



House of Lords Science & Technology Committee

Inquiry into Genomic Medicine

Submission by Roche

21 April 2008

Introduction

1 Roche welcomes the House of Lords Science & Technology Committee's inquiry into genomic medicine and the opportunity to contribute to it.

2 Headquartered in Basel, Switzerland, Roche is one of the world's leading research-based healthcare groups in the fields of pharmaceuticals and diagnostics. As the world's biggest biotech company and an innovator of products and services for the early detection, prevention, diagnosis, and treatment of diseases, the Group contributes on a broad range of fronts to improving people's health and quality of life.

3 Roche is the world leader in in-vitro diagnostics and drugs for cancer and transplantation, a market leader in virology and active in other major therapeutic areas such as autoimmune diseases, inflammation and metabolic disorders. The group employs about 79,000 people around the world. Further information is available at www.roche.com

4 Roche has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai, and invested over 8 billion Swiss francs in R&D in 2007. We are systematically using the growing understanding of the human genome to develop personalised healthcare and are committed to the significant effort and investment that this requires, as evidenced by the recent acquisition of Ventana Medical Systems Inc.

5 Given our interest in genomic medicine, our submission focuses on the following points:

- personalised healthcare – what it means in reality and the potential benefits for patients, healthcare systems and the healthcare industry;
- the public policy framework – the issues that need to be urgently addressed if these advantages are to be fully realised, including access to clinical samples, pricing and reimbursement, assessing existing therapeutic agents, and public private partnerships.
- the United Kingdom as a leader – the UK has several unique characteristics that offer the potential to capitalise on developments in genomic medicine and obtain a competitive advantage if the issues identified above can be addressed satisfactorily.

What is Personalised Healthcare?

“The Personalized Health Care Initiative will improve the safety, quality and effectiveness of healthcare for every patient in the US. By using “genomics”, or the identification of genes and how they relate to drug treatment, personalized health care will enable medicine to be tailored to each person’s needs.”¹

United States Department of Health and Human Services

6 “Personalised healthcare” is a broad term which can be used to describe a wide variety of different approaches designed to tailor diagnosis and treatment more closely to the needs and convenience of the patient. In the context of molecular medicine, it refers to the study of the human genome and how its diversity may impact on the way in which individual patients are likely to respond to different therapeutic agents. Using this information, as elucidated by specific diagnostic tests, it may be possible to tailor treatments - to meet the genomic profile of patients belonging to specific stratified groups. Indeed, Roche believes that to facilitate future progress in medicine, advanced diagnostics will play a vital role in medical decision making regarding the treatment options available.

7 Personalised healthcare is expected to have a number of significant benefits for patients, including more specific and earlier diagnosis and increasing the efficacy of treatment, while reducing the incidence of adverse reactions and side effects. It also results in the more efficient and cost effective use of resources by the healthcare system. This approach promises considerable advantages for the healthcare industry as it delivers new technology specifically targeted at meeting recognised patient needs. It will provide clinically differentiated medicines that take the diversity of disease states into account based on increasing knowledge and more sophisticated technology, including the opportunity for companion diagnostics to guide treatment decisions.,

8 It is important to note that the concept of personalised healthcare is not new. For example, blood glucose testing has been used by people with diabetes for several decades to ensure they administer the right dose of insulin. However, as our knowledge of human biology has increased through initiatives such as the human genome project we have been able to develop new diagnostics and medicines based on a growing understanding of the molecular basis for disease and the patient’s likely response to treatment. A key challenge is to create incentives to encourage efforts to translate this knowledge into clinical practice.

9 It is also equally important to manage expectations. Personalised healthcare holds great promise for patients and healthcare systems, but discovering and developing novel biomarkers and medicines is a very complex and time consuming undertaking. It is also very unclear how medicines and companion diagnostics aimed at stratified patient groups will be rewarded in the marketplace and what the potential return on investment will be once the new technology is launched. This is particularly relevant in markets which already have a poor record regarding the uptake of new technology, either for reasons of access to funding or clinical conservatism.

¹ <http://www.hhs.gov/myhealthcare>

Herceptin – Personalised Healthcare in Practice

- Herceptin was approved by the US Food & Drug Administration in 1998 and by the European Commission in 2000 and more recently for use in early stage breast cancer.
- Herceptin is the first oncongene-targeted breast treatment with proven survival benefits. It was designed specifically to target the HER2 protein, which is associated with aggressive cancer cell growth. Around 20% of women with breast cancer test positive for the HER2 gene.
- Before beginning treatment, patients are required to be tested for their HER2 status. Clinical trials have shown that “HER2-positive” individuals receiving Herceptin experience substantial improvements in survival and quality of life as compared to treatment with conventional chemotherapy alone.
- Herceptin is a practical example of how diagnostics can be used to guide targeted treatments to deliver personalised healthcare and improve patient outcomes.

The Public Policy Framework

10 These issues, both positive and negative, raise some critical questions for both Governments and the healthcare industry as they seek to harness the benefits of genomic medicine for all. Sir David Cooksey addressed some of these points in his report *A Review of UK Health Research Funding*², which made some important observations about the future framework for health research in the United Kingdom. We particularly welcomed his recommendations regarding the Office for Strategic Co-ordination of Health Research (OSCHR); creating “a stronger culture” in favour of research in the NHS; and encouraging greater collaboration between the public, private and charitable sectors.

11 We also welcome the comments made in the Department for Innovation, Universities and Skills white paper *Innovation Nation*³, which places heavy emphasis on the role of government in creating the conditions for innovation to flourish, including the areas of driving innovation through public procurement and helping to overcome barriers to business innovation. We also look forward to the publication of the government strategy for Science and Society in the autumn.

12 However, there are several critical issues that remain unresolved which are directly relevant to genomic medicine and the development of personalised healthcare:

13 **Biobanks** There is a lack of high quality clinical samples available for research purposes. There are some very promising examples including the EUDRAGENE initiative but the size and number of biobanks still needs to be expanded considerably. In our experience it can also be difficult for the commercial sector to interact with biobanks, and there is often very little focus in their remit for pharmacogenetic investigation. The pharmaceutical industry is actively engaged in establishing specimen repositories with a particular emphasis on clinical (treatment) outcomes, and an environment that facilitates these efforts will be crucial to their success.

² *A Review of UK Health Research Funding* Sir David Cooksey December 2006

³ *Innovation Nation* Department for Innovation, Universities and Skills March 2008

14 The relative technical requirements and ethical procedures involved in the collection and use samples also need to be clarified to enable commercial users to gain access on the same terms as academic users. The UK Biobank is one of the more flexible institutions in this regard and we believe this is a real competitive advantage for the UK. We would also argue that genetic information should be treated with the same degree of care as any other medical information and should not be treated differently.

15 **Pricing & Reimbursement** There is significant uncertainty concerning the impact that using biomarkers will have on research and development and ultimately on the return on investment when a product is launched. Patient stratification clearly has the potential to limit the use of a new pharmaceutical to a smaller sub population of patients, and therefore has the potential to influence the commercial return.

16 However, it also means that the product will be more effective in this subgroup than in the wider population. In this situation, how can the value of a more targeted medicine be captured in the price? Sir David Cooksey's suggestion regarding conditional licensing for new products aligned to NHS priority areas offers a possible solution - but by definition it is restricted to certain therapeutic areas.

17 Roche believes it is our responsibility to identify the specific patient groups where our drugs are most efficacious. However, the current environment offers insufficient incentives to develop medicines for stratified patient groups. We believe a new model is required consisting of flexible pricing for personalised medicines and intellectual property protection and value based reimbursement for both targeted drugs and companion diagnostics. The traditional reimbursement mechanisms for diagnostics neither reflect their increasing R&D costs nor the value they deliver to healthcare - a situation that is likely to become even more acute as personalised medicine develops.

18 The National Institute for Health & Clinical Excellence (NICE) has been involved in assessing a large number of innovative new pharmaceuticals since it was established. As personalised healthcare develops, we believe NICE should adopt a cost per QALY "premium" for medicines that can be used in clearly defined sub-groups, which would allow for greater flexibility at the margins and enable treatments for metastatic disease to be more accessible to the patients who could benefit from them. Cost-per-QALY calculations should be used as tool to help inform the appraisal process, not a rule to determine appraisal decisions alone. The correct balance may not have been found in ensuring health service efficiency and promoting equity, a core value of the NHS, making the principle of transparency in decision making even more important. It is critical that clinical freedom is not compromised as new medicines are assessed and so negatively impact the patient experience.

19 The Pharmaceutical Price Regulation Scheme (PPRS), which is currently being reviewed, should also be considered in this context. It is worth noting that the UK is amongst the slowest in Europe for adopting new medicines, even after such medicines have been approved for use by NICE. We believe that any successor that is developed to replace the current system must be allowed to remain in place for sufficient period of time, to allow the industry to adjust to the changes and enable them to plan ahead in a more stable environment. Roche supports the recommendation of the OFT report and the concern that the current scheme fails to reflect the therapeutic value of the drugs that companies are supplying to the NHS.

20 **Existing Therapeutic Agents** The current environment also acts as a major disincentive to undertake further research into the existing pharmacopeia in order to stratify patient populations with regard to their eligibility for existing medicines in order to increase efficacy and reduce adverse reactions. There is an increasing body of knowledge available – some of it dating back well over thirty years – about the impact that variations in certain genes can have on drug metabolism.

21 A good example concerns the cytochrome P450 family, the most important class of drug metabolising enzymes. Despite the weight of evidence that links DME gene polymorphisms to variability in drug response, comparatively little has been translated into clinical practice – a point highlighted in the Royal Society’s report on personalised medicines published in 2005.⁴ However, there are no commercial incentives for the pharmaceutical industry to invest in stratifying target patient populations for medicines for which pricing has been fixed, or for those that are off patent where there is no or very little return on investment likely to be forthcoming.

22 A more flexible system of price setting in situations where stratification parameters allow for more targeted, more effective, but - as a result - lower volume prescriptions would be a strong incentive for the industry to continue post-marketing efforts in generating personalised healthcare data. Intellectual property protection for biomarker-based, targeted use of off-patent medicines may be another such incentive.

23 It is also important to note that there are inadequate mechanisms available for assessing the clinical and cost effectiveness of diagnostics used independently of therapeutics. NICE does not feel its current procedures allow it to assess this kind of technology effectively and the other methods available such as the NHS R&D Health Technology Assessment programme do not fulfil the same role. As a result, the health service is not consistent in the way that it uses new diagnostic technology and this can have an impact on both patient care and the use of resources.

24 This is particularly relevant in the case of personalised medicine. If a new biomarker is identified that can provide information on the way in which individual patients are likely to respond to a therapeutic agent and help to identify the patient group that is likely to have the best response, there are no clearly established procedures currently in place to assess the potential benefits for patient care or the use of health service resources unless it is linked to the launch of a new therapeutic.

25 In keeping with our previous recommendation, we suggest that new models need to be considered to ensure that our expanding knowledge of the human genome is used to its full potential with existing as well as new products. There is enormous opportunity to improve the use of existing medicines in order to benefit patients and the wider healthcare system. One option would be to increase the research and development funding made available from public or charitable sponsorship for this purpose given the public interest involved, or the greater use of public private partnerships.

26 **Public Private Partnerships** There is increasing support from both the public and private sectors for greater collaboration in the research and development pathway. This point was made very clearly in *A Review of UK Health Research Funding*, which called for “a renewed partnership with industry and the wider research community to meet current and future health challenges.” This point has also been made frequently by a wide range of stakeholders at a series of events attended and organised by Roche in recent years, including the Academy of Medical Sciences forum on optimising stratified medicines research and development held in 2007.⁵ We strongly support this view as a means for addressing many of the issues raised above. An existing example of this concept in action is the Innovative Medicines Initiative.

⁴ *Personalised Medicine: hopes and realities* Royal Society September 2005

⁵ *Optimising Stratified Medicines R&D: addressing scientific and economic issues* Academy of Medical Science Forum 2007

The Innovative Medicines Initiative (IMI)

- The IMI is a unique initiative which has been developed jointly by the European Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA) to fund European public private partnerships in biomedical research.
- The IMI will have a total budget of 2 billion euros, half of which has been made available by the European Commission under the auspices of the 7th Framework Programme for Research (2007-13) and half of which comes from the pharmaceutical industry as in-kind contributions, for example by providing research facilities, staff and materials.
- The research grants will be awarded to public sector organisations and small and medium sized enterprises. The first calls for proposals are being invited this year, and it is hoped that the first projects will begin in the second half of 2008.
- Further details can be found at www.imi-europe.org

The UK – Untapped Potential

27 We believe the UK is uniquely well placed to capitalise on the development of genomic medicine for a number of key reasons:

28 The structure of the National Health Service means that it is exceptionally well placed to collect and analyse data on public health and health outcomes. The NHS National Programme for IT can play a key role in helping deliver this promise - the patient informatics databases being developed have enormous potential for collecting and analysing data which can be used to assess the clinical effectiveness of different treatments.

29 Until they are fully operational, the General Practice Research Database (GPRD) offers some alternative information. It is the world's largest computerised database of anonymised longitudinal medical records from primary care and is currently collecting data from over 3.4 million active patients. However, it is very limited in its ability to support the development of personalised healthcare in this context.

30 The National Institute for Health & Clinical Excellence (NICE) has developed considerable strengths in evaluation which can be used to support the development and delivery of targeted medicines and companion diagnostics.

31 *A Review of UK Health Research Funding* has set out a framework which has the potential to encourage greater collaboration and support greater innovation, particularly in the areas of translational medicine and encouraging a climate in favour of research in the NHS.

32 However, it is essential that the points in the previous section are addressed if this competitive advantage is to be used to its full potential.

Conclusion

33 Our submission has focused on the areas where we believe our experience as the world's biggest biotech company has given us particular insight, and trust our comments are a useful contribution to the Science & Technology Committee's inquiry. We would be very pleased to clarify any of the points made or to provide further information on request.