory statement, do feel free to do so.

**Professor Whitty:** I am Christopher Whitty, Professor of Public and International Health at the London School of Hygiene & Tropical Medicine. I should state for conflict of interest reasons that until six weeks ago I was also Chief Scientific Adviser at the Department for International Development, although I am not in any way representing the department now. I am a consultant physician at UCLH and the Hospital for Tropical Diseases and I chair a variety of specialist committees such as the Advisory Committee on Dangerous Pathogens.

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**The Chairman:** We are very familiar with your expertise, particularly in the international development field. Let me start with a general question. Would you give us an overview of the current impact of insect-vector-borne diseases internationally, particularly the mosquito-borne diseases? How is international development funding from the United Kingdom used currently to control vector-borne diseases?

**Professor Whitty:** A very large number of the classical tropical diseases are insect-borne, of which the biggest by some distance is malaria, although there are others. Then there are some more recent emerging infections, in particular dengue and chikungunya, which are also insect-borne. The combined impact of these on global health is very substantial. Taking the latest WHO figures, most of which are from the last couple of months, so this is relatively up to date—and one can criticise the exact figures, but I think these are as good as you are going to get—for malaria, the current estimate for the last year for which there is data is that there were around 214 million cases of malaria and around 438,000 deaths. That sounds a very large number, which it is, but it is a 60% reduction in deaths in the last 15 years. When I started in malaria work around that time, we reliably quoted over 1 million deaths a year, so that is a very major improvement.

For dengue, which is probably the second major vector-borne disease, WHO figures indicate there were between 50 and 100 million cases. It is quite difficult to tell because there is quite a large burden of asymptomatic or unrecognised infections, and they estimate around 22,000 deaths. The difference is that dengue is on the increase. Dengue has increased 30 times over the last two to three decades. Alongside it—and this has had rather less coverage from the witnesses you have seen so far—is chikungunya, which is a major vector-borne disease from the same vectors as you get for dengue. It has caused over 1 million cases in the Americas and the Caribbean. It does not kill very many people, but it does cause significant arthritis and long-term problems for people. They do eventually resolve but it can certainly last for years.

Alongside those are the classical diseases: filariasis, trypanosomiasis, sleeping sickness, lymphatic filariasis, which causes very significant disability, onchocerciasis and trachoma, which are two blinding causes. The mosquito-borne one of those is filariasis, but other insects are important, such as the tsetse fly for the trypanosomiasis and the simuliid black fly for the onchocerciasis group. There are a number of more specialist things. Then there is a whole range of arboviruses, which are viral diseases passed on by mosquitoes, of which Japanese encephalitis is probably the best known. I could spend the rest of the Committee meeting listing out the exotic names of all the others, such as o'nyong-nyong, but I will not.

**Q66 The Chairman:** It would be difficult for the record to get the spellings right. Could you tell us something about the role of DfID, and particularly international development in the United Kingdom, and this control of disease, and who the other major players might be, whether Government or charity?

**Professor Whitty:** Yes, with the clear caveat that I am not speaking for the Government on this; I am simply giving an observation. There has been a fantastic reduction, particularly in malaria but also in the other vector-borne neglected tropical diseases, which is a whole group and includes things such as sleeping sickness. Let us start off with the UK and then move more widely. The UK in general and DfID in particular put a very large emphasis, on trying to reduce these diseases, both with financial support—it is widely on the record that the UK spends around £500 million a year on malaria control activities in the round—but

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also looking at neglected tropical diseases. The other thing, and importantly for this Committee, is that not only do they support the research behind this financially, but the UK has some of the leading thinkers, from the most basic biology right through to the most applied areas in almost all of the major infective vector-borne diseases. So the UK's contribution is substantial. The other major player is the United States, by a variety of different means, and then quite a lot of other donor countries contribute—countries which are not primarily affected. Increasingly and encouragingly, the burden of both preventing and treating these diseases is being borne by the countries themselves. The number of countries that are entirely or largely donor dependent is much smaller than it was 10 years ago.

**The Chairman:** Do international charities have a role in this?

**Professor Whitty:** Yes, they have a very major role both on the delivery side and on the research side. On the research side, clearly the Gates Foundation is the pre-eminent one, but the Wellcome Trust, here in the UK, is a major supporter of the science behind this, alongside the MRC, although that clearly is not a charity. Very many of the major advances have come from those three groups—so funding from the Gates Foundation, the Wellcome Trust and the MRC. There are also charities and NGOs which are involved very heavily in the delivery side: Save the Children, Médecins Sans Frontières under certain circumstances, and a variety of others. This is a cross-sectoral area. If you move on to the neglected tropical diseases, the private sector has also played a very much bigger role than is often appreciated, donating many of the drugs for the control programme, so it is a cross-sectoral approach.

**The Chairman:** Given that it is a cross-sectoral approach, how would you describe the degree of collaboration between these different partnerships on the international scene?

**Professor Whitty:** It is surprisingly good, at least at the applied end. The group of people involved in the delivery works well under the WHO aegis on the whole. Quite a lot of the funding comes from a small number of funding groups—Gates, Wellcome, DfID and USAID in particular—and the groups of people which fund and give the technical advice tend to know one another and are relatively cohesive in their approach. My experience is that the join-up is pretty good compared to many other areas of both international development and science. The UK has its own group called the UK Collaborative on Development Sciences—UKCDS—and that tries to co-ordinate the UK efforts of the various bits of government, the research councils and government departments, but also the Wellcome Trust.

**The Chairman:** Given that this is an emerging technology, with lots of regulatory issues clearly emerging—and we find this in the evidence we have been taking—do you feel there is a role for these stakeholders that you have just been describing to collaborate and ensure that an international dialogue can be undertaken on how the possible benefits and disbenefits can be assessed and regulated?

**Professor Whitty:** In principle, the answer is yes. In a sense, within your question there is a whole series of assumptions, some of which I accept and some of which I do not fully accept. One of the assumptions is that this is an important technology for public health. For the sterile male technique equivalent technologies, it is possible but at the moment it is looking relatively niche. That may improve. For the replacement technologies, I have to say it is pretty speculative. The question is whether you are starting from a public health impact point of view or from a science point of view. From a public health impact point of view, this



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is a footnote on a footnote at this point in time. That does not mean it will necessarily remain that way. If you think about it from a science point of view, these groups of people are largely in the “How do we solve the practical problem?” end of co-ordination rather than the “How do we start with the best basic science?” end of the problem, which tends to be more in the research council space.

**Lord Peston:** I want to make sure that I understand what you have said. For example, you said that the number of people dying from malaria in the relevant countries has gone down. I think you said that categorically. Am I right then to say that is not to do with the research into the insects that we are looking at but is to do with other things? In other words, the research into the insects, which I assume our report will be about, has yet to have a payoff. Would that be a correct interpretation?

**Professor Whitty:** It would be a correct interpretation only in the narrow sense of GM insects. The incidence of new cases of malaria has gone down by about 37% and the number of deaths has gone down by about 60%. I just quoted the deaths. The incidence has gone down almost entirely due to advances in the management of the vectors—the insects—whereas the deaths, which are obviously on top of that, are on the human side. When you think about the problem of all these diseases, there are two sides of the equation you can operate on: the human side and the vector side. For some of them, you only operate on the human side; there is absolutely no point in going for the vector side. For example, we can control yellow fever completely with the yellow fever vaccine and we do not need the vectors, but for malaria it is a mixture of both.

**Lord Peston:** Thank you. That is very much a clarificatory answer.

**Lord Maxton:** What exactly are the technologies being used to reduce the incidence of malaria and the deaths from malaria at the present time?

**Professor Whitty:** Let us start off with the incidence, because that is clearly the one that is most relevant to this inquiry. The most important one is attacking the malaria vectors, and the majority of malaria vectors which cause the majority of the disease are in Africa. Fortunately, the great majority of them bite in a relatively stereotypical way—at night usually between midnight and 3 am, although there is a spread around that—and the most important of the mechanisms has been insecticide-treated bed nets. The big advance in the last 10 years is not one in basic science but in manufacturing—first in the manufacturing of long-lasting nets and secondly in the distribution. In 2000, about 10% of people were under bed nets, but now the figure is up to 40% to 60%, depending on which country you talk about. It is the science of doing it better plus a bit of engineering, using a technology—the combination of insecticides and bed nets—that has been around for quite a long time before that. That is the main one.

**Lord Maxton:** What insecticide is used in the bedding?

**Professor Whitty:** For bed nets specifically, it is a group of insecticides in the pyrethroid class of insecticides. If you are doing residual wall spraying, which also works very well for reasons I can explain if that would be useful, you have the opportunity of using DDT, which is a long-lasting insecticide. The problem we face is that there is insecticide resistance developing quite strongly now to both these insecticide classes in the mosquito populations of Africa. The impact on disease is not yet there, but I think it is only a matter of time before it becomes a very serious problem. If I can say what the clear and present danger is at the

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moment, it is the thin pipeline of new insecticides, which is due to a whole variety of issues, including political and regulatory issues. That is our immediate problem, but clearly there are other areas as well.

**Q67 Lord Krebs:** My question follows from that because you said, if I can quote back to you, that at the moment GM insects and the kind of technologies we are looking at are a footnote on a footnote. Why do you hold that view? Given what you have just said about the present mechanisms of using insecticides, bed nets and so on in relation to malaria, if they are beginning to run into problems, ought not GM insect technology be part of the armoury, and it may become much more important in the future? Then there are diseases other than malaria to which you alluded, where perhaps the kind of control measures you referred to for malaria may be less effective. Could you unpack why you said it had such a small role at the moment?

**Professor Whitty:** Absolutely. Let me stick to malaria. I want to be clear that when we come to dengue and the Aedes-transmitting mosquitoes, the opportunities for GM technologies are greater, but for malaria, my own view—and I think this is a pretty middle-of-the-road view—is that, even potentially, the opportunity for these technologies is small. Let me explain why that is. Lord Krebs, given your background, I hope you do not mind if I do a very simple bit of maths to explain why it is I think these technologies are unlikely to be very major. If  $R_0$ , the force of transmission of malaria, is 1, then one person gives it to one person who gives it to one person and the disease is stable in the population; if it is less than 1, it is dying out; if it is more than 1, say 2, then two people give it to four, and so on. In very large parts of Africa the  $R_0$  formula is over 100, so you have to come down a very long way.

Probably the most useful mathematical model in infectious epidemiology is a very simple one and a very old one. It was devised by a combination of Ronald Ross, who won the first UK Nobel Prize for Medicine, but for a different purpose, which was for his discovery relating to mosquitoes, and George Macdonald in the 1950s. It basically says—and I am simplifying it, but not much—that the vectorial capacity, which is the  $R_0$  equivalent, is proportional to  $m$ —density of mosquitoes— $a^2$ , their man-biting habits, squared because they have to bite once to acquire and once to transmit, and then  $p$ —probability of survival after they have bitten—to the power of  $n$ , which is the number of days in the intrinsic cycle.

I am sorry I have hit you with maths, but the reason for that is that if you want to reduce malaria by killing mosquitoes, you are going to have to kill a lot of mosquitoes. It is very inefficient as a way of delivering malaria control. However, if you shorten the life of a mosquito that has bitten a human or is about to bite a human—you get several hits at this, because at any time between the time a mosquito bites and it becomes infected and the time it becomes infectious, which in tropical countries is between nine and 10 days and in Europe is higher than that—that mosquito does not transmit. Because it is to the power of nine or 10, that is enormously efficient. With the most efficient methods, which include bed nets and indoor spraying, you can reduce their probability of survival by, let us say, 20%, but because it is to the power of nine or 10, that is massively efficient in reducing transmission, whereas reducing the number of mosquitoes, which is what we used to do, is extraordinarily mathematically inefficient, leaving aside the very large populations involved. That is a fundamental flaw with any method that seeks to reduce numbers as its basis. It is not a very efficient method. There is a number of other reasons as well, but that is the fundamental one.

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**Lord Krebs:** But the maths could be different for different diseases.

**Professor Whitty:** The maths is different for different diseases, but the basic equation is applicable to the majority of vector-borne diseases. This is the big difference with vector-borne diseases compared to, let us say, screwworm, which is often used as the example from sterile male technique working. The problem with screwworm is the screwworm itself, whereas for vector-borne diseases the problem is not the vector; the problem is the disease you get, so these mathematical advantages from intervening at different parts of the cycle start to be a lot more important.

**Lord Fox:** You mentioned that the pressing need is probably more for insecticides rather than other technologies, not least, I guess, because, as you just said, it is part of that barrier at that point. Is there any sense that the technologies we are talking about—GMO insects—are distracting from the resources or attention to the insecticide development which you feel is more important?

**Professor Whitty:** No, I do not think there is any reason to think that, because it is a relatively niche product. Those who are supporting them, including the Wellcome Trust and the Gates Foundation, all say this is a niche product. It is possible that we may find uses for it in due course, but no one is diverting large amounts of resources or anything else. My slightly bigger concern is that, if you read some of the colour supplements, you get the impression that GM mosquitoes are going to solve the problem. What we found in the past is that, whenever you have a technology where people grow to believe that something can solve the problem when it will not, that can reduce people's feeling of urgency, and there is serious urgency to deal with this.

**Lord Fox:** That was really the sense of my question.

**Professor Whitty:** There is no diversion of resources that is in any meaningful sense a worry, no.

**Q68 Viscount Ridley:** Thank you for the clearest seminar on population dynamics since Lord Krebs taught me the subject 40 years ago, which I have forgotten in between. Can I bring you to dengue in general and chikungunya, as well as Europe and the UK? First, you said that dengue has increased 30-fold. I presume this is largely because of the spread of the mosquito rather than the disease—the day-biting tiger mosquito, the Aedes, or am I getting muddled here?

**Professor Whitty:** No, you are not getting muddled at all.

**Viscount Ridley:** How much further is that going to go? Is it going to travel to the UK? I do not want to be too parochial about it, but give us a feel for that question.

**Professor Whitty:** There is a certain amount of hand-waving about exactly what the reason is, but it is a combination of the spread of mosquitoes, which is due primarily to transport links rather than anything else, plus changes in habitat. Many human habitats, particularly ones without piped water, are perfect for the major vectors. There is a major and a minor vector for these two diseases, both of which are Aedes species. Aedes aegypti is the major species in most of the tropics and is an efficient vector for the mathematical reasons I gave earlier, which are that it takes most of its blood meals from humans and that is squared, which therefore makes it more efficient. Aedes albopictus is the other vector.

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The reason I have differentiated those is partly that the GM technology around—the Oxitec technology—is aiming at *Aedes aegypti*, which is the major vector in many countries, and also that the *Aedes albopictus*, which is the Asian tiger mosquito, can overwinter through its eggs, which *Aedes aegypti* cannot. Although, from time to time, *Aedes aegypti* can establish itself in the UK, and we have had reports of that going back to the 1910s, it dies out, whereas *Aedes albopictus*, in principle, can overwinter in the UK—probably in lowish numbers, but it can do it, and certainly it has started to move up through Europe for a variety of reasons. The contribution that climate change adds to that is very debatable but the fact is it has moved. That is the vector of these diseases which is probably the bigger concern in Europe.

**Viscount Ridley:** Both dengue and chikungunya?

**Professor Whitty:** No. Just as from time to time there are transmissions of malaria in Europe, and in theory there are mosquitoes in the UK that can transmit malaria, from time to time there are transmissions of dengue and chikungunya in Europe, but so far they have not taken off as a major problem. With the number of *albopictus* there are now in southern Europe, there is at least the potential for epidemics—not on the Latin American scale, because, as I say, it is not a hugely efficient vector, but certainly on a significant scale.

**Viscount Ridley:** Could you touch on the West Nile virus?

**Professor Whitty:** West Nile virus is a *Culex*-transmitted virus. The main vector in this part of the world, ie Europe, is *Culex pipiens*. There are no major ones in the UK. There is a sub variety that lives in the London Underground, but I do not think that is a major worry. As far as we know, it is not a vector, but certainly some of the more efficient vectors are there in central Europe. There is a slightly higher risk that those could move to the UK but I would say slightly, not very.

**Q69 Lord Cameron of Dillington:** As usual, Professor Whitty, the enthusiasm of this Committee means that even if I am asking only the third question, it has already been answered. If I was an anti-GM campaigner, I would probably pick up on what you have been saying so far and say that GM is not worth very much and there are other more effective methods of controlling malaria, for example. Could you outline some of the drawbacks? How effective is bed netting? You have talked about the reduction of cases. Where are the weaknesses and where do you think GM mosquitoes in the future could have more effect?

**Professor Whitty:** To be clear, I have gone firmly on record saying that where GM is useful we should use GM. I am not an anti-GM person at all on this, but always you have to balance both sides of the argument: do not overstate the disbenefits but do not overstate the benefits either. If any GM person grabbed on to what I said to say we should not do GM, I would strongly reprimand them, if I had the opportunity.

We have quite a large number of efficient ways of dealing with malaria at this present time, with the big caveat about the rise of insecticide resistance and, in due course, drug resistance. I think, personally, neither of those is going to be solved by GM insects. When it comes to *Aedes* on the other hand, I think the number of options we have is much smaller, so the ability to target *Aedes* is poorer. There are broadly two approaches. The first is to reduce the habitats, provide people with piped water, cover pots and so on, but also in epidemics to do fogging, which is where every couple of days you push insecticide up into

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the air. That has a whole series of pretty obvious ecological downsides to it, because these are non-specific, broad spectrum methods.

In those kinds of areas, the advantage of a more targeted approach, which is what GM potentially offers, has some very clear attractions. The other potential attraction of GM technology is that it is the only technology when you are trying to eradicate or eliminate an insect which gets more efficient the closer you get to the end point. I am talking about the sterile male rather than the change in population method. That is because you start off with a situation where, let us say, your sterile or soon-to-be sterile males are one to one with the population and, as time goes by, the number of sterile males stays the same, the wild type goes down and eventually you end up overwhelming them with numbers. That is the theoretical advantage. In reality, the evidence that this is an effective method has still to be case proven, but there are some attractions to it. It is for those kinds of relatively niche but quite important areas that I think we should be considering this.

**The Chairman:** You say that there are some attractions, but it is important that we do not overstate the opportunities. We must keep a clear view that has to be looked at on its own merits. You described it earlier as a footnote on a footnote. Would you explain how you reconcile those two observations? To my mind you have sold it quite well, but a footnote on a footnote seems to be of vanishingly small relevance.

**Professor Whitty:** I used to enjoy reading my footnotes. The thing to understand is that there are multiple other experimental technologies and techniques which are being used. Let us take dengue. There are two completely separate strands of work which have multiple sciences attached to them, one of which is around dengue vaccines. We now have a vaccine that is probably about 60% effective and 80% effective at preventing severe disease. That probably means we can improve on that, so the human side is improving.

In Aedes control, there is a whole variety of new methods being used, ranging from giving ivermectin, which is something which any of you involved in farming will probably be very familiar with, as seed corn to birds so that when the mosquitoes bite the birds they die, through to wolbachia infections with bacteria, which prevent the mosquitoes becoming infected via another form of biological control that works pretty well but has some quite serious side effects, through to trying to infect them with a variety of new fungi. This is one of a very large number of approaches, most of which will probably bite the dust in reality, because what you want at the end of the day is something that is effective, cost-effective and able to be maintained for long periods of time. It is possible that GM mosquitoes are one of the technologies that will see its way through to the finishing line, but there is a high chance, in my view, it will not. I think it is worth exploring just for that reason. What I would not want to do is think this is the only experimental technique. There are lots of others.

**Lord Fox:** You have singled out the sterile male technique. Is that because you dismiss the others or because that is the only one that is far enough down the track for you to assess?

**Professor Whitty:** I was using sterile male in the very loosest sense, as in anything which aims to reduce the population via mating, whether it is sterile male or through to the Oxitec mechanisms, which I think have some attractions. I must admit as a public health person I have quite a bit of scepticism—this is a personal view—about the population replacement models.

**Lord Fox:** The gene drive-type things.

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**Professor Whitty:** There are multiple steps in the logic that these things have to work, for each one of which the probability is significantly less than one. It has to work by reducing transmission. You have to have a gene drive system that works as well. That gene drive system has to have nothing attached to it that you do not want. That is a big risk. The gene drive system has to get through huge populations which are incredibly well adapted and fit. The population of Anophelines in Africa is massive. It has to have no significant resistance early on in a situation and no disbenefits that you realise too late when you have let the thing go. Then it has to be cost-effective. To get a high score in each one of those boxes strikes me as not impossible but fairly improbable.

**Q70 Lord Patel:** Thank you for your evidence. It is very revealing on the science side, but I am going to be a bit more challenging to you. You said that your view about GM insects is a middle-of-the-road view. Is that correct?

**Professor Whitty:** That is correct.

**Lord Patel:** What is the mainline view?

**Professor Whitty:** What I have said is that if you took 100 entomologists and asked them these questions—but under anonymity so they were not going to have their grants removed by people who back this more strongly—the majority of them would say, “This is a lovely theory. I think the science is great. I hope they get an FRS, but this won’t have any impact on disease”. That is my own view.

**Lord Patel:** Why should we invest in the science of this technology at all?

**Professor Whitty:** There are quite a lot of things where you should invest on the basis that this is an interesting bet and it might have an impact in due course that you do not know about. For example, whilst I am cautious about some of the claims made for malaria, let us say theoretically a zoonosis emerged that could be transmitted by insects unknown, where those insects took up residence in the UK and where this was an efficient way to eliminate the insects from the local population; we would then be thankful we had gone quite a long way down the technological line, without necessarily believing the rhetoric that these things were going to solve current problems. The idea that this is going to solve current problems, apart from dengue, under certain niche conditions, strikes me as a low probability, but the possibility that this technology might become useful at some later stage strikes me as entirely plausible. For that reason, I am certainly not against investing in it, but what I would not want to do, to go back to a previous question, is take money away from, let us say, investing in getting new insecticides into this technology on the basis that these are somehow comparable. That does not strike me as realistic.

**Baroness Morgan of Huyton:** I am intrigued by what you have been saying about insecticides. I am not a scientist, but it sounds to me as if you think insecticides are almost neutral and there are no negatives associated with them, whereas I think it is right to say we have received a fair amount of evidence from other people of a concern about needing stronger and stronger insecticides in order to combat these diseases. Is any part of you anxious about our overdependence on insecticides?

**Professor Whitty:** Let me be clear that I differentiate very sharply between insecticides for human disease use—if you have a disease which is killing over 400 thousand children a year, that is a serious problem—and spreading insecticides more widely for marginal gains in agricultural use. I am not saying even that the second of those is inappropriate; I am just

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saying there is a spectrum. The insecticides we are talking about are used under very narrow circumstances. They are used in houses, either on walls or on bed nets. The environmental impact is completely different from using them in cotton production. Again, I am not knocking cotton production; I am just saying clearly there is a risk. No one is going to use an insecticide if there is no disease, but the trade-off between the risk of malaria and the risk of insecticide is so hugely on the side of using insecticide appropriately that I do not think anyone rational looking at it is going to say we should not be doing that. Clearly the trade-offs become more balanced the more widely they are used and the lower the marginal gain you are going to achieve. That is where I would differentiate. Incidentally, the difficulty we have with insecticides for human use, on the other hand, is they have to be safe for humans. If you put a bed net around a child, that child is going to suck that bed net. Having an insecticide which kills insects but also kills children is not good news. Our problem is designing effective insecticides that are also non-toxic to humans.

**Q71 Lord Peston:** We may have pre-empted some of Lord Cameron’s question, but he still led us into an important area. Again, I would like some clarification. Do you agree logically that the fact that something is working or doing some good does not mean you should not look at other things as well? To take an obvious example, what many of the countries in sub-Saharan Africa with which we are concerned need is access to clean water. If I was asked what I would spend my money on first, I would say, “Guarantee a clean water supply for everyone in those countries”. The second thing they need is a decent transport system if they need to get to hospital quickly. I would not infer from that that all the interventions you have talked about therefore are a waste of money. I take it that a multi-intervention approach is what you are trying to get over to us. Is that right?

**Professor Whitty:** That is absolutely right. If you take malaria, clearly everyone would agree that we need to have a combination of things that would: reduce the incidence via vector control; reduce the incidence via controlling cases early, because that also has an impact on number of cases, though a lesser impact; reduce the number of people who are getting severe disease; and reduce the number of people who are dying. Each one of those has a slightly different approach and in reality you need several approaches for all of them. You have a bundle of approaches. My caution about GM for malaria specifically is largely because I do not think the mathematics stacks up compared to alternatives, not because in principle I am against the idea that you should have a portfolio of things you are doing—clearly you should.

**Viscount Ridley:** Just to follow up on that, are you guiding us towards saying, “Look, this may not be a terribly important technology at the moment for human vector-borne diseases but, for example, for insect pests in agriculture it could be a far more important one”? You mentioned screwworms and things like that. I know that is not your area of expertise but, given what you said about insecticides in agriculture, and the fact that this technology should work better when you are trying to target the insect directly rather than as a vector, are we right in concluding that this technology could be very valuable in agriculture but might only be a niche thing in human vector-borne diseases?

**Professor Whitty:** Starting with agriculture, I certainly think the logic of using it when your main aim is to reduce the total number of insects because it is a pest makes it a lot more attractive, because there is not an alternative, whereas when you are dealing with vector-borne diseases, you are dealing with mathematical non-linearities that favour alternative

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approaches, essentially. That is a rather pompous way of saying that it is not very efficient just to kill lots of mosquitoes. That said, I do not want to imply that there is no role for this in the management of Aedes, which is what Oxitec is doing. The role of it is not yet clear. Fundamentally, it is going to come down to the question of under what conditions and what is the most cost-effective or ecologically non-damaging approach compared to alternatives. I do not want to say that it is completely useless at all; that is not my point. My point is simply that it is a relatively small product at this point for that disease. Where I get nervous is when people make wild claims, in my view, for diseases such as malaria, where there are multiple alternative routes which seem the more logical bundle of things to do.

**Q72 Lord Hunt of Chesterton:** You have mentioned dengue once or twice. I have been to meetings on climate and, as I understand it, dengue is one of the diseases that, as you commented, in central and eastern Europe is a growing danger. In those areas with a greater propensity in Europe or eastern Europe, are those countries looking at research on this? Are they taking this idea of GM insects as one of the techniques, or what is being done about it?

**Professor Whitty:** I regret to say—and this is ignorance on my part—that my knowledge of GM insect research in central Europe is zero. I am not aware of any, but that does not mean it is not going on. It is not an area I have looked at. It is not my own area of research.

**Lord Hunt of Chesterton:** You did say, as I understood it, that dengue was a disease where this technique might be useful.

**Professor Whitty:** Yes, that is the case and if I was worried in Europe I would not be going down the Aedes aegypti line; I would be going down the Aedes albopictus line. I would be aiming to look at this particular technique but in a different mosquito vector.

**Lord Krebs:** I would like to come back to this question of efficacy. When Oxitec submitted evidence to us, one claim from their trials in Brazil was that it has reduced the population of the vector by more than 90%. Could you help us to clarify whether a 90% reduction in the vector population is an effective way of controlling dengue or whether this other point you referred to in relation to malaria about the lifespan of the individual vector is more important?

**Professor Whitty:** There are two sides to that. First, it has a relatively effective but linear impact on disease. The Ross-Macdonald equation works potentially for all vectors. The time in the mosquito is shorter for dengue, so the advantages are smaller. It is probably seven to nine days rather than nine to 14 days. You should also remember that killing Aedes is not in itself that difficult. The problem is that they rebound incredibly quickly. They have a very fast regeneration time so, essentially, you have to maintain the pressure on them for very long periods. The problem with killing Aedes is not killing them; it is killing Aedes in a cost-effective way that does not cause other damage due to the very widespread use of insecticides.

**Lord Hunt of Chesterton:** My second question was to do with how the scientific community is dealing with this question in discussion. Does the scientific community advocate more regulations? There is the government world that you were in but now you are a scientist in this other world and, obviously, the non-governmental scientific community has some input into policies and regulations. Do the issues we are talking about here have a good and effective focus in the non-governmental scientific community?



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**Professor Whitty:** I would not want it to stand that being in government means that you are not a scientist; I think it is possible to be both. My view is that there are at least two and possibly three different discussions going on, and they do not get connected. There is a group of discussions by people who are in public health and they start from, “Okay, we have got this problem; what are the multiple solutions we could use and what is the most efficient bundle of them that is going to get us there?”, and they do not tend to talk about GM mosquitoes much for the reasons I have just given. Clearly there is then a group of people who are interested in insect biology, and they talk a lot about this because they are interested in the fundamental science. As I say, I do not want to imply that there are not potentially very significant spin-offs from that, but they do not tend to be starting from the problem. They often talk about malaria or dengue in their grant applications, but that is only two lines and the rest is fundamental science. There is nothing wrong with that, but that is the way it is. You have those two conversations going on. The closest there has been to joining them up is the WHO document, in which I had no part, so I can say this without any conflict of interest. I thought it was a pretty thoughtful and sensible attempt to be balanced in its approach. It does not say anything about regulation but it does provide a framework for thinking about these matters in a broader sense.

**Lord Hunt of Chesterton:** The WHO is effective in bringing the scientific community and the governmental side together.

**Professor Whitty:** As it should. My view is that that is very much part of its central function. I think it is one of the things it should be doing. In this case it seemed to me a sensible and appropriate document.

**Lord Hunt of Chesterton:** In many of these United Nations agencies, which I knew about, they have the regular programme and then they have extra-budgetary programmes. Does the UK contribute to both?

**Professor Whitty:** I am in danger of getting into what I am not allowed to do which is to defend the UK Government.

**Lord Hunt of Chesterton:** I just asked what they did.

**Professor Whitty:** My simple answer is that the UK Government do both. There is a more complicated answer, which I think you need to ask a Minister about.

**Lord Hunt of Chesterton:** That is useful, thank you.

**Lord Maxton:** You mentioned the difference between agricultural use and human use. Is agriculture the only industry? It springs to mind that the tourist industry is affected by insect bites. In the west of Scotland it is the midge, but more particularly it is the side effects of drugs you have to take if you go to places such as Kenya, for instance, in order to combat malaria, which has an impact upon the tourist industry.

**Professor Whitty:** Absolutely. Let me take two examples, one from human health and one from potentially human health. On human health, an area where a sterile male or equivalent technique for *Aedes* would strike me as very attractive is in tourist islands in the Maldives, where they depend on tourism very heavily for their economy. It is an island so therefore you can eliminate an insect and its re-invasion will take quite a long time. It is controlled. It is

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not going to go anywhere<sup>193</sup>. That seems to me an ideal example of the kind of area where a sterile male technique might be the right tool. That is one example.

The midge is an interesting one. Clearly, it is a pest. Being a detribalised Highlander myself, I am well aware of the downsides of Highland midges. What we do know is that the last two serious animal diseases into the UK—bluetongue and Schmallenberg—are both midge transmitted. That has demonstrated the principle that midges, of which the UK has a lot as opposed to other vectors, can transmit quite serious diseases. There is no principled reason, in my view, why in due course a disease could not emerge that was midge transmitted. In that situation we would not just think about this as a tourist problem; we would see this as a public health problem. We have to think a little bit ahead about this.

**Viscount Ridley:** Would you be prepared to comment on Lyme disease? I know it is transmitted not by an insect but by an arthropod.

**Professor Whitty:** There are a number of potential and real tick-transmitted infections in the UK. It is the one area where we do have that. Lyme disease is the most important but it is still a relatively small number. The PHE numbers are around 1,000 a year. Clearly, the true numbers would be higher than that, but nowhere near what you would believe if you read some of the more hysterical press commentary. It is not a huge problem in the UK, but it is an issue. That is a sort of bacterial disease and we have a viral disease, louping ill, which affects primarily sheep and red grouse but can infect humans from time to time, and, in theory, we have a parasitic disease, babesiosis. Tick-borne diseases exist already in the UK and, in principle, there is no reason why there could not be others.

**Q73 Lord Fox:** You have indicated quite clearly that you think this is a niche, but you have also indicated that we should perhaps place a bet or buy a potential insurance policy for what may happen. Who and where should that money come from? Clearly with the Gates Foundation and the Wellcome Trust we are seeing philanthropic organisations and we have heard opinions from some of the evidence that it is not really a business model. Should this come from the international development funding from the UK rather than medical research? Where should we invest from in this?

**Professor Whitty:** I need to be careful in answering that I do not appear to be giving advice to my very distinguished and able successor in my previous role. However, with that caveat, I would separate out a variety of different issues. Let us take malaria as an example. DfID has taken the view that its primary aim is to reduce the number of people who die from malaria and the number of pregnant woman who get malaria and so on. The Gates Foundation has taken as its primary aim eliminating malaria, where it can be eliminated. Those lead to very different strategic and then tactical decisions about what should be backed. If I think about elimination, I would think a bit more seriously about GM products because they may have niches in areas where nothing else works. If I am trying to stop children dying from malaria in northern Nigeria, it is about getting new insecticides and about how to get children not sleeping under a bed net to sleep under one. I would be cautious about diverting that away. On malaria that would be an answer.

Dengue has a slightly different set of answers. I will defend a decision that I took about the advice I gave around a dengue vaccine. I was doubtful that UK development funds should be put into a dengue vaccine, not because I did not think it would work—I thought the science

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<sup>193</sup> Following the evidence session Professor Whitty added: using insecticides near coral reefs is not ideal.

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was moving in the right direction very rapidly—but because this is primarily a disease which has affected middle-income countries with highly developed biotechnology systems, such as Brazil and India, and where there is a big travellers’ market, so it seemed to me likely that the private sector would move into this and they would happily take our money, but whether or not we were there, they would deal with this. That is indeed what happened. Sanofi Pasteur, which did the first vaccine, refused public money I gather, because they did not want to be bound by all the conditions on pricing that would come with that. There are slightly different arguments depending on what it is you are talking about.

**Lord Vallance of Tummel:** Is that a generic approach that a government department would take? In other words, it would look to see whether the private sector would take something up before it decided to put public money into it.

**Professor Whitty:** I would be very cautious about speaking for other government departments. My own logical answer to that would be that the question is whether all you are doing is providing money which they would have used anyway, so in a sense it is completely fungible money, or whether you need to pump-prime or provide some degree of subsidy essentially to get something through that you want. I realise that is a very bland answer.

**Lord Vallance of Tummel:** You take a judgment as to whether the market would work or not.

**Professor Whitty:** Yes.

**Q74 Lord Hennessy of Nympsfield:** Given your warnings about the danger in overselling GM techniques, how do you think the public debate should be shaped about this? Do you think it needs stirring up or is the worry that it might spill over into a version of GM foods and the Europeans then get agitated in their role of congenital snag hunters?

**Professor Whitty:** I wrote an editorial for *Nature* in which I said we should be trying to make sure that Africa and Asia do not catch the European irrationality on GM for crops. In my own judgment, there is a danger on GM that we had people on the one side massively overstating the risks and disbenefits but also people on the other side overstating the potential benefits, and then they are easy to shoot down. The public sit in the middle. If they feel you are being very straight with them and saying, “Let us not exaggerate the benefits, as there are some clear benefits here, but also let us not exaggerate the risks”, that seems to me the right approach, and that is what I am arguing for here. Let us not get carried away but also let us not dismiss it.

**Lord Hennessy of Nympsfield:** May I have a footnote on a footnote? It is the midge question. Is the science there to eradicate midges in the Western Isles and the Highlands? This could save the union, you know.

**Professor Whitty:** The short answer is no, without doing things that would be so draconian and environmentally unacceptable that it would simply not be a runner.

**Lord Maxton:** That is a way of eliminating it.

**Baroness Morgan of Huyton:** Could I go back to the previous question? You were describing the type of public debate that is required, with which I suspect we all agree, and that is to get the balance right. Who on earth is going to orchestrate that? Who the public are going to believe is one of the questions we are grappling with.

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**Professor Whitty:** The kind of report that I suspect your Lordships will come up with is exactly the kind of thing that is needed, which does the—

**Baroness Morgan of Huyton:** On the one hand and on the other.

**Professor Whitty:** —on the one hand and on the other, but we are being serious about this. We are not believing the most extreme on one end or the most extreme on the other.

**The Chairman:** Let me confess my own concerns about the danger of the public debate which I think you are encouraging us to recommend. It might be captured either by people who overstate the benefits or other people who might overstate the disbenefits or the risks. If the debate was held at the European level, one only has to see what has happened on GM crops to realise that that is not necessarily a very successful forum in which to conduct this particular exercise, and yet of course competence in this area lies to a large extent at the European level. We must not overstate any potential beneficiaries, but you suggested there might indeed be niches where this could be usefully deployed, although it remains to be seen. Surely such beneficiaries should have a stake in the dialogue. It is quite difficult to structure a dialogue where some of the beneficiaries might be places such as the Maldives, as you have described, or it might be somewhere else. How would you like to see such a dialogue structured where we have the opportunity for people who are not going to take extreme views but who have a relevant interest to participate, so that eventually when policies have to be made by national Governments or organisations, such as the European Union, they are informed by that sort of debate?

**Professor Whitty:** I am straying beyond my own skillset as a scientist, but let me point to the role that small island states have had in the debate on climate, where they have been one of the most powerful advocates for getting the science right and understanding the impact of climate issues. Certainly Brazil, where the Oxitec experiments are going on, is more than capable of having serious debates around technology. They have one of the best science/technology/research nexuses in the world and, although one can call them out about the politics, the fact is that Latin America has been surprisingly successful in having technical debates between scientists and the public, often cutting out government completely in doing so. I do not think it is impossible to do, but I am definitely not the expert to say how it should be done.

**The Chairman:** Who should advise us on this issue?

**Professor Whitty:** I suspect the people around this table have a much better idea on that than I do.

**The Chairman:** That is a very helpful answer, thank you. We have probably come to the end of our questioning. I am very relieved that you were on your own because you have been able to impart so much information to us in a relatively short time and we would not have wanted it diluted by a further contribution. Thank you very much, Professor Whitty. You have been enormously helpful to us.

## **Professor Christopher Whitty, London School of Hygiene and Tropical Medicine – Supplementary written evidence (GMI0032)**

Professor Michael Bonsall, who is helping the Committee on their enquiry on GM insects has sent me three questions for clarification following my oral evidence. This is my attempt to reply. The first two are technical questions with technical (semi-mathematical) answers; the third is probably more generally useful.

### *1) How does the Ross-MacDonald model apply to dengue fever?*

I did not fully answer one of Lord Krebs' questions. He asked whether the Ross-Macdonald model applied to dengue as well as malaria. I replied yes (which is accurate) but did not pick up on the question implied behind that- why then treat dengue and malaria differently in terms of sterile-male type methods?

1) The more important reason; with malaria we have proven methods to reduce  $p$  (average probability of surviving a full day after biting when that is to the power  $n$  which is generally around 9) because for the major vectors especially in Africa they bite in a predictable time at night in a predictable place and then do a predictable thing (rest on walls) meaning this can be targeted. Aedes bite during the day in multiple areas making targeting  $p$  much harder. Aedes therefore has no equivalent of insecticide-treated bednets or indoor residual spraying of DDT/ pyrethroids, which are both aimed at  $p$  (although they also reduce populations a bit). Therefore it is less that the Ross-Macdonald equation does not apply, than that with malaria we can use the mathematical advantages because we have tools effectively to target  $p$  for the major vectors (especially in Africa), whereas with Aedes we do not.

There are some malaria vectors, especially in SE Asia and Latin America, which do not bite indoors or rest on walls, so targeting  $p$  is not as easy. On the other hand it is not obvious they could easily be targeted by genetically modified vectors either.

2)  $R_0$  (VC) for malaria can be over 100, so reducing it to less than 1 with something which is strictly proportional like density of mosquitoes is tough.  $R_0$  for dengue is generally much lower so halving can have a serious impact.

As a result the difference between realistic measures which target  $m$  (density of mosquitoes) and  $p$  (probability of survival) is substantial for the main Anopheles vectors but not so substantial for Aedes, so the sterile male variants, which target  $m$ , are not at such a disadvantage for Aedes, hence dengue.

In the unlikely event you want a fuller version of the mathematics behind it this paper is a reasonable summary of the history.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3320609/>

There are many versions of the Ross-Macdonald model, but they are versions of the same thing and I quoted a simplified version of the most widely used one. The extrinsic mosquito

cycle (the 'n to the power of' in the model) is both temperature and species of parasite/virus dependent, but in tropical climates around 9 for falciparum malaria and closer to 7 for dengue is a reasonable estimate. In cooler climates, like the UK, the extrinsic cycle is longer (because it is a biological process in a non-mammal) so n is greater and the advantages of targeting p even greater.

*2) What the advantages and limitations of focusing on mosquito longevity for determining disease spread? What are the other parameters in the equation for the basic reproductive number that are also key to determining disease spread?*

The big advantage is that if you can reduce p (longevity after biting an infected person) it provides a very substantial mathematical advantage because it is to the power n the time in the extrinsic cycle so even a small reduction will have a big effect on vectorial capacity (R).

Man-biting habit (a, anthropophily) is squared as vectors have to bite once to acquire and once to transmit, so if you can reduce that it has bigger than arithmetic effects. For species for vector which are indifferent to their source of blood meal this is realistic, either by providing barriers to biting humans (eg screening windows and doors) which divert them to other species or providing alternative blood meals (eg tethering animals between breeding sites and human habitation). For ones which almost exclusively use human blood meals this makes less difference as if they are diverted from one human they find another. Major malaria vectors such as *A. gambiae* fall into this group.

The other factors are mainly linear, including density of vectors, longevity of infectiousness in humans, and how well adapted vectors are to acquire infection. For all of these halving the risk factor will halve VC (R).

*3) Based these epidemiological principles, how important are self-limiting insect strategies for the control of dengue (or similar vector-borne diseases spread by Aedes mosquitoes)?*

Mathematically they are linear. The real public health question is however: what are the alternatives and what is the optimal mix? Control strategies should not be considered in isolation of alternatives. Control of vector-borne diseases is a mixture of vector-side and human-side interventions of varying effectiveness and cost-effectiveness. The aim in resource-constrained settings is to get the mix which is most cost-effective in the local context, and then see what additional benefits other interventions might bring and their incremental cost-effectiveness. If for example control of Aedes by GM technology was the only way to reduce dengue it would be much more attractive than if it has to be seen as one technology among many.

What makes this more difficult is that GM is not the only technology that is progressing scientifically. The model is therefore not one where the science of GM moves forward, but all others remain static. In evidence to the Committee I suggested some of the parallel vector-side approaches which are being tried (eg Wolbachia). Possibly more important however are the human-side approaches, in particular vaccines. If a highly effective vaccine for dengue at a reasonable price structure were developed it is likely all vector-side interventions for that disease would become redundant. For Aedes-transmitted infections

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the model is Yellow Fever; vector side interventions are irrelevant because the vaccine is for practical purposes 100% effective. Dengue would not require a 100% effective vaccine because it is purely a human disease (unlike Yellow Fever). Therefore there is a herd effect; if enough of the population are protected they protect the rest of the population. If 80% of people around me are immune I am very unlikely to get a disease from them and major epidemics are very unlikely.

In 2015 there is one vaccine in late-stage clinical trials which looks over 50% effective (and likely to be licensed). For the trial data see <http://www.nejm.org/doi/full/10.1056/NEJMoa1411037>, but there are now many other vaccine candidates in earlier development which may improve on this and there are major private sector, public sector and foundation investments pushing many vaccine paths.

Therefore there is a fair chance that all of the experimental vector methods which are currently in development, of which GM is only one, for dengue will be rendered largely redundant for widespread use by a human-side vaccine for dengue (but this is by no means certain). An example where human-side interventions have recently largely or completely supplanted vector control is lymphatic filariasis where mass drug administration has been proven more effective so human-side interventions have become the main or sole control method.

My own opinion, which may well be wrong as it is a prediction about future science, is that it is unlikely widespread use GM insect technology will become cost-effective for public health use compared to other methods for dengue, but not because they cannot work in theory despite its mathematical disadvantages. It is because the combination of widely spreading piped water with development (which removes a lot of the breeding sites for *Aedes aegypti* from water storage) and a moderately or highly effective vaccine are likely to render them redundant before they become cost-effective. The point about the GM technologies used for control is that they have to be cost-effective compared to other methods- being effective is not enough- and the self-limiting methods have indefinite costs unless elimination/eradication is aimed for and achieved. It is however entirely possible I am wrong in this prediction and GM is the science which progresses and the others all founder.

I highlighted two exceptions; niche indications, and Chikungunya. The reason for Chikungunya was because vaccine development is currently well behind dengue (itself not an easy vaccine candidate) so the human-side developments are less likely in the timeframe within which GM is developing. The niche indications would include situations where you want to eradicate rather than control *Aedes* vectors, where self-limiting methods have particular advantages, and some specific environmental niches. The example that came up in the Committee was the Maldives where tourists might not want vaccination for a 1 week holiday. Small, ecologically isolated, with clear economic benefits and in an environment (coral reefs) where continuous insecticide use has serious downsides this is an example where a self-limiting method might be very attractive.

One final question I did not answer adequately, although previous witnesses did, on agricultural use of GM insects asked by Lord Ridley. I answered (correctly) that because the

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problem was the insect, not their vectorial capacity, the mathematical advantages of the Ross-Macdonald equation did not apply. What I should have add were two points:

1) agricultural use for insecticides tends to be many multiples of scale and ecological impact of that for human use because it is being used in large quantities, outside (this argues for GM) but

2) as the Oxitech evidence accurately and admirably pointed out, in agricultural use insecticides are often used to reduce multiple insect pest species attacking a crop rather than just one. GM is less useful in this situation.

*13 November 2015*