Scientific Workshop "Future perspectives, benefits and bottlenecks of Neuro-biobanks"

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SIXTH FRAMEWORK PROGRAMME

Contents

The Workshop was introduced by a welcome word from the NEURON Coordinator Dr. Marlies Dorlöchter in order to explain the ERANET Neuron Scheme and the scope of the Workshop.

This Workshop is part of Work Package 2
STRATEGIC PREPARATION OF PROGRAMME COORDINATION AND PROGRAMME OPENING ACTIVITIES,
Work Package Leader is FNR.
Powerpoint presentations are available upon request from the Work Package Leader.

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Introduction

The ERA-Net NEURON (see also http://www.neuron-eranet.eu) is a project that is funded under the ERA-Net scheme in FP6 by the European Commission for 4 years (2007-2010). The aim of the "Network of European Funding for Neuroscience Research" (NEURON) project is to link 15 national research funding programs and funding activities in the field of disease-related neurosciences. In NEURON as well as in other ERA-Nets, national funding organizations of different European member states exchange information about their work and develop strategies for cooperation. Coordinated by Germany, fifteen ministries and funding agencies are currently members of the Network: FWF[1] (Austria), AKA[2] (Finland), INSERM[3] (France), CNRS[4] (France), ANR[5] (France), PT-DLR/BMBF[6] (Germany), CSO-MOH[7] (Israel), MOH[8] (Italy), FNR[9] (Luxemburg), NCBIR[10] (Poland), MEdR[11] (Romania), MEC[12] (Spain), FCSAI/ISCIII[13] (Spain), SRC[14] (Sweden), MRC[15] (UK).

Many of the world's most devastating diseases are caused by complex interactions between genes, environment and lifestyle. Advances in genomics and proteomics have begun to enable us understanding the molecular mechanisms of disease, and thus bring closer the promise of a more personalized approach to the diagnosis and treatment of disease.
However, to accelerate this paradigm of personalized medicine, researchers and clinicians not only need access to molecular information but also the corresponding phenotypic information often contained in medical records or collected in the course of clinical trials.

Biomaterial banks (Biobanks)

Biobanks are institutions that collect, process and store samples of human body substances or materials, amend these samples by personal or disease or treatment related medical data of patients and provide these material samples and data for research purposes. A biobank is thus (in most cases) not a stand-alone research project, but an important long-term oriented research tool for biomedical research. Europe has well-organized biobanks and health databases of high quality. Such biobanks – sometimes also called biorepositories or tissue banks – provide both types of critical information, and have been identified as important translational bridge between research and clinical practice to accelerate the development of more personalized medicine. They are considered a major resource to enable research into the interaction between genes, environment, lifestyle and disease, and – in close cooperation between scientists and clinicians – to support the implementation of the knowledge into clinical practice through innovative diagnostics, therapeutics and preventive treatment strategies.

Neuro-biobanks

Neuro-biobanks are a subset of the general biobank concept and understanding and precise delineations are often not a simple matter. Particularly in the fields of disease-related neurosciences, well characterized human tissues are an essential resource for research into the aetiology, diagnosis and treatment of neurological and psychiatric disease. Tissue banks of neuropathological material, e.g. brain samples or cerebro-spinal fluid (CSF) have made an essential contribution to progress in these fields. This is evidenced by scientific breakthroughs such as the discovery of amyloid deposition in Alzheimer's disease, Lewy bodies in Parkinson's disease, variant Creutzfeldt-Jakob Disease (vCJD) and the role of glutamate in Schizophrenia.

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[1] Austrian Science Fund
[2] Academy of Finland
[3] National Institute for Health and Medical Research
[4] French National Centre for Scientific Research
[5] L'Agence Nationale de la Recherche
[6] Project Management Agency in the German Aerospace Centre (PT-DLR) for the Federal Ministry of Education and Research (BMBF)
[7] Chief Scientist Office-Ministry of Health
[8] Ministry of Health
[9] National Research Fund
[10] Nardowe Centrum Badani I Rozwoju
[11] Ministry of Education and Research
[12] Ministry of Education and Science
[13] Institute of Health Carlos III, Fund for Health Research
[14] Swedish Research Council
[15] Medical Research Council

For both funding organizations as well as scientific research there are however a number of areas that require particular attention.

Improved co-ordination or networking of biobanks would allow more efficient use of infrastructure, enable sharing of best practice and help avoid any unnecessary duplication of effort or resource.
Common database systems could greatly aid researchers in designing their experiments and acquiring the necessary samples for their research. Harmonized database architecture and grid computing technology are key features to significantly support integrative IT-infrastructure.
Indispensable for such networking on international level is the harmonization of ethical and legal regulations.

There are a number of recent national and EU-wide directed developments that impact directly on this field. Examples are the Human Tissue Act (HTA) and the *European Strategy Forum on Research Infrastructures (ESFRI)* Biobanking and Biomolecular Resources Research Infrastructure (BBMRI).

In addition, particularly for research into neurological and mental diseases the lack of suitable control (non-diseased) brain material and respective donors has been a longstanding problem. Brain banks aspire to support research in CNS disorders but they face the challenge of declining autopsy rates in all countries. Due to such declines and changes in the societal attitudes to death and despite successful brain donor programs as e.g. for dementing and neurodegenerative conditions this type of tissue and information thereof is still most needed for medical research.
Furthermore, among disease entities neurological disease cases with defined neuropathology tend to be relatively well represented in specific collections whilst there is a scarcity of material available for research into mental health disorders.

In view of the opportunities and limitations highlighted above, within NEURON a specific working group (PT-DLR/BMBF, Germany, FNR, Luxemburg, MRC, UK) was established to give consideration to the development, provision and bottlenecks of such major resources/services. The first step in this process was to convene a workshop for adequate information and discussion of the key themes (e.g. legislation, infrastructure, quality assurance, networking). The agenda and delegate list can be found at Annexes 1 and 2 of this report.
This report lays out the main issues and opinions expressed on the day and to serve as a base for further discussion and more detailed strategy development.

The workshop

The theme of the meeting was 'Future perspectives, benefits and bottlenecks of Neuro-biobanks' and focused upon both, current legal and ethical regulations and guidelines and recent national and international activities to develop the field.
Specifically, the aims of the workshop were to:

- bring together the funding organizations within NEURON and members of the material and specifically brain banking community to discuss issues of strategic importance
- sharing of information and best practice
- identify strengths, weaknesses, gaps and opportunities
- inform NEURON in what will be required in developing strategies to help foster an environment conducive to European wide integrated neuropathological research
- facilitate networking in this area to ensure optimal support for brain banking

Following a number of presentations key issues were further discussed in a round table discussion.

Conclusions of the round table discussion

Legislation
Currently very few specific legal regulations pertaining to biobanks exist. Where such regulations do exist, they vary greatly between different countries, and a solid experience of legal practice is widely lacking in the field of biobanking. Recent legislation from the Human Tissue Authority had been received positively in the UK and begun to make some impact on the field through licensing of banks and developing best practice.
Ethical approval is desirable, but not an absolute requirement in some EC countries, for all aspects of brain bank activities, including removal, storage and dispersal of samples to users. In some other EC countries, ethical approval is required only for research projects and not for tissue banking *per se*.
Ethical guidelines and their implementation (e. g. informed consent) vary between individual EC countries, and may even prohibit exchange of material, but all brain banks in EC (BrainNetEurope) subscribe to the overarching guidelines encoded in documents such as the Helsinki declaration of the World Medical Association[16] and the Opinion on Ethical Aspects of Human Tissue Banking by the European Group on Ethics in Science and New Technologies in respect of Human Tissue Banking[17].

Quality assurance
Since high quality clinical and biochemical data to accompany samples are understood as essential for the values of bio- and brain banks these should now be considered as routine. Data security and privacy are crucial issues associated with biobanking implementing the principles of coding/anonymisation so that neither data nor samples can be traced to individual persons. Services like extraction of DNA/RNA and protein are not the primary focus of brain banks but may add value.

Networking
Given the huge challenges of networking, including but not limited to legislation, ethics, physical and electronic bank systems, management, logistics etc. there are some promising examples of both national and international networking although some EC countries have import and export regulations concerning the movement of human tissue across borders.

Funding
Since bio- and brainbanks are long term oriented facilities funding/resourcing of such entities in view of maintenance and sustainability appears a major challenge. Some EC countries operate with institutional funding whilst others provide grant or project related funding, this may include full economic costing. Cost recovery mechanisms for e.g. provision of material are not commonly implemented. It should however be noticed that a break-even mode with cost recovery only mechanisms can realistically not be reached.

[16] WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI, 2004, Ethical Principles for Medical Research Involving Human Subjects
[17] Council_of_Europe Opinion of the European Group on Ethics in Science and New Technologies to the European Commission. Ethical Aspects of Human Tissue Banking, 21 July 1998

Contributions by invited speakers

Legislation and Ethics

- Regulations and guidelines around biobanking' (p. 9)
  Juergen Goebel as member of the Working Group on Biobanks of the Telematics Platform of Medical Research Networks summarized current EU legislation and general legal issues relating to biobanks. The paucity of legal regulations specifically pertaining to biobanks, international differences in terms of legal regulations or different handling of the provisions of international law as for e.g. data protection together with a relative lack of practical legal experience in the field of biobanking were considered as major bottlenecks for international cooperation and interoperability.

- Biobanking harmonisation – Ethical and legal challenges (p.14)
  Andrea Cook from the UK Biobank Ethics and Governance Council reviewed establishment, aims and tasks of the EGC among which the formulation and monitoring of a respective framework for the UK biobank addressed the need to engender confidence in the public for this project. With the goal of harmonization the ethical and legal challenges were summarized as those relating to biobanking *per se*, those relating to the practical issue of trying to harmonising and find common language and those relating to ensuring adequate consent and security measures to maximise sample and data-sharing while protecting the interests of participants.

- The Human Tissue Act - Implementation and impact on research (p.18)
  James Ironside from the University of Edinburgh gave from his dual perspective as Director of a UK Brain bank and Deputy Chair of the Human Tissue Authority (HTA) an overview of the HTA and its impact on research. He explained the background to the Act that was designed to be supportive of research. The HTA which had been established as a regulatory body developed flexible codes of practice for researchers to follow. The implementation of licensing standards for research tissue banks had been an important step forward and provides a clear, consistent and proportionate regulatory system.

- BMB-EUCOOP - A Legal Basis of an EU-wide Biobank-Cooperation (p.20)
  Thomas Pickard from the Competence Network Congential Heart Defects and as member of the Working Group on Biobanks of the Telematics Platform of Medical Research Networks introduced an ongoing project on collection and publication of recommendations and template text files covering e.g. informed consents, transfer agreements, conciliation agreements and contracts for international research projects in both German and English language.

Infrastructure

- BBMRI - European research infrastructure for biobanks and biomolecular resources (p. 22)
  Kurt Zatloukal from the University of Graz gave an overview of the Biobanking and BioMolecular Resources Infrastructure (BBMRI) project. Following the European Strategy Forum on Research Infrastructures (ESFRI) 'roadmap' BBMRI, comprising 51 participants in 21 countries and 149 associated organisations intends to integrate biobanks in a pan-european research infrastructure.

Networking

- BrainNet Europe (p. 24)
  Hans Kretzschmar from the University of Munich reported about the EU funded 'Network of Excellence' BrainNet Europe (BNE). He addressed principles of brain bank management and drew on the experience of the 18 brain banks that make up the consortium, representing post-mortem practice in the constituent member states. For brain banks themselves, inclusion in a network fostered the sharing of protocols, development of best practice and quality control and assistance of individual brain banks to effectively manage the increasingly complex legal and ethical framework for brain banking.

- UK National network for DNA sample management (p.27)
  Martin Yuille from the University of Manchester described the history, structure and functioning of the UK DNA Banking Network (UDBN) project as part of a new initiative for human genome research and attempted to draw lessons from strengths and weaknesses of the project. Located at the Centre for Integrated Genomic Medical Research (CIGMR) the project aims at creating a community resource in post-genomic translational research.

1. Regulations and guidelines around biobanking

Professor Dr. Jürgen W. Goebel, Legal Practitioner, Bad Homburg v. d. H., Germany
Working Group on Biobanks of the Telematics Platform of Medical Research Networks (TMF e.V.), Germany

1. Introduction

Biobanks are an absolute requirement for modern, particularly biomolecular medical research. However, serious concerns have been raised not only in Germany, but also at a European level, about the legal basis and framework of such endeavours. Indeed, many of the scientific institutions, which are currently in the process of establishing or using biobanks may be operating in a legal "grey zone", because there are currently very few specific legal regulations pertaining to such collections. Where such regulations do exist, they vary greatly between different countries, and a solid experience of legal practice is widely lacking in the field of biobanking. Furthermore, a comprehensive assessment of the legal standing of a biobank would severely strain the logistical and financial resources of most interested institutions. Although this is particularly true for international collaborations, the practical need for legal advice to biobanks currently seems to be more pressing for regional recruitment and research activities within individual countries. Therefore, in 2004, the Working Group "Biobanks" of the German Telematics Platform for Medical Research Networks (TMF e.V.) initiated a project to construct a generalized legal basis for the establishment and operation of biobanks in Germany. In a second TMF project, currently ongoing and alluded to in more detail at a later stage, the specific problems arising for German biobanks from their collaboration with foreign (mainly EU-based) institutions are being dealt with. Both these activities have aimed at clarifying the actual status of, and the need for, regulations and guidelines around biobanking, which I will briefly describe and discuss in my presentation.

2. Main Problems and International Regulations

When asking for the most important legal issues related to the implementation and operation of biobanks, the same questions and problem arise at both a national and an international level. These can be summarised as follows:
(1) Who is the legal owner of the biomaterials kept by a biobank?
Who has the right to use these materials, and in which way?
(2) Which data protection rules govern the handling of biomaterials and the associated data?
(3) Do biomaterials represent commercial goods, or should they be subject to a ban on commercialisation? To what extent are the donors legally entitled to sharing the benefits of the scientific research carried out with their materials?
(4) How should the fact that biomaterials are carriers of personality rights be taken into account, and which legal entitlements of the donors emerge from this fact?
(5) To what extent are biomaterials and/or the scientific results derived from them subject to intellectual property rights, or even patentable?
(6) Which consequences regarding the handling of biomaterials arise from medical professional regulations or from the penal law, particularly in terms of protecting the biomaterials and data against confiscation by the police?
(7) Are there any supranational or international regulations that govern the use of biomaterials? Are these regulations legally binding (hard law/ soft law)?
(8) Are there any "Alternative Dispute Resolution Models (ADR)" for resolving legal confrontations over the use of biomaterials?

These and similar questions arise at both a national and an international level, particularly when it comes to collaborations between biobanks and/or research institutions in different countries. In order to ensure the legally sound handling of biomaterials by all participants, these questions have to be answered in timely fashion.

3. The German Experience

The Telematics Platform of Medical Research Networks (TMF e.V.) has initiated two projects to identify currently existing regulations and guidelines for biobanking[18]. A detailed and comprehensive report of the results would be beyond the scope of this short presentation. Nevertheless, the main outcome can be summarised as follows:

(1) At an international level, several codifications exist of which some are legally binding whereas others only constitute soft law. Examples include

[18] Simon et al., (2007) A legal framework for biobanking: the German experience. *Europ. J. Hum. Gen.* 1-5

- The European Convention on Human Rights and Biomedicine (1997)
- The Additional Protocol (to the above) Concerning the Transplantation of Organs and Tissues of Human Origin (2006)
- The UNESCO Universal Declaration on the Human Genome and Human Rights (1999)
- The UNESCO Universal Declaration on Bioethics and Human Rights (2005)
- Directive 2004/23/EC of the European Parliament and of the Council on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells (2004)
- The WMA Declaration of Helsinki (in its 2004 version, addressing questions of research ethics)
- Various EU guidelines on data protection and the European Charter of Human Rights
- The WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS)
- Directive 98/44/EC of the European Parliament and of the Council on the legal protection of biotechnological inventions (1998)

(2) Similar issues as above also arise at the national level in Germany. However, in addition to existing legal regulations, some of which are implementations of the supranational directives listed above, several country-specific normative aspects have to be taken into account, including

- Germany's comprehensive codification of the national law (particular as regards property issues)
- the constitutional law (e.g., the protection of general personality rights)

- relevant court decisions (if available)
- recommendations and guidelines by national associations and ethics councils (e.g., "Stellungnahme des Nationalen Ethikrats zu Biobanken" in Germany)
- the practice of decision making by local ethics committees, universities or research institutions.

Owing to their multitude and diversity, the abovementioned national and international regulations may pose serious obstacles to the routine operation of biobanks. This situation calls for extensive harmonisation and standardisation efforts on the side of the legislative authorities. However, since the necessary improvements are likely to constitute a long and complicated process, SOPs and contractual agreements developed by the biobank community itself appear a more promising means to ease the current situation more efficiently.

4. Open Questions

Even if the majority of problems related to biobanking were to be solved at a national level, the many EU-wide or global collaborations of biobanks envisaged for the near future are likely to pose new and even more complicated legal challenges to the scientific community. Instead of being related to actual regulatory issues, the following problems are expected to become most important:

(1) How can the legal rights of donors and biobanks be enforced in different countries?
(2) How can appropriate contractual agreements help to secure fruitful and mutually beneficial scientific collaborations?
(3) How can the above problems be solved in collaborations involving countries of different jurisdiction, different ethical frameworks, or different law enforcement policies?

In the long run, it would be most helpful if the responsible institutions were to establish clear legal regulations for the handling of biomaterials, if and when these regulations become necessary. On the other hand, bureaucratic over-regulation may easily jeopardise the collaborative initiatives currently emerging in the field of biobanking, and should therefore be avoided. This requires a balanced view of the problems and perspectives of biobanking.

Telematics Platform of Medical Research Networks (TMF e.V.): www.tmf-ev.de

2. Biobanking harmonisation – Ethical and legal challenges

Andrea Cook OBE, UK Biobank Ethics and Governance Council

UK Biobank is a major national project funded primarily by the Wellcome Trust medical research charity and the UK's Medical Research Council. The project aims to set up a resource that will support a diverse range of health-related research and data intended to improve the prevention, diagnosis and treatment of health throughout society. It will recruit 500,000 people between the ages of 40-69 and their data and biological samples will be stored for use by researchers, both from the UK and internationally, to study the effects of genetics, lifestyle and environment on the onset of disease.

In providing valuable information for researchers, the project also raises key ethical, legal and governance issues. These are addressed in an Ethics and Governance Framework which describes the standards which UK Biobank will adhere to during the creation, maintenance and use of the resource. This is a public document which has been created to strengthen public trust and confidence in the project. An independent Ethics and Governance Council monitors UK Biobank's compliance with the Framework and provides constructive challenge and advice on the development of policies which raise ethical issues.

UK Biobank has gained much in knowledge and experience. Harmonisation with biobanking activities in other countries would encourage the sharing of data, identify and promote good practice and highlight the learning which has taken place. In doing so it must be sympathetic to the local environment in which a biobank is operating. There is no template which can be adopted by all biobanks, however areas which would lend themselves to harmonisation are potentially the method and taking of a sample; processing a sample; the questions asked of participants; the consent given by participants, the levels of protection for samples and data; and the conditions of access.

So how can we achieve harmonisation? Some countries, for example Iceland and Estonia, have adopted national biobanking specific legislation. Others have adopted various models for governance or issued their own guidelines. International collaboration can be limited as a result of the detail of these different approaches. Harmonisation through European legislation may therefore be the only comprehensive, coherent and consistent way of dealing with issues raised by biobanks. However in the case of European Directives where a 'margin of appreciation' is allowed according to the historical, cultural and social norms of the particular country, consistent implementation in the Member States is not guaranteed.

Harmonisation is being achieved through a number of established initiatives: firstly, the Public Population Project in Genomics (P3G) which aims to promote collaboration between researchers in the field of population genomics; secondly, the Promoting Harmonisation of Epidemiological Biobanks (PHOEBE) project which aims to establish a collective network to ensure the best use of population-based biobanks and longitudinal cohort studies in Europe; and thirdly, the Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) initiative which aims to co-ordinate, harmonise, standardise and integrate a number of individual resources into a European research infrastructure. The key to harmonisation is finding a common language in which to communicate where there is agreement on terminologies and their meaning, for example such terms as 'anonymised', 'coded' and even the term 'biobank'.

Harmonisation also brings ethical and legal challenges. It is important here to distinguish between the ethical and legal challenges which biobanks face and the ethical and legal challenges which arise because of the result of harmonisation and of maximising data and samples sharing. Biobanks in general need to consider issues such as consent, recruitment, the right to withdraw, access by third parties and data confidentiality. P3G aims to assist in this area by providing a generic participant information leaflet and consent form. However harmonisation also throws up new challenges in relation to the intended sharing of samples and data between biobanks. This can be illustrated by two areas where the Ethics and Governance Council has played a key role in advising UK Biobank – consent and confidentiality.

A biobank needs to acquire consent that informs participants of the broad array of research uses and users. This includes the fact that the biobank material may be accessed by users from other countries and those with commercial interests. Will consent provide sufficiently broad use of data and samples to facilitate harmonisation? This issue has been addressed by UK Biobank through the adoption of a 'broad consent' in which participants are asked to consent to their samples being used for 'health-related research purposes'. This approach is intimately linked with the participant's ability to withdraw from participation at any time, and with the provision of ongoing communication from the biobank about the use to which the resource is being put.

Research commissioned by the Ethics and Governance Council would suggest that there is a reluctance amongst some people for data and samples to be shared internationally, unless certain limits are in place. UK Biobank's participant information leaflet is explicit on this point to foster transparency and trust. Reluctance has also been expressed by some members of the public in relation to access to the resource by researchers with commercial links. It would be advisable as part of a thorough procedure of gaining consent from potential participants for them to be advised of the possibility of commercialisation of the research outcomes. If a participant expresses doubt over this aspect of the study, they should be advised not to take part.

Biobanks also need to assure each other that they can provide the same level of confidentiality of data and samples – including the security measures to protect participant privacy. If the standards are not appropriately harmonised this will undermine confidence in data sharing at a European level and within individual biobanks. This could be achieved by providing only reversibly anonymised data, by reducing the risk of identification of participants from released data sets through confidentiality agreements or by adopting international, auditable standards for data security.
The most significant steps towards harmonisation are being achieved by the co-ordinated actions of organisations and networks such as P3G, PHOEBE, BBMRI – and NEURON. These are addressing the challenges of harmonisation by sharing experiences and benefits, identifying challenges and bottlenecks and attempting to find a common language through which biobanking harmonisation can be promoted in the public interest.
Ethics and Governance Council: http://www.egcukbiobank.org.uk/

3. Human Tissue Act 2004: implementation and impact on research in UK

Professor Dr. James W. Ironside, University of Edinburgh, Edinburgh, UK

The Human Tissue Authority (HTA) was established as a publicly accountable regulatory authority responsible for the implementation of the Human Tissue Act 2004 in the United Kingdom. Subsequent legislation in Scotland (Human Tissue (Scotland) Act 2006) had many similarities in its scope to the Human Tissue Act but does not legislate on the use of tissue from the living individuals. The Human Tissue Authority is composed of over 30 full time staff (Executive) and around 17 members, with a majority of lay members. The strategic aim of the HTA is to create a regulatory system of removal, use and disposal of human tissue and organs that is clear, consistent and proportionate and in which professionals, patients, families and members of the public have confidence. The HTA regulates across six sectors: tissue for human application, research, post mortem, anatomy, public display and living donor transplants. The HTA has prepared Codes of Practice which help translate the legislation into a working framework; these Codes of Practice address the six broad sectors listed above. In England, Wales and Northern Ireland licences are required for activities in these sectors, including research. The Codes of Practice relevant for research are those for consent, removal, storage and disposal of human organs and tissue and post mortem examination. The Licensing Standards for Research Tissue Banks cover consent, governance and quality systems, facilities and equipment and disposal.

Organisations undertaking activity in these regulated fields apply for a licence initially by completing a compliance report online and this will be followed by an inspection according to the deemed risk of the organisation in terms of compliance with the Human Tissue Act. The licensing system is proposed to be as unburdensome as possible, supporting existing professional standards and allowing for further development of these standards. Licence fees are applicable and these are reviewed on a regular basis. At present in the UK, there are 219 licences for medical research, representing the second largest sector which is under the regulation of the HTA. In a recent survey of the regulated sectors it was found that the majority felt that the HTA and its implementation of the legislation had had a positive impact on their practices. The HTA commissioned a leading polling organisation to conduct general public, professional and opinion leader research in 2007 which indicated that stakeholders were positive about the HTA and had confidence in its activities. The HTA aims to ensure that implementation of the Human Tissue Act does not place unnecessary constraints on tissue based research in the UK, and will work closely with the regulated sector, funders and other stakeholders to monitor the situation closely.

Human Tissue Act: http://www.opsi.gov.uk/ACTS/acts2004/ukpga_20040030_en_1

4. BMB-EUCOOP - A Legal Basis of an EU-wide Biobank-Cooperation

Dr. Thomas Pickardt, Professor Dr. Jürgen W. Goebel, Working Group on Biobanks of the Telematics Platform of Medical Research Networks (TMF e.V.), Germany

The project BMB-EUCoop (Biomaterial Bank – EU wide Cooperation) is funded by the German Telematics Platform for Research Networks in Medicine (TMF, http://www.tmf-ev.de/site/EN/int/c_homepage.php). BMB-EUCoop was applied by the Competence Network for Congenital Heart Defects, that participates in a FP6 EU Project (Heart Failure and Cardiac Repair), where it provides DNA-samples from concerned German patients to research partners in Newcastle and Amsterdam. The aim of BMB-EUCoop is to clarify

- Up to what extent property rights, personality rights, privacy and self determination of the German donor are concerned or affected by foreign laws?
- Are property- and exploitation rights of the collaborating German scientists/institutions affected, when samples are transferred to research groups to other EU countries?
- How to implement the rights and ethical considerations of the German donor and the German research institution?

In an expert workshop a project consortium was established, consisting of lawyers with expertise in privacy, data protection, ethics, biobanking, and health care laws.

The consortium agreed that expert opinions are necessary to be prepared on

- Data privacy and protection
- Commercialisation and benefit sharing
- Property rights, legal right of use
- Personality rights
- Intellectual property rights
- Medical and health law
- Criminal law
- International legal frameworks
- Dispute settlement mechanisms (ADR)

In order to limit the complexity expert opinions will consider only four selected countries (UK, Netherlands, Austria, Switzerland).

In addition to the expert opinions the expected outcome of BMB-EUCoop are recommendations for research institutions, and specimen texts, covering informed consents, transfer agreements, conciliation agreements, contracts, in German and English language.
The project has started in July 2007, the final versions of expert opinions and specimen texts are expected at the end of May 2008.
Competence Network for Congenital Heart Defects: http://www.kompetenznetz-ahf.de
Telematics Platform of Medical Research Networks (TMF e.V.): www.tmf-ev.de

5. BBMRI - European research infrastructure for biobanks and biomolecular resources

Professor Dr. Kurt Zatloukal, Institute of Pathology, Medical University of Graz and coordinator of the BBMRI consortium

Human biological samples, such as blood, tissues or DNA including associated medical data, as well as biomolecular research tools are a key resource in unravelling genetic and environmental factors causing diseases and influence their outcome. Furthermore these resources are required for identification of new targets for therapy and may help to reduce attrition in drug discovery and development.
The European roadmap for research infrastructures foresees a pan-European infrastructure to further develop these resources and to provide access to academia and industry. The planning of the construction of a pan-European Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) will occur within the FP7 capacities program. BBMRI will build on existing sample collections, resources, technologies, and expertise, which will be specifically complemented with innovative components. In particular, BBMRI will comprise
i) all major population-based and disease-oriented biobank formats,
ii) biomolecular resources, such as collections of antibodies and other affinity binders and a variety of molecular tools to decipher protein interactions and function,
iii) bio-computing and sample storage infrastructure.
All resources will be integrated into a pan-European distributed hub structure-like network, and will be properly embedded into European scientific, ethical, legal and societal frameworks. Specific tasks in the planning of BBMRI are the preparation of an inventory of existing resources, implementation of common standards and access rules, establishment of incentives for resource providers, and to develop solutions for international exchange of biological samples and data which properly consider the heterogeneity of pertinent national legislation and ethical principles.
The planning consortium comprises 51 participants including several ministries and funding organizations from 21 European Member States and more than 150 associated organizations. BBMRI should increase the scientific excellence and efficacy of European research in the biomedical sciences as well as expand and secure competitiveness of European research and industry in a global context.
BBMRI: www.biobanks.eu

6. BrainNet Europe

Professor Dr. Hans A. Kretzschmar, Centre for Neuropathology and Prion Research Ludwig-Maximilians-University Munich, Germany and coordinator of the BrainNet Europe

BrainNet Europe is a network of 18 established brain banks across Europe. Its main objective is collecting human high-quality post mortem brain tissue and fostering research in the cellular and molecular basis of neurological and mental disorders and diseases, gender aspects and the ageing process. Diseases of high frequency and outstanding medical and social importance such as Alzheimer's, Parkinson's, motorneuron disease, prion diseases, multiple sclerosis, schizophrenia and affective disorders are the focus of the network. In addition BNE contributes to research in rare diseases, a research branch, which can only be worked on successfully on an international European level.
The main objectives of BrainNet Europe are:

1. To exchange experiences in all matters of brain banking between all partners of the BNE consortium with focus on brain bank management, tissue sampling, tissue storage, quality control of the tissue, safety aspects, ethical and legal aspects to reach a common high level of excellence.
2. To harmonize neuropathological diagnostics.
3. To perform staining and diagnostic quality control exercises.
4. To determine the influence of pre- and post-mortem factors and tissue storage on tissue quality.
5. To determine the limits of the usability of human post-mortem tissue for sophisticated molecular techniques.
6. To develop gold standards for
   - safety provisions
   - histological and immunohistochemical stainings in neuropathological diagnostics
   - neuropathological diagnostic criteria
   - working with human brain tissue using modern technologies (such as laser capture microscopy, mass spectrometry, gene expression profiling etc.)
   - the usage of morphometric methods in neuropathological diagnostics
   - tissue storage and handling
   - the quality of human post mortem tissue samples
   - DNA, RNA and protein extraction
7. To contribute to the harmonization of the ethical codes of conduct of the participating countries.
8. To identify the legislation concerning import/export of frozen samples, autopsy, storage and use of frozen and fixed human tissue samples, data protection etc. in participating countries and to give impulses to uniform this legislation.
9. To foster the establishment of donor programs in participating countries.
10. To collect brain tissue of patients with psychiatric diseases.
11. To exchange cases with difficult or atypical neuropathology ("mystery cases") within the consortium to reach a consensus diagnosis and to improve diagnostic security.
12. To utilize the Internet for
    - internal exchange of information
    - spreading of excellence within the consortium
    - spreading of excellence outside the consortium
    - raising scientific awareness regarding human post mortem tissue samples
    - announcement of internal and external training sessions and courses
    - dissemination of information to the general public
    - running a common data base with highest possible IT security and protection of data.
13. To train researchers of the consortium and external researchers in the use and application of human nervous system tissues for research, by means of short term visits to other centres, training fellowships, and workshops.
14. To spread excellence beyond the network not only via the BNE website but also by
    - publishing in scientific journals,
    - presenting posters and giving lectures at national and international meetings in the field of neuroscience
    - using electronic media
15. To acquire and distribute well-characterized and high-quality tissues for basic research in neuroscience
16. To disseminate information to the public on the necessity of brain banking in general and on BNEII in particular, on research activities on human post-mortem tissues samples and their results, on donor programs.
17. To increase the awareness of standardized neuropathological and clinical diagnosis in neurology and psychiatry at a European level
18. To provide a basis and quality control system for RTD projects dealing with clinical or epidemiological aspects of neurological and psychiatric diseases
19. To integrate new members

20. To investigate important neural parameters in schizophrenia and the influence of pre- and post-mortem variables on these parameters.

All objectives will be reached by having established a rigorous decision making and management system resting on the members of the Network Coordination Committee and being assisted by a company for process organization as a partner of the consortium. A Joint Program of Activities was worked out dividing the work into 25 work packages.

The BNE consortium has published extensively on inter-rater reliability of neuropathologic diagnosis, quality control of tissue staining, the quality of post-mortem proteins, DNA and RNA, the management and ethics of brain banking. A shared database for available samples has been established. Continued public support will be necessary to pursue the work of BrainNet Europe in the future.
www.brainnet.net
BrainNet Europe: www.brainnet-europe.de

7. UK National network for DNA sample management

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UDBN was funded as a biobanking research infrastructure in 2003 by the UK Medical Research Council (MRC) in order to manage samples and data accrued by a dozen consortia of collectors who, with MRC support, were each focussing their collections from clinical centres on specific high-impact diseases.

The research infrastructure comprises a coordinating centre and DNA bank in the University of Manchester, a bank for peripheral blood lymphocytes (PBL) and EBV-transformed derivatives at the European Collection of Cell Cultures and Azura, a software consultancy. All three centres have ISO9001-2000 accreditation. This provides reassurance of quality management to collectors and delivers a standard of management that research laboratories usually do not - and arguably should not - attain.

UDBN currently manages over 30,000 samples (with ca 3 aliquots per sample). All DNA samples have a 'mirror' copy on a second site (at UK BioBank) to guard against catastrophic loss. UDBN has distributed over 30,000 aliquots on which over 6 billion genotype tests have been performed. Some 15,000 samples are stored as PBLs and 7,500 as cell lines. DNA sample management is largely automated using off-the-shelf robotic equipment and is supported by a Laboratory Management Information System. An online Collaboration Management System has been developed that enables *bona fide* researchers to initiate collaborations with UDBN collectors after inspection of summary datasets. The critical advantage of access via collaboration is that it corresponds to existing practices which are self-monitoring and which we know work well.

Essential activities linked to biobanking are undertaken:

- MRC has supported network cohesion through regular meetings of UDBN members (i.e. biobankers and collectors).
- Biobanking-specific research has been initiated via an observational study on comparative study of DNA concentration estimation involving academic and commercial laboratories in the UK, elsewhere in Europe and internationally.
- UDBN supports sample and data accrual as well as storage and distribution.
- UDBN undertakes policy development and policy implementation to regulate access to resource. This evolved in a pragmatic manner, with the support of an MRC-appointed Steering Committee, and has resulted in the establishment of "Fair Access" principles. These principles seek to specify arrangements that ensure fairness to patients and subjects, to collectors, to recipients of aliquots and data and to institutions.

Lessons to be drawn from UDBN's current experience include

- The need to fund shared biobanking infrastructure before accrual starts.
- The need for a Preparatory Phase in which the funder organises national workshops to explain vision for national infrastructure; establishes an international committee to promote the OECD vision of a global Biological Resources Centre network and to increase national cohesion; develops 'fair access' principles; promotes harmonisation and standardisation with other relevant funders.
- The funder should then issue a call for proposals to host the infrastructure and select applicants with experience in service provision; large-scale infrastructure management; web-based data networks; laboratory methods research; genetics, epidemiology, cell culture. Applications should be accepted from academic centres as well as public-private consortia.
- The Construction Phase should include policy development activities (e.g. on access policy); biobanking infrastructure development (hardware, software, replenishment, ISO, R&D); and initial operations (serving Pathfinder Projects, harmonising with genotypers, linking to a suitable common data centre).
- Pathfinder Projects have the aim to structure and troubleshoot Operational Phase. They should comprise new collections with novel conditions of grant (patient gifts sample to funder; patient gives informed general consent; use of data standards; the resource will be a "shared scientific resource" made available for collaboration after publication). Applicants should be advised that on-time completion of pathfinder deliverables will lead to a tailored call for genotyping etc. The genotyping will be undertaken following a design specified by the investigators but commissioned by the biobank.
- The normal running of the Operational Phase should be funded over the longer term (measured in decades) to meet a number of challenges (e.g. biobanking R&D is essential to comply with ISO 9001:2000; data management becomes increasingly complex; operational development to handle new sample types; management of legacy collections; development of international links; problems

of staff turnover and professional development; the need for an effective public engagement policy and activity; activities to develop the trust of the research community).

www.medicine.manchester.ac.uk/cigmr/
UK DNA Banking Network: www.dna-network.ac.uk