

Submission to the House of Lords Science and Technology Committee's Subcommittee on Genomic Medicine, 23 April 2008

*By individual*

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The ALSPAC laboratory with its robot-assisted facility for banking immortalised cell lines and DNA processing/handling expertise is responsible for the genetic resource of the **British 1958 Birth Cohort** ([www.b58cgene.sgul.ac.uk](http://www.b58cgene.sgul.ac.uk)). Having helped set up the cell-line backed, national DNA control series for case control studies based on the B58BC, I became one of the principle investigators of the **Wellcome Trust Case Control Consortium** (WTCCC)

As a clinical geneticist (heading up genetics at Great Ormond Street Hospital and the Institute of Child Health from 1979-1998) I have witnessed the development of genetic testing services for individually rare Mendelian and other high-risk inherited disorders through to the recent contemplation of genetic susceptibility testing for common multifactorial disorders.

As Consultant Adviser in Genetics to the Chief Medical Officer, Department of Health (1989-1998) and Chair of Progress Educational Trust, I have gained some experience on policy development. As a member of the Advisory Committee on Genetic Testing, I chaired the ACGT Sub-committee on 'Over the Counter Genetic Testing' that published the first *Code of Practice and Guidance on Human Genetic Testing Service Offered Direct to the Public*, in September 1997.

Below I respond to just those questions where I have direct experience *and* feel some issues need to be addressed. I am happy to give oral evidence if that would be helpful. I am happy to provide references in support of some of the points I make.

## **1. Policy Framework**

### **1.1** *Who is in charge of setting and reviewing policy in this area?*

Increasingly – by default – the Wellcome Trust (WT) is having a disproportionate influence on policy and yet is answerable to just a few governors. With its huge financial resources the Wellcome Trust has become the major lead on research in genomic medicine (see below) and this has led to the WT trying to dictate policy in a number of areas. A good example has been on the issue of wide access to data generated by WT funded projects, which naively, in my opinion, attempted to just apply what worked for the human genome project without appreciating-

- a) how much more complex it is when linking genetic data with phenotypic measures / outcomes from ongoing cohort studies and
- b) what impact the policy would have on those investigators running the cohorts.

**1.2** There is an attempt by the MRC, ESRC and WT to devise an overarching governance policy for all cohort studies. This one-fits-all approach is flawed in my view and may be at odds with the established policy of the study principal investigators seeking ethical approval and assuming the responsibility for sticking to the approved protocol. This move by the funders has created uncertainty and in the meanwhile, for example, the oversight of and management of access to the British 1958 birth cohort has been floundering over the last year.

**1.3** *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?*

It is not clear to me that a system exists for balanced, independent scientific advice on policy development. At present big projects are launched, the direction and detailed designs of which are determined by the (most assertive) scientists involved. What happens may or may not become 'the model' of how it should be done.

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

As you can gather from the above, the system is not optimal. Regulatory gaps currently exist in part because of the 18-month delay in the WT (+MRC & ESRC) coming up with *their* proposal for overarching governance - that should then, in my opinion, be assessed by your sub-committee or by the Human Genetics Commission or in some other independent way before being imposed by these funders.

**1.5** *In what way is science and clinical policy decision-making informed by social, ethical and legal considerations?*

This is through local or national research ethics committees and specific project related committees such as the ALSPAC law and ethics committee. There are big challenges ahead, for example when to switch from undisclosed genotyping in basic epidemiological research to disclosing the genotype to the participants in clinical/ public health studies.

## **2. Research and Scientific Development**

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

The state of knowledge about specific genetic effects and epigenetic influences (the capture of developmental experience through programming gene expression patterns) on common disease risk is very rudimentary indeed. New concepts and entirely new genome-related mechanisms concerning gene-environment interactions (including transgenerational effects) are likely to be discovered. The rate of development of (epi)genome analysis techniques is very fast as is what can be done with living cells

in terms of re-programming in the laboratory. However, there are some ‘knowable futures’ that must be kept in mind. Whatever the future discoveries in genomics and epigenetic responses, their impact on public health and an assessment of disease prevention strategies will always need longitudinal cohort health data, physiological measurement, environmental exposures data and suitable biological samples including immortalised cells. These cohorts require huge commitment by both the investigators and participants over decades and maintaining motivation is crucial for the future of research in genomic medicine. Undermine this and you undermine the future of biomedical research. Whilst the WTCCC was timely, case-control designs have significant limitations and need to be complemented by other approaches.

## **2.2** *Who is taking the lead in the consideration and co-ordination of research and the development of new technologies?*

The lead in research is taken, in affect, by the scientists and the funders of research. Despite peer-review by grant awarding panels, my impression is that much of the *strategic* advice taken by the WT, for example, comes from senior research fellows funded by the WT. The emergence and final nature of the WTCCC is an example. The WTCCC, with the Wellcome Trust’s name nailed to the mast, has become something of a flagship. In the grand scale of things its contribution whilst important is likely to be modest because of design limitations. There is a risk that it will be seen as ‘the model’ and distort future research planning.

Industry is driving most of the new technologies in genomics.

## **3. Data Use and Interpretation**

### **3.1** *Is other medical information recorded in a suitable format to allow optimal interpretation of genomic data? How should genomic data be brought together with other health information?*

Genomic analysis *per se* without linkage to phenotypic data (health measures etc) does not get you very far in genomic medicine research – it just discovers the nature and scale of genetic variation within the sample analysed. There is also a problem with diagnostic medical labels (acknowledged by the later question ‘*What impact will genomic information have on the classification of disease? How will it affect disease aetiology and diagnostic labels?*’). Much of the current disease classification is rather arbitrary and may not map well onto human biology. The great challenge is to develop research resources that can link genomic data with intermediate metabolic phenotypes and cellular responses to specific challenges.

### **3.2** *What are the implications of the generation and storage of genome data on personal data security and privacy, and on its potential use or abuse in employment and insurance? How should these be addressed?*

There are concerns that the rush to link phenotypic outcomes and genotypes at the level of the individual, plus the pressure to make data as widely accessible as possible, could lead to inadvertent disclosure of a participant’s genotype. The public release of a ‘phenome scan’ with aggregated data that shows the relationship between a genotype and a physiological outcome is a safe and valuable way forward (for meta

analysis for example). The British 1958 birth cohort genetics website developed by Prof David Strachan provides a good example ([www.b58cgene.sgul.ac.uk](http://www.b58cgene.sgul.ac.uk)).