

House of Lords Science and Technology Committee Call for evidence: Genomic medicine

(Specific sections responded to are identified in each paragraph)

1. Policy Framework, 2nd bullet point. Who provides scientific advice on policy development? Who monitors and anticipates potential scientific developments and their relevance to future policy? How effective are these mechanisms? In this rapidly evolving field a major source of scientific advice is the expert scientists, either individually or collectively through expert committees brought together for the purpose. For example a selected scientific advisory panel supported the Human Genetics Commission as it deliberated with officials of the Department of Health (DH) with respect to the 2003 White Paper on the future provision of genetic services in the UK. Expert genetic scientists however can disagree on the significance of particular data even at the fundamental level with respect to its technical validity and certainty; even before addressing the overlay of clinical relevance. Tools for testing characteristics of scientific data are at the heart of the UK's National Measurement System (NMS) which is funded by DIUS. The accuracy of genetic data and technology is the focus of a number of programmes researched by LGC as the designated National Measurement Institute for Chemistry and Biochemistry. The NMS anticipates and aims to address the measurement issues associated with the scientific developments within genetics and genetic technologies, working with industry and academics as appropriate. The output of this work informs industry and Government. The efforts would benefit from a stronger link between the NMS and DH to give a more effective underpinning of applied genetics in the UK.

2. Policy Framework, 3rd bullet point. Does the existing regulatory framework provide for optimal development and translation of new technologies? Are there any regulatory gaps? There are two distinct and somewhat parallel frameworks for the conversion of genetic knowledge into applied genetics tests. Within the NHS the Regional Genetic Laboratories have associated into the UK Genetic Testing Network (UKGTN). The UKGTN has procedures in place to assess and approve new clinically applied genetic tests. The UKGTN laboratories sell their services within an internal NHS market, particularly reflecting the particular expertise and local clinical focus of each laboratory. The transfer of these services is deemed to fall outside of the EU Directive concerning InVitro Diagnostics (98/79/EC). Conversely the development and provision of genetic test services from the private sector are subject to little legislation excepting this EU Directive. The UKGTN emphasizes the clinical relevance of genetic tests, whilst the IVDD emphasizes the technical performance. Clearly there is a lack of a unified approach to the provision of genetic services within the UK. However the related clinical and industrial community has recognised the value of collaborating in developing a standards framework for genetic testing. The NHS Genetics Reference laboratories (part of

the UKGTN) and LGC are associated with a number of international initiatives developing best practice guidelines in support of genetic testing standardisation.

3. Research & Scientific Development ,1st bullet point. What is the state of the science? What new developments are there? What is the rate of change?

Genetics is simplistically viewed as the understanding of a personal blueprint that nature converts into a biological endpoint, such that a single genetic variation directly relates to a clinical or medical condition for the individual. However there is increasing awareness that this simple linear relationship does not hold in practice. Much of the human genome is now thought to consist of varying levels of gene duplication. Further the conversion of the DNA message via the intermediate RNA into protein is now known to be subject to numerous control mechanisms. Additionally the multiplicities of protein forms that can derive from a single gene are difficult to predict. For example, array-based technologies have the potential to probe all the key biochemical variables known to underpin a particular clinical condition. However the rate of understanding of such variation as it relates to the relevance of a genomic information is severely hampered by limited research funding. Fundamental research is particularly required to understand the true diversity at the genomic product i.e. protein (or proteomic) level.

The rate of technological change is extremely rapid. For instance, new DNA sequencing technologies are now capable of sequencing the whole human genome in six weeks and the costs are falling dramatically.

4. Research & Scientific Development, 2nd bullet. Who is taking the lead in the consideration and co-ordination of research and the development of new technologies?

Within the NHS the new National Institute for Health Research (NIHR) with its central commissioning facility has control over research funding. Thus the NIHR will take a pivotal oversight of research projects funded by the NHS including those involving genomic medicine. Additionally DIUS is supporting collaborative research through the Technology Strategy Programme. The recent Health Technologies call aims to bring together academic, clinical and industrial consortia to develop technological innovation including point of care tests and microarray applications. From a UK plc perspective, as well as to maximise healthcare impact, it is clearly beneficial if technological innovation can be aided at a fundamental level e.g. promoting best practice in the use of genetic micro-array applications. In this respect work funded by the National Measurement System is looking to co-ordinate the interests of the stakeholder business community, and research programmes are designed to address underpinning analytical processes.

5. Research & Scientific Development, 6th bullet point. What is the role of industry? How much cross-sector collaboration takes place? The extent and nature of genetic research collaborations between individual pharmaceutical,

diagnostic, clinical and academic teams can be expected to be extensive but are not obviously collated or co-ordinated by an over-arching body. The UK National Measurement System places great emphasis on collaboration and dissemination within the industry stakeholder communities (e.g. pharmaceutical, diagnostics), The National Measurement System devises research programmes, including genetic methodology and technologies, to reflect shared interests. For example, improvements in measurement accuracy of DNA sequence information at very low copy conditions, such as in single cell situations, will support cell-based array technologies for drug discovery as well as early stage, non-invasive diagnostic procedures at or near the bedside.

6. Data & Interpretation, 2nd bullet point. Who should provide the framework for optimal evaluation of data and translational opportunities? What policy and funding mechanisms are in place for recognising and utilising potential opportunities? The question implies that one body should be designated with the responsibility to oversee the evaluation of data and the translation of such research into practical application. This may be an unnecessary simplification with oversight being fit for purpose e.g. the driving of a new model of car on the road needs the distinctly different assessments of the technology robustness as well as the skill of the driver to use the new technology. In this respect the fundamental need to ensure that genetic data is valid and accurately assessed is distinctly different to the assessment of the relevant mode of clinical application. If the data is incorrect or its uncertainty not understood then the subsequent translational opportunities could be wasted money and time. The National Measurement System and its Institutes may be the appropriate organisation to take a more prominent role in this underpinning evaluation.

7. Translation, 1st bullet point. What opportunities are there for diagnostics, therapeutics and prognostics now and in the future? There is no doubt that eventually genetic understanding must translate into better care procedures with opportunities arising for diagnostics, therapeutics and prognostics. However at this juncture current research is revealing the increasing complexity of interactions between many genes and their proteins etc. It may be that opportunities for simple diagnostics (e.g. one gene variation being solely causative of one disorder or adverse reaction) will have some specific but limited applications (e.g. in pharmacogenetics). Over the next 5-10 years, basing clinical decisions on variations in multiple genes or their expression patterns will require thorough metrological underpinning as well as critical appraisal on a case-by-case basis.

8. Translation, 3rd bullet point. Given the pace of technological advance how future-proof is healthcare investment in this area? This is a very relevant observation. It may be important to seek and support incremental improvement in the application of genetic know-how whilst still recognising the

limitations caused. For instance it has been discovered that certain genetic variations greatly increase the risk of severe adverse reaction for patients to the leading treatment for AIDS, but that same knowledge does not provide an equally effective replacement treatment for such individuals. It is to be hoped that future research can redress such an imbalance but application of the current knowledge is clearly relevant and beneficial if still incomplete. The criteria of new genomic medicine being 'fit for purpose' and advocating small advances should be welcomed rather than awaiting ultimate understanding and complex solutions.

9. Translation, 5th bullet point. How meaningful are genetic tests which use genomic variation data? What progress has been made in the regulation of such tests? Genetic tests are only as good as the validity of the genomic variation data they are based on. It is to be expected that many respondents to this question will emphasise the importance of assessing the clinical utility of such information. Whilst not disagreeing with this perspective it is essential to first ensure that the actual biomolecular data that is the basis of subsequent clinical evaluation is robust to start with. For instance the pressure to achieve DNA sequence data as economically as possible may be reducing accuracy of data resulting in potential missing, or misleading associations of genetic variation with the endpoint under study. Only the use of appropriate controls and standards can highlight such errors. Greater awareness of genetic technical quality matters is essential in the subsequent clinical trials assessment.