Report on the Workshop on Human Biological Sample Collections 5 November 1999, The Wellcome Trust, London

The Governors of the Wellcome Trust decided in June 1997 to fund a programme of research into the social, ethical, and public policy implications of advances in biomedicine, under the title The Biomedical Ethics Programme. This is a relatively new area for the Trust, its response to the growing recognition over recent years that advances in biomedical science raise questions of ethics and of social impact which require careful examination and in some cases suitable regulatory supervision.

Research grants for this programme are funded in responsive mode, open to UK-based researchers with expertise in social, ethics and policy research. It is up to the research community to identify research themes. In addition to responsive mode funding, the Trust has recently called for proposals on two specified topics: the collection of human biomedical samples for DNA and other analysis; and pharmacogenetics. To encourage work on these themes, a workshop was organised on each so that interested researchers could familiarise themselves with the scientific developments, and identify areas of social, ethics and public policy research which need to be done. The workshops were not intended to debate issues, but rather to try to identify research questions. Researchers, it is hoped, will be stimulated to submit good project grant proposals to the programme. Ultimately, the results of research and analysis might feed into public policy-making.

This paper reports the results of the workshop on human biological sample collections which was held on 5 November 1999 at the Wellcome Trust in London.

The Trust commissioned a background paper on this topic from Dr Paul Martin of the Genetics and Society Unit, University of Nottingham, and Ms Jane Kaye, University of Oxford. Professor Tom Meade of the MRC Epidemiology and Medical Care Unit, Wolfson Institute of Preventive Medicine, London was invited to speak. Professor Meade chaired the MRC and Wellcome Trust Expert Working Group on UK population collection.

The workshop attracted much more interest than anticipated. Some 40 delegates attended, including clinicians and researchers from a range of disciplines including genetics, law, social science, philosophy. Chatham House Rules allowed delegates to speak as freely as possible about recent scientific and legal developments.

Legal and regulatory matters are central to any discussion of biological sample collections, and this was true at the workshop. A result was that the workshop produced policy pointers (as well as themes for further social, ethics and policy research) even though this was not the main purpose of the meeting.

Much of the recent international discussion of the issues raised by the use of biological sample collections has been stimulated by developments in Iceland, where a proposal for an electronic database containing detailed information from the entire population's medical records has been championed by the biotechnology company deCODE Genetics. This has aroused wide concerns about the potential abuse of human genetic research. Comparison

between developments in the UK and those in Iceland produced the surprising conclusion that Iceland appears to be superior to the UK in many respects.

This paper is divided into three main components: Scientific context; Policy points; Themes for social, ethical, legal and public policy research

Scientific context

Specific scientific issues and questions which were highlighted in the workshop. Those identified in this report complement the exposition outlined in the Martin and Kaye background paper, which were also discussed at the workshop but which will not be repeated here.

Funding for genetic epidemiological research over the next few years in the UK is likely to be around £25 million. The MRC and Wellcome Trust formed an expert working group to address the question of how to get the best science for the money. The working group reviewed existing population studies and considered how knowledge of gene-environment interactions may enhance prediction and preventive treatment for common diseases of adult life such as cardiovascular disease and cancers. The number of people needed for such studies is around 500,000 individuals. A new, large prospective UK population cohort to be co-ordinated by the MRC and the Wellcome Trust in conjunction with the NHS is currently under discussion. Personal medical information from the NHS records will need to be linked to the samples.

Important scientific aspects of these developments to bear in mind are:

- Nothing is settled about the science, which is at its earliest stage.
- A UK population collection would need to have a very large number of samples due to the heterogeneity of the population.
- Only 6 or 7 out of all UK centres doing DNA research can cope with DNA processing and research on half a million people.
- There is interest in studying genotype-phenotype correlations by looking at socio-economic factors including behaviour ("lifestyle") and ethnicity.
- The ESRC Millennium Cohort could provide a resource for studying some infectious diseases of childhood and the relationship between genotype and phenotype for health factors such as cholesterol. (In the Comprehensive Spending Review, the ESRC was allocated £2.2million dedicated to conducting a millennium cohort study, to collect lifetime data on those born in the year 2000 across a range of areas covering England, Northern Ireland, Scotland and Wales. A consultation exercise with the academic and user communities on the form and content of the study is underway).

In response, one delegate asked if the working group had considering "joined up" studies of already existing collections. Others pointed out that biomedical interest in social outcomes and genotype-phenotype correlation raises questions about the demarcation between scientific and social agendas in regard to "genetics and intelligence" and behaviour.

Policy Points

The scientific community recognises several ethical, legal and regulatory issues, mainly on:

- Unanticipated use of stored material for analysis and the issue of implied consent for long-term use of samples
- Confidentiality with respect to personal medical information
- Ownership and control of samples and information
- The demarcation between biomedical and social outcomes particularly with the use of birth cohort collections.

These issues are clearly central to any policy discussion, but there are other ways of responding to the social and ethical impact of genomics research which both inform these issues and widen them. A discussion of these follows.

Reciprocal altruism

Before discussing the "technical" aspects of consent and confidentiality, there must be a prior consideration of why people donate biological samples. People make *social* judgements when they give their consent to donation of biological samples for research. People make judgements about the uses of the research and the professionals they deal with. Much has been made of the "gift relationship"[1] and "reciprocal altruism" as models for understanding why people have been willing to donate blood and organs for medical use, but it is not clear that these are workable or the best models in the current climate. Use of samples for biomedical research is somewhat different to donating blood or organs for therapeutic use. In addition, commercial exploitation of genes and other biological material are changing the social context of donation.

Social perspectives thus wish to take account of issues of public trust, the relationship between public and private research, and public and professional access to biomedical research.

It became clear that a feature of biomedical genomics research which needs to be borne in mind is that it is as much if not more about *informatics* and use of genetic and biomedical *information* as it is about access to and use of material *samples*.

Consent and unanticipated use of stored material

The general view in the UK is that personal information in epidemiological studies should be anonymous, and if the research does not harm the individual, and if a research ethics committee has given approval, then additional consent is not required. Autonomy is said to be upheld by "opting out" provisions at earlier stages. The Medical Research Council's interim ethical guidelines on "Collections of human tissue and biological samples for use in research" confirm this approach as an accepted and necessary medical practice.

[1] Richard M Titmuss, *The Gift Relationship: from human blood to social policy*, first published 1970 by Allen and Unwin; republished with new chapters edited by Ann Oakley and John Ashton, 1997, LSE books

However, this view is being challenged as the terms of scientific and medical research change. In a recent High Court judgement[2] *R v Dept of Health ex parte Source Informatics*, Judge Latham ruled that personal information collected for the purposes of health care cannot be given to a third party without the consent of the patients who are subject of the data even when that data is anonymised. The Latham ruling did not necessarily jeopardise the practice of sharing of confidential information between members of the medical profession. Nevertheless, it raised wide concern about its possible implications for medical use of samples.

Consent for future use of donated samples is likely to become more problematic and contestable, and there is a need to clarify the secondary use of existing samples.

Confidentiality

Protecting confidentiality for those about whom personal medical data is collected is a fundamental ethical and policy issue. There is great confusion about the three technical fixes that can be employed to enhance confidentiality: anonymity, encoding, and encrpyption. Many commentators appear to use the terms interchangeably, which causes confusion as each refers to a different procedure. Public discussion of the Icelandic databases has used the terminology of anonymisation but it is not clear how the separate databases can be linked to yield scientifically useful information if the data is truly anonymous rather than merely encoded.

There is a need to clarify the technical processes of anonymisation, encoding and encryption. This is a complex social issue, not merely a technical one. These processes raise questions about the social nature of confidence and its protection. What social values underlie anonymisation? What are the obligations of dataholders and who shall own and use personal information?

Public trust

Consent and confidentiality are not simply ends in themselves. They are a means to achieve a higher end. Confidentiality means showing respect for private life, respect for persons. If people do not trust the organisation and the people in it to show respect then they will not trust those organisations to do the anonymising properly. People need to agree with the goals of the research, the goals of the institutions involved, and they need to feel that they can place their trust in them. This could easily be called into question if people felt that their confidence was not being kept, or if they felt that medical information was being used for commercial gain. With closer links being forged between academia and industry in genomic research, the distinction between public and private good and the distinction between use of

[2] *R v Dept of Health ex parte Source Informatics*, Lloyds Law Report Medical. August 1999 264. Since the workshop was held, the High Court judgement was overturned on appeal to the Law Lords. Anonymous information can be used without consent by third parties for commercial gain. (The Department of Health has been adamant that the use of anonymous information should be limited to the public interest.)

patient information for commercial and medical or non-commercial reasons are being blurred.

A criticism of the Iceland situation is the potential dangers associated with commercial ownership of a national population database. Yet, the UK compares unfavourably with Iceland in other respects: in terms of democratic decision making and research governance. Changes to the Icelandic bill, the result of public pressure, created a stronger process of governance on how doctors and researchers treat information and samples than exists elsewhere in Europe, highlighting the UK's weaker institutional framework for governance.

Research governance

In Iceland, a national agency has been set up to ***do*** the coding and encryption independently of the interests of users. In the UK, medical and scientific practitioners are trusted to carrying out the anonymising of data in conformity with their own codes or practice. The UK Data Protection Registrar does not control individual records and information. The issue is not so much one of acceptable standards but of having an independent agency to enforce those standards either because the agency controls the records or because it has powers of inspection and enforcement.

There are no public records of existing collections in the UK. There is no place for the public to put its trust.

Compared to Iceland, public involvement in decision-making in the UK is at a low level of informed debate, and there has been no public consultation so far on these matters.

Research ethics committees are crucial to the decision making process in regards to use of biological samples and information, but their competency and quality is known to be uneven. Adequate support and training of research ethics committees is crucial if they are to do a good job.

Biomedical and social outcomes

Demarcation between biological and social outcomes, including the genetics of behaviour and intelligence, is a growing interest in human genomics research. The distinction between research into diseases and non-disease conditions is not always clear, and this interest raises ethical questions about the proper use of population collections, particularly birth cohort studies. Narrow biological models of intelligence and other characteristics and behaviour could dominate. There is a need to ensure that the realities of socio-economic factors are understood and are not subsumed into biochemical models.

The debate over Iceland showed that faulty assumptions of social reality underlie some of the claims of benefit of a population data bank. Iceland's genealogical records are enviable in their completeness. However, the assumption that these wholly reflect biological genetic reality is clearly mistaken. Genealogies for medical use are naturally implicated since the historical records may be "wrong" due to people's different understandings of biological relatedness and kinship, and multiplicity of family forms.

Professional biomedical understanding of a concept may differ from that of other members of the public. “Genetic relationship” is one such example.

Public and professional awareness

The social world is more complex than biochemical reality. Careful ethnographic and socio-historical analyses can demonstrate precisely what happens in the complex “social reality”. Nevertheless, narrow biological models of intelligence and other characteristics and behaviour could dominate. There is a need to ensure that the realities of socio-economic factors are understood and are not subsumed into biochemical models. Awareness of these issues needs to be raised among biomedical professionals as well as the public at large.

If high-quality and relevant social and ethics research on the questions which arise from these policy points is to be done, researchers need access to sites where biomedical research is being done

In summary, the main policy points drawn from the workshop discussion are:

- Secondary use of existing samples, and the requirement for consent for future unanticipated use of such samples, needs to be clarified.
- The different processes of anonymistation, encoding and encryption need to be clarified.
- Independent institutional and administrative procedures need to be constructed to demonstrate the trustworthiness of the organisations doing the collections.
- Openness and public involvement are crucial.
- Support for training of research ethics committees is needed.
- Awareness of social realities as distinct from biochemical models needs to be raised among biomedical professionals and policy makers who are understandably focused on the technical biomedical aspects of issues.
- Differences in professional and “lay” knowledge, understanding and uses of language need to be understood by scientific policy makers.
- Social, ethics and public policy researchers need access to sites where biomedical research is being done to address some of the questions arising from the scientific research. Technical people need to be involved.

Themes for social, ethical, legal and policy research

Research themes on the social, ethical, legal and public policy aspects of sample collections include questions on consent, confidentiality, public participation, and social outcome, but also questions on commodification of the human body and personal information tied to it. Research on these areas should help inform what is permissible in different contexts, and regulation.

A fundamental issue is why people donate biological samples for research.

- How is donation of samples for research, as opposed to donation for immediate medical use, conceptualised? What model should be encouraged? The gift relationship and concepts of abandonment and reciprocal altruism need to be revisited in the present context where commercialisation is an issue.

- What are the implications of the distinction between the use of patient information for commercial, medical, and non-commercial uses? What is public opinion on these uses?

- What do people want and need to know before they give consent? How do cultural variations change the answers?

- Comparative work on different national, regional attitudes and values will help.

How should confidentiality be protected, and what are the social values underlying it?

- What is the quality of confidentiality?

- What kind of information requires confidentiality?

- What is public opinion on the distinctions between the use of patient information for commercial, medical and non-commercial uses?

- How have attitudes changed about this? What cultural variation exists?

- Who owns information of the sort kept and generated in sample collections, and who should have access. What safeguards are needed to ensure beneficial use as well as protection of individuals?

Is the human body a form of property?

- How is property in the body conceived in jurisprudence? How do concepts of human dignity bear on this question? How do legal frameworks and cultural and social values compare between different countries? Legal research, including the anthropology and sociology of law, will help inform these questions.

- How are moral arguments over commodification of body parts and of information settled? These questions are becoming more urgent in regards to sample collections. More ethnographic accounts and socio-historical analysis are needed which illuminate the various locations where decisions are made. Anthropological and feminist research perspectives on the commodification of nature and problems of seeing the body as object are relevant.

- Should the body be commodified?

- How do attitudes toward the human body and toward marketing of bodies and samples differ? Is there a difference between how science sees the body and how the body is experienced? How are bodies conceived in policy making?

- If people are more than objects to be studied, what does this mean for biological research?

Research into genotype-phenotype relationships raise a set of political questions which require examination on

- Struggles over different reading of science, as exemplified by the scientific perspectives of the Green parties
- The use of birth cohorts and interest in sociological themes
- Multiplicity of scientific and social understandings of genealogy, kinship relationships in a multicultural society
- Nationalism and political uses of population information

Are biochemical models on causes of behavioural characteristics setting the social agenda about behaviour, intelligence? If so, how? What are the real effects on attitudes to things such as reproductive decision making?

How do social and scientific ideas of genetic relationship and genealogy differ, and how are they similar? Work needs to be done on different understanding of concepts and language. There seems to be a gap in key terms, for example, in the meaning of a donated sample as a gift. How do concepts of genetics and patenting travel through population?

What do members of research ethic committee want to know and need to know? The members themselves and prospective members need to be asked.

Professionals have identified the major ethical and policy issues, but what does the public think the issues are?

Conclusion

The workshop on human biological sample collections aimed to provide a forum to identify research questions. It was successful in this regard, but it also, importantly, identified pointers to policy.

Many of the themes and points were raised at the pharmacogenetics workshop which was held the week before. This should not be surprising since long-term research using stored biological sample are relevant to much genomics research.

The two workshops demonstrated that the topics chosen are not only important issues in themselves, but that they can, as was hoped, act as exemplars of social and ethics research on the new genetics. Delegates took the opportunity to became aware of the science. In turn they identified ethical and social realities tied to the scientific developments which policy making needs to take account of, and the questions they raise.

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