Information Paper

Governance and Benefit Sharing of Biobanks of Genomic Materials

1. Introduction

"Biobanks" are emerging infrastructures for the deposition and management of human body tissue or samples and the related data. The emerging state of this sector provides unique opportunities for the ethical governance and capacity building. This needs to bring together lessons from the international state of the art in science, ethics and administration with insights about the special requirements within the regions involved, such as in China. There is hope that an internationally and interdisciplinarily integrated system for regulating biobanks can be developed that that can contribute to the health of populations both in China and Europe, and in other countries.

Ever since the Human Genome Project and Celera Genomics Corporation announced the completion of the first working draft of the human genome in June 2000, expectations have been high that novel ways to prevent, diagnose, treat and cure disease would emerge from 21st century genomic research. The sequencing of the human genome was a milestone in itself, with China contributing 1% of the total sequencing work as the only developing country involved. Since that time, a number of developments have led to a 'step change' in genetic research:

- Sequencing technology has improved drastically – making it faster, cheaper and more accurate.
- Genome-wide association studies (GWAS) have been made possible, relocating genetic inquiry into disease origins from a focus on single genes to a study of the impact of genomic variation across the entire genome.
- A consensus has emerged that 'single gene' approaches are not appropriate for the study of common complex diseases, (such as cancer, diabetes or heart disease), which are most likely to arise from the interaction of variations in multiple genes with environmental factors.
- The ethical, legal, social and cultural issues involved in the science itself and in the ways science is organised, are being taken more seriously, as intrinsic challenges arising from international and interdisciplinary research.

Biobanks have become a vital resource for geneticists as they seek to translate basic knowledge into preventive, diagnostic and therapeutic applications. At the same time, these developments have also raised a number of ethical questions around issues of privacy, informed consent, traceability and feedback of information to participating research subjects, all of which are given a particular salience in the context of international collaboration.

In this leaflet, key findings arising from the work of BIONET are summarised, with a particular emphasis on the ways in which the ethical challenges identified relate to international scientific collaborations.

2. Collecting samples and sharing benefits

Biobanks have been compiled and maintained for many years as archives of human biological materials, used for the purposes of teaching, diagnosis, therapy or research. They have differed in terms of the population included (e.g. family, cohort, population or disease-based), the nature and size of the biological specimens (e.g. blood, tissue, urine), context of the collection, form of storage, underlying scientific purpose (e.g. forensics, therapy, research), funding (public, commercial, both), etc. Within 21st century genomics research, a key focus has been on the development of biobanks that are not just collections of biological samples (genetic data), but also of related medical records, health data, lifestyle information and sometimes also genealogical information for whole populations. The commercial aspects of this work, implied in the very term "bank", have also become clear with the reappraisal of many types of human tissue as potentially powerful resource for the generation of knowledge, health and wealth rather than disposable "waste".

A biobank can be defined as a biospecimen resource: a collection of human biological specimens and associated data for research purposes, including not only the physical entity where the collection is stored, but also all relevant processes and policies involved, including governance.

This definition highlights the different components of biobanks:

- the biospecimens themselves
- associated data (usually stored in the form of databases)
- physical storage site for biospecimens and data
- processes and policies governing their administration, use and maintenance

The development of such institutions as biobanks raise questions of data collection: how biological samples are collected from voluntary donors; what donors are consenting to when providing a sample and medical information; what forms of safeguards should be in place to protect their privacy; as well as the extent to which any benefits arising from biobank research can be fed back to research participants.

In recent years, many have regarded issues of informed consent and privacy as the key ethical challenges surrounding biobank research. However, informed consent, especially when presented in its established forms, is not seen as sufficient to ensure ethical research and may not be the most important ethical issue in biobank research. Nonetheless, properly achieved informed consent can be recognised as a mark of the necessary minimum respect in communicative practice between researchers and research participants in the collection of biological materials.

Other important ethical issues concern: 1) public's trust and support for biobank research; 2) what kinds of risks participants face; and 3) how feedback of information, and other benefits to research participants, should be conceptualised, communicated and organised.

Public trust: With so much public investment going into biobank research, it seems prudent for the scientists involved to make their case for gaining and deserving public trust and support for this research and also to ensure that these are actually scientifically worthy projects. This is particularly the case with biobanks, as their nature and significance may not be widely understood, and the implications of donation of samples and of current and future medical information may not be clear to potential participants.

There are examples of trust building measures at work in European and Chinese institutions, which warrant attention. Such measures include the use of local national minority languages to communicate with potential research participants with the support of local minority doctors, village teachers, cadres and sometimes also local religious leaders. The context in which research subject recruitment and consenting procedures took place is important, as it can either render informed consent disempowering – a mere ritual - or empowering – giving the participants a real voice and insight into the work of the biobank and the meaning and implications of their participation. Thus, informed consent in relation to such novel scientific developments as biobanks is possible but requires adequate investment in research and capacity building, especially in international collaborations.

Risks: The focus of ethical governance should go beyond the risks related to giving a blood sample. Longer term risks of having DNA samples analysed and stored on file should be taken into account, as well as risks arising from the information and knowledge arising out of the research. There are also some complex ethical questions regarding feedback of information to participants, and these also relate to possibilities of stigmatisation, discrimination or 'loss of face' if certain details became public (despite assurances of privacy). Here lies a huge task for the ethical governance of biobanks and the related sampling, as there appears to be a close link between the perceived credibility of the institution in relation to such questions of privacy, confidentiality and potential stigma, and the readiness among potential donors to trust the researchers and to donate their samples.

The questions of trust and risk also matters if there is any possibility that medical biobanks might become used in forensic investigations. Informed consent for participants usually makes it clear that biological samples would only be used for research purposes. If such material is used for non-research purposes, as in forensics, this might have serious impact on the acceptance of biobanks and on the practicality of international collaborations. It is clear, therefore, that appropriate protocols and

institutional designs must be put in place to regulate the relation between biomedical research and forensic banks in an effective and transparent manner.

Benefits: Informed consent procedures should always make explicit the arrangements for feedback and for potential benefits of participation. Some examples may clarify this issue. In one study in China, those agreeing to participate confirmed, in signing the informed consent forms, that they were aware that "you will not benefit directly from participating in this study. However, your participation will benefit the general population by increasing knowledge related to genome diversity and its significance in diseases". In another example, from a biobank research project from southern France, participants were informed, that, "the participant could not obtain individual results concerning his genome". This raises open questions about benefits and feedback – what should research participants rightfully and reasonably expect to get out of participating? This is not merely a question of addressing immediate health benefits, but also of the benefits of the basic knowledge to be generated through biobank research in the medium term. Evidence suggests that many donors participate in biobank research from altruistic motives, but they nonetheless would expect a governance system that regulates the institution of the biobank fairly.

As far as individual health benefits are concerned, technical instruments could play a role in reducing the problems of data protection while making best use of personal health information. For example, some have suggested that biobanks could communicate individual clinically relevant information to research participants, through an anonymous and automated process. However, since donated biological samples are often screened against a number of standard analytic tests, and as most findings suggest probabilities of disease susceptibility rather than immediate medical concerns, this leaves open the question of the kinds of results that are sufficiently clinically meaningful to be communicated to patients.

One solution that has been proposed is to organise biobanks in the spirit of a "cooperative economic community", with an obligation to make public and accessible all knowledge

arising from research carried out using the data and samples from a specific biobank. This could be done in the form of an annual report or a website which was updated regularly. This would mean that any research participant who was interested in receiving this information could find it easily, albeit not specifically addressing the individual case. Such practice would be culturally supported, for example, in the UK as it relates to the well-established Freedom of Information Act, but not in all other countries. Here lies another significant area for cross-cultural diversities. Not at least, it should be made clear that any governance model comes along with specific legal issues and potential disputes that need to be anticipated when designing the structure of the enterprise.

Although BIONET considered this issue specifically in the context of EU-CN relations, it can be argued in general that 'benefit sharing' and 'informed consent' belong among the 'missing essentials' for a desirable regulatory and conceptual governance framework.

3. Processing of genomic materials for biobanking and genomic research

It is certain that the number of samples (and associated health-related data) procured for storage in biobanks will continue to increase in the coming years as large sample sizes are required for the high power multivariate analyses necessary to capture genetic variation. The BIONET discussed a cautionary approach to the promises of benefits, but this should not overlook the genuine grounds for optimism about the results of such research. However, to date, achievements have been made in the areas of building institutions, infrastructures and cooperation agendas, with hopes for fundamental scientific discoveries in the future, rather than health benefits for the near future.

Once samples and data have been collected and stored, the task of analysis begins. Storing requires continued data protection and sample quality assurance measures. With genomic research, a first step is to sequence the collected biological samples, because it is the correlations between diseases, lifestyle factors and variations in DNA sequences that are the target of genomic studies. Previously single gene studies of disease were the norm, but it has become clear that these are not helpful in understanding the genomic

variations linked to common complex diseases. A number of individual genomes have also been sequenced. Yet while these examples might act as good 'reference genomes' they lack explanatory power when it comes to disease. However, given advances in gene sequencing and the very significant cost reductions of such work, in the near future it may become possible to combine the full genome sequences from hundreds of thousands of human subjects with their medical data, making it possible to carry out far more complex calculations.

The falling cost and increasing speed of sequencing technology also creates considerable market-potential. This raises a number of ethical and governance questions. A market for personal genomics is emerging where individuals send in a DNA sample (in the form of a cheek swab or saliva sample) and then have their genome sequenced and interpreted by experts who then provide them with information on their relative levels of susceptibility to particular diseases. This are raises numerous regulatory difficulties, both nationally and internationally. Many suggest that the bulk of the information provided by such services is clinically irrelevant, and that users of such services may be unaware of this, or overestimate the individual clinical relevance of such data. As these issues are being debated at the very early stages of such developments, this may allow ethicists, clinicians, and genomic researchers, together with those who are developing these commercial services, jointly to work towards sound and perhaps innovative ethical governance models.

This raises questions as to whether the knowledge made possible by new sequencing technologies would ever really be translatable into therapeutic or diagnostic possibilities. Will there ever be health benefits from such genomic research, or, will benefits rather in the form of basic knowledge? Other scientific developments, such as in epigenetics, indicate that one genotype can lead to multiple outcomes depending on life history and that there is a complex system of interaction at stake. This renders many traditional ways of thinking about genetics, and much folk wisdom, obsolete or even misleading. Sober-minded planning of biobanks and the accompanying research will need to take these implications into account, and deal realistically with the likely benefits of the research.

4. Emerging issues for Sino-European collaborations

A key theme in the discussions about Sino-European collaborations is, how to ensure good quality data as well as how to ensure harmonisation of data recording practices and standards. This latter objective is important since larger and larger populations are required to ensure sufficient statistical power. Moreover, comparable quality standards and an effective infrastructure are crucial for cross-institutional and international collaborations. In Europe, there is a research infrastructure for Biobanking and Biomolecular Resources emerging within which some of the many challenges of harmonising biobank research in a European context can help anticipate the forthcoming Sino-European situation. At this point in time, Europe is seeking to overcome the problems arising from multiple isolated and fragmented small and middle-sized institutions, building an integrated system of "research infrastructures" to connect up these different endeavours. In China, the path seems to be towards the development of large centralised biobanks. A number of questions arise regarding China and Sino-European collaborations in this area:

- How should evidence-based standards and harmonized processes be ensured?
- What incentives were there to contribute to European scale biobank infrastructures?
- What should be the access rules?
- How to deal with the heterogeneous European ethical and legal landscape – with a diversity of national regulatory regimes - in collaborations with China?
- How to assess data protection in biobanking
- How to generate sustainable funding, especially for the related capacity building, social scientific research and ethical governance?

Harmonisation and standardisation could be approached using an 'adapter model' as an appropriate way of thinking . Standardisation in the sense of uniformity of data collection methods, of data recording methods as well as of data storage methods on a European

scale would be an impractical and unnecessary aspiration. It is more useful to agree on technical standards which samples and data can be combined pragmatically and according to the particular project in question. Notably, this refers to dealing with technical and legal standards rather than with standards of science and ethics, where matters of translation-research between languages, cultures and other relevant systems should be considered. The latter question is still open and requires careful elaboration.

The challenges of harmonisation and data sharing are especially relevant for international collaborations between Europe and China, where many of the described technical conditions do not exist. How should such collaborations be monitored and how should access to samples and data be managed if they were shared across borders and continents?

China and Europe, with their internal regional diversities, share the challenges from the new generation of 'secondary biobanks'. At the same time, biobanks present us with an opportunity to think ahead, on how ethical governance of biobanks and biobanking-related activities should be organised, within and between the regions.

China, and in particular the Pearl River Delta, can be seen as an emerging hub in the area of biobanks and the related sciences. However, the region still faces considerable challenges. Projects that combine scientific and technological growth with ELSI-related capacity building are underdeveloped. Much work remains to be done on the co-ordination of such developments, and the appropriate forms of good governance both within the region and in collaborations between the region and Europe. The complex administrative situation between special zones such as Hong Kong, Shenzhen and Shanghai (according to the slogan, "one country, two systems") require particular efforts of coordination when it comes to overarching funding or governance. There is a need for concrete steps from Europe in this regard, as future collaborations are likely to increase.

A major focus in this regards is the possibility of an integrated approach to capacity and capability building. The continued education and training of staff in ELSI matters and

the qualification of IRB members could be complimented by measures for a better understanding about the differences within and between the regions of China and Europe, to add human skills and good governance mechanisms to technological, economic and scientific capability.

Europe and China share the task to find appropriate ways to develop legal cultures and social cultures of trust that can sustain good science in healthy societies. This must grow from dialogic interaction and the ability to understand and overcome potential conflicts. These may result from “hard” factors such as systemic differences, but also from “soft” factors, such as different cultures, with their differing ethical languages, world-views and moral principles. Although we are still some way from answering these challenges, the problem itself has been identified and calls for action.

The topic of the ethical governance of biobanks is not only significant and challenging in itself, but it thus presents the opportunity to stimulate fresh approaches to the ways in which we discuss and organise bioethical governance in transnational contexts.