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POSTNOTE

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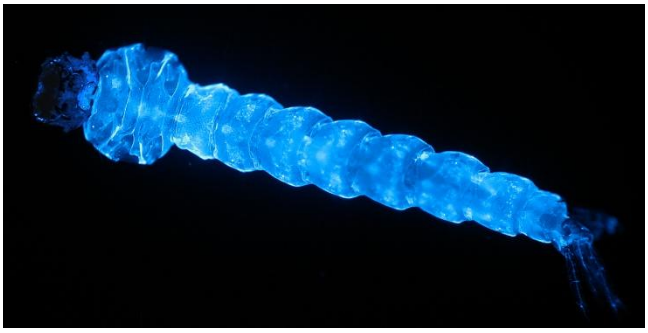
Genetically Modified Insects



Overview

- Insect-borne diseases impose a huge burden on health worldwide, with about half the world's population at risk of infection.
- Insect pests are responsible for severe economic losses through damage to crops and livestock.
- Insecticide and drug resistance have made insect pests an increasing global problem.
- Genetic engineering of insects to reduce populations or to replace them with less harmful varieties is a new control method.
- The risks and potential benefits of genetically modified (GM) insects are disputed.
- Guidelines for the release of GM insects are currently lacking, and several international efforts are currently under way to draft them.

Insects are essential to global ecology and show remarkably varied adaptations to their environment. They are also responsible for economic and social harm worldwide through the transmission of disease to humans and animals, and damage to crops. Their genetic modification has been proposed as a new way of controlling insect pests. However, regulatory guidelines governing the use of such technology have not yet been fully developed.

Background

Health Impacts of Insect-borne Diseases

Approximately half the world's population is at risk from insect-borne diseases (Box 1). Malaria alone kills nearly one million people annually with 3.3 billion people in 109 countries at risk of infection. Those most at risk live in developing countries, concentrated in Africa and South East Asia[1]. There are currently no vaccines against most of these diseases and in some cases drug-resistance is making existing treatments less effective (POSTnote 284). Thus, disease-control programmes focus on reducing the populations of insects responsible for transmission of the disease (known as vectors). However, these have not prevented the continued spread and resurgence of many of these diseases. To meet the challenges posed by these diseases, the World Health Organisation (WHO) has identified that innovative solutions are needed for control programmes, to work alongside traditional interventions[2].

Economic Impact of Insects

Insect-borne diseases cause significant economic losses in countries where they are endemic through lost productivity and healthcare expenditure. Malaria alone can decrease gross domestic product (GDP) by as much as 1.3% in countries with high levels of transmission and is a serious barrier to economic development. Insects also cause economic harm through direct damage and disease transmission to crops. Field vegetables, grasses and citrus fruit are all seriously affected by insects and insect-borne diseases.

Box 1. Major Insect-borne Diseases

The World Health Organisation (WHO) publishes data on the incidence of insect-borne human diseases – those where an infectious agent such as a virus or parasite is transmitted by an insect. Exact figures are difficult to obtain due to the difficulty of collecting complete data in many countries.

- **Malaria** is caused by parasites transmitted by several species of mosquito. In 2008, there were 247 million cases of malaria worldwide and nearly one million deaths, most of these in Africa.
- **Dengue Fever** is caused by viruses transmitted by mosquitoes. It infects 50-100 million people annually with 2.5 billion worldwide at risk; it causes severe fever and may be fatal.
- **Chagas Disease** is caused by a parasite spread by assassin bugs in the Americas. It can cause lifelong debilitating medical problems. 16-18 million people are infected and 21,000 die annually.
- **Human African Trypanosomiasis**, also known as sleeping sickness, is caused by a parasite spread by certain species of tsetse fly in sub-Saharan Africa. Millions are at risk and 50-70,000 infections occur every year; causing neurological symptoms and death if untreated.

The problem is particularly acute in developing nations and a single insect pest of maize causes economic losses of $25-60 million dollars in some African nations[3]. Livestock is also affected by insect-borne diseases such as bluetongue virus, with the potential cost of an outbreak in the UK as high as £230 million[4]. Scientists believe that climate change, changes in land use and global trade are all leading to expansions in the ranges and prevalence of many agricultural insect pests.

Current Insect Control Strategies

Insecticides

Chemical insecticides are the primary means of controlling insect pests for agriculture and public health. For example, two important control strategies targeting mosquitoes are indoor spraying of residual insecticides, such as DDT, and the use of insecticide-treated bed nets. However, some insecticides are linked to environmental harms, such as the decline of beneficial insect pollinators (POSTnote 348). This has lead to tighter regulation of their use globally, such as by the Stockholm Convention on Persistent Organic Pollutants and the EU Directive on the Sustainable Use of Pesticides (POSTnote 336). This has resulted in many products being taken off the market and some scientists fear that the current lack of alternative insecticides may lead to an increase in insecticide resistance in insect pests, a problem that is already occurring in mosquito control programmes around the world.

Alternative Control Strategies

An insecticide-free method to control insect pests is the Sterile Insect Technique in which laboratory-reared male insects, sterilised by radiation, are released over an area. These compete with fertile wild males to mate with wild females in a form of area-wide birth-control that can be used for elimination of an insect population from an area. This is a widely used method but can be employed only for a limited number of insect species. Environmental management is also an important control method. For example, removal of breeding sites around human habitations can be an effective way of controlling mosquito populations in urban areas.

Genetic Modification of Insects

Genetically modified (GM) insects are produced by inserting new genes into their DNA (Box 2).

Box 2. Creating GM Insects

Many genes have been identified that can alter the behaviour and biology of insects. When these genes are inserted into an insect's genome they are called transgenes and the insect is described as transgenic or genetically modified. Transgenes are usually inserted using short sequences of DNA that randomly integrate into the insect's genome, carrying the transgenes with them. By injecting DNA containing the desired genes into the eggs of insects, genetically modified strains can be created carrying complex arrangements of transgenes. Researchers use a wide variety of transgenes, derived from a variety of organisms, to modify insects:

- Marker genes are used to make the insects fluoresce. These allow researchers to distinguish them from the unmodified variety, which is important for monitoring them in the environment.
- Lethal genes cause the insect to die, or make it unable to reproduce.
- Refractory genes confer resistance to a particular pathogen rendering the insect unable to transmit the disease any longer.

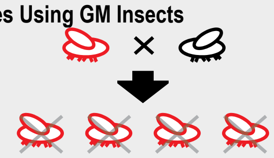
Novel methods to manipulate genes over the last ten years have allowed many insects to be genetically engineered including agricultural pests such as the Mediterranean fruit fly as well as disease vectors such as mosquitoes.

Researchers are preparing some GM insects for trial releases into the environment, with the 2006 release of a GM pink bollworm moth (a pest of cotton), containing a marker gene, in the United States being the first use of GM insects in a plant pest control programme[5].

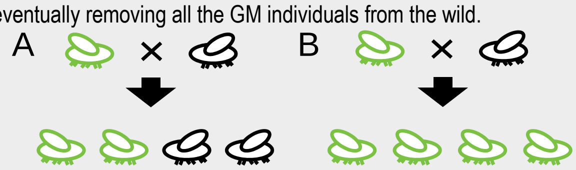
Potential Control Strategies

Scientists have proposed two distinct strategies involving the release of GM insects: population suppression and population replacement (Box 3)[6]. Population suppression strategies are potentially an improvement of the Sterile Insect Technique that do not require radiation sterilisation. They are also applicable to a wide range of pest insects as the design of the genes inserted may be readily adapted to new species. This strategy is the furthest forward in development. A UK company, Oxitec ltd. has engineered GM mosquitoes for suppressing the vector of dengue fever. Trial releases into the wild are imminent in several countries.

Box 3. Strategies Using GM Insects



Population suppression; is a method in which insects are engineered to ensure that when they mate with wild individuals no viable offspring are produced. This is achieved by creating GM insects carrying a lethal gene (red in the picture above). When they mate with the wild insects (black in the picture above) the lethal gene, which is suppressed before release, is passed to the offspring causing them to die. If enough of the GM males were to be released to inundate the wild females this would result in the elimination of the insect population from the area. Most suppression strategies are self-limiting because the lethal genes are designed to kill successive generations, eventually removing all the GM individuals from the wild.



Population replacement strategies involve permanently replacing wild populations of insects with GM varieties that have been altered to render them less able to transmit disease. This requires the use not only of a genetically engineered system to give the insects the desired characteristics but also a system, called a 'gene drive', to spread that desirable gene. Normally an engineered gene (green in the picture above), such as one granting immunity to a disease, would be passed to only half of the next generation, A above. However, a gene drive ensures that this desirable gene is passed on to more than half of the offspring, B above. This means that, over time, the desirable gene will spread through the population, eventually replacing it. Because this strategy is self-propagating, a smaller number of GM individuals needs to be released to begin the process of replacement.

Population replacement technologies are more applicable to public health applications than agricultural ones. Mosquitoes less able to transmit dengue fever have already been created and scientists believe they are close to the more technically challenging goal of creating mosquitoes less able to transmit malaria. Despite this, population replacement technologies suitable for use in the environment are still 5-10 years away, as technologies to drive the desirable genes into wild populations have yet to be developed for any insect pest. Disease control experts agree that, should a population replacement strategy for a major insect disease vector be developed, it could be a 'powerful and sustainable' way to prevent the spread of insect-borne diseases.

Developing GM Insect Technologies

When fully implemented, existing control strategies such as insecticidal bed nets can reduce the burden caused by diseases such as malaria. However, the difficulties in implementing these strategies on a large scale, limited resources and insecticide resistance have been identified as reasons to develop new control strategies. GM insects are one of the technologies being explored by funding bodies such as the Grand Challenges in Global Health (GCGH) initiative and intergovernmental bodies like the WHO[7].

The Potential Benefits of GM Insect Strategies

Proponents of GM insects consider them to be a tool to complement existing control methods. Several unique benefits of GM insects have been proposed:

- they would target only a single insect pest species, leaving beneficial insects unharmed
- by using insects' natural propensity to find one another, pest populations inaccessible to traditional control methods could be eliminated
- GM insects could reduce the need for insecticides and any associated toxic residues in the environment
- when used in disease control programmes GM insects would protect everyone in the release area, irrespective of socio-economic status.
- disease control using GM insects would require less community involvement and so would be less vulnerable to the failure of individuals to participate in a control programme.

Possible Risks of GM Insects

The use of GM technologies is controversial. Some organisations, such as GeneWatch UK and EcoNexus, that monitor the use of genetic technologies, fear that reliance on high-tech solutions, such as genetic modification, detracts from more effective but poorly deployed measures to combat the harm caused by insects. Furthermore, environmental NGOs such as Greenpeace suggest that GM insects could have unintended and wide ranging impacts on the environment and human health due to the complexity of ecosystems and the high number of unknown factors, making risk assessment difficult. They have raised several concerns about the release of GM insects:

- new insects or diseases may fill the ecological niche left by the insects suppressed or replaced, possibly resulting in new public health or agricultural problems
- the new genes engineered into the insects may 'jump' into other species, a process called horizontal transfer, causing unintended consequences to the ecosystem.
- releases would be impossible to monitor and irreversible, as would any damage done to the environment.

Researchers developing GM insects acknowledge the need to proceed cautiously. However, they argue that the insect pests targeted by their technologies are often not native species and that traditional control methods cause more harm than would the introduction of GM insects. Furthermore they argue that:

- GM insects would be deployed only if they were able to reduce successfully the targeted harm and that any ecological impacts would be detected during trial releases.
- horizontal transfer is a concern. However, no study has yet identified a mechanism through which it could occur in insects and furthermore methods have been developed to inactivate transgenes to prevent their 'jumping' into other species.
- self-limiting strategies are designed to remove themselves from the environment after release, preventing persistence of any GM individuals in the wild.
- although self-propagating strategies are designed to maximise the transgenes' spread in the environment, recall mechanisms are being designed that should allow their spread to be reversed if need be.

Funding the Development of GM Insects

Development of GM insect technologies receives funding from various sources, among them the EU's Seventh Framework programme[8], initiatives such as the GCGH and biotechnology companies. International partnerships such as 'Roll Back Malaria' and the WHO (that are supported through the £1.5 billion the UK has committed to the sixth Millennium Development Goal to combat malaria) do not fund research directly but would consider GM insects a potential control strategy if their efficacy could be proven. Were GM strategies to be successfully developed, like any other new control tool, they would require extensive funding to move out of the research and development phase. The involvement of public health authorities at the national and international level, to manage release programmes, would be necessary.

The Regulation of GM Insects

Existing Regulation

At the international level, the Cartagena Protocol on Biosafety applies to the transboundary movement, transit, handling and use of all GM organisms (GMOs) that may "have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health". The ability of insects to travel long distances and to cross international borders means regulation of transboundary movement will be required, particularly in the case of a self-propagating population-replacement strategy that could spread over entire continents[9].

The release of a GM insect within any EU member state is controlled by European Directive 2001/18/EC, known as the Deliberate Release Directive, which regulates deliberate release of all GMOs into the environment (Box 4). Legislation regulating GMOs has been widely initiated in the rest of the world since the ratification of the Cartagena programme, but is often poorly implemented. In Africa, the African Union has drafted the African Model Law on Biosafety, and recently individual countries, such as Kenya with its Biosafety Act of 2009, have created legislation regulating the release of GMOs into the environment. However, in some nations GMO regulation remains undeveloped.

The Suitability of Existing Regulation

Existing legislation was designed to govern all GMOs but its implementation has so far focused on the regulation of GM *crops*; this has been described as the "plant paradigm". The lack of appropriate guidance on how to apply regulation to GM insects may slow down the development of these technologies or deter investment by preventing trial releases.

Box 4. Approving the Release of a GM Insect in the UK

Release of GM insects in the UK is controlled by the Deliberate Release Directive. With non-commercial releases, such as a field trial, the decision to approve is made at the national level by the Department for Environment, Food and Rural Affairs (Defra) in consultation with the independent scientific experts of its Advisory Committee on Releases to the Environment (ACRE), which is responsible for assessing the risks of the technology. If this committee recommended that the insects should be released, it is for Defra ministers to consider this advice in either approving or denying release.

For a commercial release, Defra would perform an initial evaluation of the application with ACRE's input. This application would then be sent to every EU member state, with the European Food Safety Authority (EFSA) providing a scientific opinion. Member states must then, by a qualified majority, approve any release based on the scientific evidence. If member states fail to reach a decision, the application then passes to the European Commission which can approve or deny the application based on the scientific opinion of EFSA.

The European Commission Directorate - Food, Agriculture and Biotechnology considers that "from a regulatory point of view, the application and release of GM-insects, at least within the EU, is far from being a reality". Commercial and scientific developers of GM insects have been pushing for the development of unified international guidance to allow for consistency in evaluation of any technology. The North American Plant Protection Organisation has already drafted guidance on the release of GM insects in its member nations. Currently several international efforts are under way to draft guidelines for regulators and scientists in countries that have not yet developed their own (Box 5)[10].

Box 5. Efforts to Develop Guidance on the Release of GM Insects

- The WHO Special Programme in Research and Training in Tropical Diseases, in collaboration with the US Foundation for the National Institutes of Health, is developing guidance on the "safety, efficacy, regulation and ethical, social and cultural issues" surrounding the release of GM mosquitoes.
- The European Food Safety Authority (EFSA) is constructing guidelines for the environmental risk assessment of GM insects for commercial use in the EU.
- The Cartagena Protocol on Biosafety has just released the conclusions of an ad hoc technical expert group on risk assessment and management of GMOs that includes provisions for GM insects.
- MosqGuide is a project funded to develop "guidance on the potential deployment of different types of GM mosquitoes to control vector borne disease, specifically malaria and dengue fever".

Risk Assessment

The Deliberate Release Directive and the Cartagena Protocol on Biosafety require regulators to consider all possible risks particularly when there is scientific uncertainty about their existence or extent. In most regulatory regimes, including the EU, a formal risk assessment is the mechanism by which the risks of the release of a GMO are evaluated. The potential benefits of such a release are not taken into account within a risk assessment. Environmentalists support this precautionary approach as a way to deal with uncertainty and minimise harm to the environment. However, researchers involved in developing GM technologies feel that regulators should also consider the potential benefits and weigh those against the risks.

Public Perception of GM Insects

Public opinion of GM technologies varies greatly between nations. In the EU, public perception of GM technologies largely has been defined by the GM crop debate (POSTnote 211). The lack of public acceptance of GM technologies led to a 12 year *de facto* moratorium on approval of any GM crops in the EU. This ended only in March 2010, though "delays remain", and makes release of a GM insect in the EU in the near future unlikely. Public consultations on attitudes to GM insects have yet to be conducted in many countries. In the EU, polls have shown a year on year increase in positive responses to GM technology, especially its medical applications[11]. In other nations, particularly those most likely to benefit, the public response to GM technologies has often not been investigated. Many communities are sceptical about the benefits and regulation of genetic modification which is often perceived as 'unnatural' and as such undesirable.

Public Engagement

Engagement with the communities that will be affected by GM insects will be needed if the technology is to be accepted by the public and eventually deployed. This process is already ongoing in countries where releases of GM mosquitoes for disease control are planned[12]. For example, the communities around a test-site in Mexico have been involved with the international collaboration responsible for the last four years. Engagement with communities and local scientists in Asian and African countries is being led by bodies such as the WHO's Special Programme for Research and Training in Tropical Diseases and those that fund research into GM mosquitoes, including the Grand Challenges in Global Health and the Wellcome Trust. It is hoped that this early engagement, combined with the potential benefits of GM insect technologies, will lead to their social acceptance.

Endnotes

1 www.rollbackmalaria.org/keyfacts.html
2 WHO, 2009, *World Malaria Report 2009*
3 Frisen, 2004, *Integrated approaches to higher maize productivity in the new millennium*, CIMMYT
4 Defra, 2007, Bluetongue: Economic assessment of moving bluetongue SZ to All England
5 USDA, 2008, *Use of Genetically Engineered Fruit Fly and Pink Bollworm in APHIS Plant Pest Control Programs*
6 Gould, F., 2004, *Annual Reviews in Entomology*, 49, 193-217
7 WHO-TDR, 2009, Innovative vector control interventions - 2009 annual report
8 For example, ec.europa.eu/research/infrastructures/pdf/infravec.pdf
9 Benedict, M. *et al.,* 2008, *Vector-Borne And Zoonotic Diseases*, 8(2), 127-166
10 Beech, C. J. *et al.,* 2009, *Asia-Pacific Journal of Molecular Biology and Biotechnology*, 17(3), 75-85
11 European Commission' DiG Research, 2006, *Europeans and Biotechnology in 2005: Patterns and Trends*
12 Marshall, J. M. *et al*., 2010, *Malaria Journal,* 9, 128

POST is an office of both Houses of Parliament, charged with providing independent and balanced analysis of policy issues that have a basis in science and technology. POST is grateful to Mr Oliver St John for researching this briefing, to the BBSRC for funding his parliamentary fellowship, and to all contributors and reviewers. For further information on this subject, please contact the co-author, Dr Jonathan Wentworth.