

House of Lords Science and Technology Committee Inquiry on Genomic Medicine

Response from Wyeth

1. Wyeth welcomes the Inquiry on Genomic Medicine and we agree that it is timely to review current research achievements and future prospects in this area in order to assess the issues for policy across a broad front for science, innovation and health.
2. Genomic medicine is an important part of the R&D effort of the pharmaceutical sector and, therefore, will contribute to UK health and wealth creation. In aggregate, pharmaceutical companies carry out more than one quarter of all business R&D performed in the UK. One in five of the world's top medicines were discovered and developed in the UK and this success has been achieved by innovation, built on sustained investment in R&D. As a leading R&D-intensive US company investing in innovation in the UK, the experience of Wyeth may prove helpful in setting into context the issues for the UK in an era of ever-increasing global competition¹. In order to provide a succinct response, we have focused on a relatively small number of the questions posed by the Committee but we would be happy to provide further information on any point.

What is the state of the science? What new developments are there? What is the rate of change?

3. The research that will advance the development of genomic medicine continues at a rapid pace even though the first phase – the sequencing of the human genome – may be considered accomplished. There is now much to be done to characterise the genome, particularly in terms of understanding the genetic contribution to disease and the selection of new targets for therapeutic approaches. There is still surprisingly limited understanding of the mechanisms underlying human physiology and the pathophysiology of most common diseases. New initiatives rendered possible by advances in technology, in particular genome-wide association studies, will be of great importance in accelerating the rate of understanding of these processes.
4. Disappointment has been sometimes expressed that genomics has apparently not yet contributed significantly to the emergence of new drugs. But this view underestimates the amount of work involved in drug discovery and development and the need to create better tools, models and processes to capitalise on genomic data to identify, select and validate targets. Obtaining genome sequence data and postulating its association with a putative function is only the first step – elucidation of target characteristics and the development of assay methodology in animal models and clinical studies are essential next steps in drug discovery and development².

¹ Recent survey results (20 March 2008) are noteworthy in showing that many UK-based pharmaceutical companies are generally increasingly pessimistic about the UK as a place in which to invest in R&D and conduct clinical trials. See www.abpi.org.uk/press/press_releases_08/200308.asp

² These issues are discussed in detail in a report of a meeting “Experimental Medicine” organised by the Academy of Medical Sciences. Wyeth presented case studies from diverse disease areas (Cardiovascular, Alzheimer’s Disease, oncology) to illustrate how the outputs from genomic research must be integrated into

5. Broadly defined, genomic medicine encompasses specific objectives that build on the identification of novel targets, to include:

- The introduction of stratified medicine (“personalized medicine” in the older terminology) for better focusing of therapeutic interventions on well-defined subgroups of patients. The better understanding of molecular variation in disease should enable delivery of safer and more efficacious drugs with greater certainty of success to those in need.
- The extension of genetic testing for more common conditions. This is not a particular business focus for Wyeth currently but although we will not be responding to the specific questions relating to genetic testing we recommend the recent OECD publication that provides a valuable international comparison on quality assurance in genetic testing with accompanying discussion of the issues for sample and data handling³.
- The development of novel biological therapies. Wyeth recently (October 2007) acquired Haptogen Ltd, a company spun out of the University of Aberdeen, expert in next-generation biotechnology discovery platforms that allow for the discovery and optimization of protein therapeutics with significantly improved profile over the current generation of therapies.

What is the role of industry? How much cross-sector collaboration takes place?

6. Many companies in the pharmaceutical sector are perceived to be encountering problems with R&D productivity associated with weak pipelines, impending patent expiries and consequent loss of revenue, and increasingly costly R&D processes. Despite these problems, the sector is poised to develop a wave of innovative medicines discovered and developed following the decoding of the human genome. The outputs from genomics research has led to an increasing flow of compounds into the R&D pipeline and many of these compounds address novel, “unprecedented”, targets for hitherto hard-to-treat diseases. In consequence of this novelty, there is a growing clinical attrition rate – but the high failure rate and long life cycle in drug development are not economically sustainable for the sector. Thus, genomic medicine will only succeed if the ambition to select unprecedented targets is accompanied by new approaches to validate targets and provide proof of concept in humans earlier in development. By this means, there is prospect of improving confidence in lead compound selection and optimization and enhancing cost-effective decision-making, while providing meaningful benefit to patients. It is critically important to take an integrated view “from gene to community”.

7. Translational Medicine is rapidly emerging as a tool to bridge the gap between pre-clinical and clinical studies so as to improve early understanding of drug safety and efficacy in patients. Wyeth helped to pioneer the application of Translational Medicine in terms of biomarker discovery and the validation of drug targets and Wyeth worked closely with Regulatory Authorities in developing guidelines for the submission of

a broad range of other activities in pharmaceutical R&D. See www.acmedsci.ac.uk/download.php?file=/images/event/EMSummar.pdf

³ OECD, “Genetic Testing: A Survey of Quality Assurance and Proficiency Standards”, October 2007, www.oecd.org

genomic data in support of drug registration. In 2004, Wyeth was the first company to provide genomic data to the FDA in the Voluntary Genomic Data Submission programme.

8. A significant degree of cross-sector collaboration takes place at the pre-competitive level, to assess the value of genomic information. The SNPs Consortium in the 1990s helped to create the starting point for understanding the importance of individual genetic variation in disease propensity. The US Biomarkers Consortium (established 2006) involves the FDA, NIH, pharmaceutical companies and patient group in work to find and validate disease markers. The European Innovative Medicines Initiative (starting 2008) involves companies, academia, regulatory agencies and patient groups across the EU in research on biomarkers for drug safety and efficacy assessment.

How does research in the UK compare internationally? How much collaboration is there?

9. In our view an important component in successful progress is strong problem-solving academia-industry collaboration. Wyeth has introduced a novel concept in partnership to focus on Translational Medicine in the UK. This capitalises on public sector excellence in biomedical research, building a new collaborative model in Scotland between the research capabilities of Wyeth and a consortium of the four medical universities (Glasgow, Edinburgh, Dundee, Aberdeen) and Health Boards and Scottish Enterprise. In our innovative model focusing on disease mechanisms, ideas are jointly-derived, the research plan is modified by mutual agreement, background Intellectual Property is protected, with shared ownership of jointly-generated deliverables. This initiative, sharing risks and rewards, now in its second year, covers diverse disease areas and academic disciplines with particular focus on biomarkers research and imaging techniques. Scotland is deemed an attractive location for this endeavour because of strengths in pre-clinical and clinical research, university-NHS networks, health informatics and tissue banks. Success of the collaboration will be measured in various ways – in better understanding of pathophysiology, in shared generation of ideas and hypotheses, in standardising new models and tools, in development of new therapeutics, better patient care and economic growth. We commend these measures as equally relevant to the UK as a whole in evaluating the achievements of genomic medicine.

Does the existing regulatory and advisory framework provide for optimal development and translation of new technologies? Are there any regulatory gaps?

How effective is the policy and investment framework in supporting research in this area?

10. The scientific advances will continue to create new opportunities for health care innovation if there is an encouraging environment for innovation. Wyeth has made a major investment to capitalise on scientific excellence in the UK and this type of inward investment is most likely to succeed if:

- There is a proactive approach by public policy makers to build research infrastructure. Government also has an important enabling role to ensure that partnerships generate value – this requires effective protection of Intellectual Property⁴.
- There is availability of skilled researchers and the flexibility to organise them into research teams with diverse expertise in pursuit of new directions rather than focusing unduly on individual disciplinary strengths.
- Support is given to new forms of partnership and promotion of the NHS as a leading research resource.
- Public engagement efforts include communication on the value of public-private partnerships.

11. The advent of Stratified Medicine in consequence of advances in genomics research warrants consideration of new options for regulatory and pricing frameworks for both therapeutics and diagnostics in order to create flexibility to assess health care value and reward the innovator. One option for regulatory reform is conditional licensing – allowing new drugs in NHS priority areas to be made available to patients following preliminary safety studies and proof of efficacy. This conditional licensing approval would be subject to continuing clinical study employing the new technologies (in particular, biomarkers) central to evaluation in genomic medicine⁵.

How is the study of genetic factors and biomarkers integrated for translational purposes?

12. Biomarkers have important roles in Translational Medicine – across the R&D lifecycle and into clinical practice. For example:

- Understanding, monitoring and predicting disease processes, including the earliest and most sensitive markers of altered pathophysiology.
- Providing evidence for target validation and for drug-target engagement during the discovery phase.
- Selecting patients – to ascertain which subjects are most likely to respond to the drug.
- Evaluating efficacy and safety in clinical trials and assessing optimal dosing regimens.
- Post-marketing, to inform the continuing need to understand the determinants of efficacy and safety.

⁴ With particular regard to the licensing of genetic interventions, the recent guidelines from the OECD (www.oecd.org/sti/biotechnology/licensing) are useful in setting out principles and examples of best practice for health care inventions in the international context, seeking to foster the twin objectives of stimulating innovation, while maintaining appropriate access to health products and services.

⁵ The scientific and regulatory issues for Stratified Medicine are discussed in detail in the recent report from the Academy of Medical Sciences, December 2007, produced following a meeting in which Wyeth participated.

What opportunities are there for diagnostics, therapeutics and prognostics? Who is responsible for translation to clinical practice?

13. We have addressed these questions in our previous paragraphs but we would like to take this opportunity to emphasise that this is an exciting time for Translational Medicine. We welcome the inception of the Office for Strategic Coordination of Health Research (OSCHR) established following the Cooksey Review of Health Research. Implementing the new OSCHR strategy promises to develop new momentum in building partnership between industry, academia and the NHS. We reiterate that the NHS can become a leading research resource for genomic medicine and should be regarded as a major asset to generate and delivery innovation. This requires improving research culture, capabilities and capacities within the NHS.

How should genomics data be brought together with other health information?

What impact will genome data have on data emerging from projects such as UK BioBank, Generation Scotland and other biobanks?

14. The NHS National Plan for IT provides the unparalleled opportunity to use health care records for research and, in due course, will be a major resource with which to interpret genomic data. The collection of well-phenotyped patient data is often the rate-limiting step. There is continuing need for national health care IT systems to be developed so as to support the objectives of research.

15. The pioneering work of the Generation Scotland initiative in providing a population-based resource to explore genetic epidemiology of common diseases is of particular potential value. Unfortunately, some other large-scale genetic databases have been controversial or relatively slow to progress and public policy makers must take the initiative to advocate the value of such activity⁶.

What are the implications of developments in genomic technologies for the training of medical specialists and other health professionals? Are there any gaps that need addressing?

16. As discussed previously, the use of genomic technologies to improve health care will only be successful if the advances in fundamental sciences can be translated into new products and services. This requires attention to developing training programmes for physician scientists and others in Translational Medicine and drug discovery and development. There are particular gaps in supply of some of the in vivo experimental skills, pharmacology, toxicology and clinical pharmacology. Wyeth is currently supporting a bid for training fellowships in clinical pharmacology with the four medical universities in Scotland and this will involve fellows spending a period of time in industry.

⁶ The report on Stratified Medicines (footnote 5) describes some of the needs for future biobanks, particularly prospective collection for the purpose of monitoring therapeutic responses.

17. It is important to encourage mobility between sectors, institutions, disciplines and countries. The introduction of the new approaches to public-private research collaboration will help to facilitate researcher mobility. Nonetheless, it is still necessary for some universities to understand – and to communicate to their students – that a research career in industry does not represent a failure for a skilled young scientist.