GeneLibrary Ireland

An all–Island Biomedical Research Infrastructure

Design Phase

Molecular Medicine Ireland in association with Queens University Belfast and University of Ulster

February 2009
The GeneLibrary Ireland Design Phase report was commissioned by the Health Research Board and Research and Development Office
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1.0 GeneLibrary Ireland - Introduction

1.1 Introduction
Biobanks of human biological material are increasingly appreciated as major assets in disease research. As biomedical research moves from the study of simple monogenetic disorders to the investigation of complex diseases, the availability of biological materials along with well-annotated clinical and medical information, lifestyle and environment factors will allow the investigation of the interplay of genetic factors that contribute to complex polygenic diseases (1). In order to study these complex and often subtle effects of genes on health and disease, there is a need to study information and samples from a large cohort of people (2-5). Typically, researchers will study patient groups with the same disease. The data generated are then compared with samples from a group of ‘normal / healthy’ people. By comparing information from each of these groups, we can discover more about the genes involved in disease.

1.2 Objectives of GeneLibrary Ireland
GeneLibrary Ireland will be a biomedical research infrastructure to enable and support the continued development of translational and genetic research on the island of Ireland. The biobank of 10,000 DNA and blood samples from volunteers on the island, together with key phenotypic information will serve as a control population to study the genetic determinants of common diseases that significantly impact patients in Ireland and Northern Ireland. These diseases include cardiovascular disease, cancer, diabetes, arthritis, respiratory disease and cognitive disorders along with key disease areas that are over represented in the population, such as coeliac disease, multiple sclerosis, cystic fibrosis and haemachromatosis. In addition, this biomedical resource will in itself provide a valuable cohort to study the genetic background of the population on the island of Ireland.

GeneLibrary Ireland, with DNA and biological samples donated by volunteers across the island of Ireland, together with information about their health, will provide ready access to samples for a variety of biomedical studies. The development of this important biological resource will facilitate high quality research into disease by providing a carefully characterised collection of DNA for control experiments. This will ensure that investigators can complete research investigations in a more timely and cost effective manner.

The creation of GeneLibrary Ireland will lead to sustained primary and secondary benefits to the people of Ireland through the;

- Establishment of a carefully phenotyped control population to facilitate disease research.
- Creation of a unique, all-island resource of genetic material and health information.
- Provision of a valuable datasets for additional research into the health and genetic make-up of the population.
- Avoidance of duplication of resources and effort.
- Creation of a vibrant all-island research partnership that connects the biomedical research community North and South.
- Provision of a standardised format for biobanking initiatives, which will support clinical research studies.
- Assistance to investigators in leveraging additional research funding.
- Provision of a unique opportunity for the island of Ireland to partner with international efforts in biobanking and genetics.
- Further embedding the genetics and biotechnology industries in Ireland.
- Complement recent exchequer investment in health research and research infrastructure.
1.3 Overview

Biomedical researchers need to study information and samples from large numbers of people, particularly in the investigation of the complex and sometimes subtle effects that genes can have on our health. Such information and samples are not easily obtained and collection often proves costly and time consuming. The primary aim of GeneLibrary Ireland is to establish a biomedical research infrastructure, which will provide a common resource of samples, which researchers can use to study the role that different genes play in disease and health. This will be a powerful and valuable resource for health research on the island of Ireland which, fuelled by the human genome project, will lead to discoveries about causes of disease, new diagnostic tests, new drugs and even new cures. This resource will help health researchers to achieve cost-effective results more rapidly and efficiently. Some diseases are more common in certain parts of Ireland and the genetic background of the Irish population varies. The all-island aspect of this project will allow researchers to investigate these effects and take account of them in their studies.

The proposed library will contain DNA and blood samples collected from 10,000 volunteers throughout the island of Ireland, the results of a detailed medical examination and phenotypic data on aspects of medical history, lifestyle and environment. This combination of samples and health information will make the archive extremely useful to researchers. GeneLibrary Ireland will serve as a large ‘control group’, providing essential health information on a cohort of the population as a whole. Scientists studying a particular disease will need to collect samples only from people with the disease that they will then be able to compare with samples from the library. In this way, the resource will be an important and enduring part of the health research infrastructure on the island of Ireland. Researchers in Ireland and Northern Ireland, and researchers elsewhere with whom reciprocal arrangements exist, will be free to access the facility, provided that: they submit their research plan to a Scientific Steering Committee for approval, bear the cost of any DNA analyses, and add their results back into the resource when they have published their research. In this way, the library and all its users will benefit from each study.

1.4 Strategic Importance

There is a concerted effort on the island to create a harmonised and world-class clinical research infrastructure that will allow Ireland and Northern Ireland to be competitive in the era of personalised medicine. This has been facilitated through the significant investment by both the Irish and UK Governments and the Wellcome Trust in the construction and implementation of major, world-class clinical research centres (CRCs) in Dublin, Belfast, Cork, Galway and Derry which will be networked via the Irish Clinical Research Infrastructure Network (ICRIN) in Ireland and the Northern Ireland Clinical Research Infrastructure Network (NICRIN) in Northern Ireland. A key element of these translational and clinical research initiatives is the opportunity presented to assemble and store collections of biological materials in a harmonised manner. These collections need to be assembled in a manner that allows them to be linked with other similar collections at an all-island level if increased sample size is required. GeneLibrary Ireland will not only provide the control bio-resource for these disease networks but will also provide a standardised framework for biobanking activities across the island and ensure harmonisation internationally.

Over the last number of years, researchers in Ireland and Northern Ireland have contributed to international research in identifying genes that play a key role in disease susceptibility and risk. Some of these genetic research studies include the identification of genes associated with the Irish schizophrenia population (6), the expression of an airway epithelial gene in the diagnostic evaluation of smokers with suspect lung cancer (7), the demonstration of a role for the DNA repair genes, XRCC3, XRCC4, XRCC5 in the aetiology of myeloma (8), the recognition of seven new genes associated with coeliac disease (9), the detection of mutations in the gene encoding filaggrin that cause ichthyosis vulgaris and predispose to eczema and secondary allergic
diseases (10) and the identification of a role for the gene NET1 in the development and progression of gastric cancer (11).

This research has been supported on the island by investment from the PRTLI through the Programme for Human Genomics, Science Foundation Ireland, the Health Research Board (HRB), the Research and Development (R&D) Office, the US National Institutes for Health and the Wellcome Trust. This investment has enabled the development of valuable bio-collections by researchers in major disease areas including coeliac disease, cardiovascular disease and neuropsychiatric disorders. While there is no figure available for the total investment that has been made for biobanking samples by the major funding agencies in Ireland and Northern Ireland, it is evident that significant funding has been committed over the years to individual investigators, which has enabled the establishment of valuable bio-collections in specific disease areas. These collections however may not contain large numbers of control samples. Furthermore these bio-resources are associated with the specific disease studies that have funded them and may not be stored longer-term. In contrast, GeneLibrary Ireland as an infrastructure to support research will make standardised bio-resources available to all academic and commercial research under defined rules of access.

A number of reports published in Ireland in recent times have identified that such a biomedical research infrastructure is needed to assist in the translation of biomedical research to clinical practice and inform the questions that researchers ask. The Advisory Council to Science, in its Report Towards Better Health: Achieving a step change in Health Research in Ireland (November 2006) recommended additional investment to address the infrastructural deficit in translational and clinical research, including the provision of biobanking and a gene library. In May 2007 Enterprise Ireland commissioned the CIRCA group to make recommendations on infrastructural and other initiatives that would improve the environment for the creation of economic activity from the expertise and research and technology development in the Irish healthcare system. Recommendations included clinical trial facilities, biobanks, stem cell production facilities, biomarker identification and validation. In addition, the Higher Education Authority and Forfás commissioned report entitled ‘Research Infrastructure in Ireland – Building for Tomorrow 2007’ recognised ‘genebanks and biobanks’ as a specific research infrastructure requirement for the instrument and medical devices industry in Ireland.

The establishment of GeneLibrary Ireland as a research infrastructure will not only provide a strong framework to support and foster large research studies to identify genetic associations with common diseases in Ireland and Northern Ireland but also allow researchers on the island to share this bio-resource internationally through participation in large, statistically powered studies.

1.5 The International Context

A number of European countries have established well-organised population-based, disease orientated and/or case-control bio-resources. These biobanks, include HUNT in Norway (12), the UK Biobank (13), the Estonian Population Biobank (14), Islandic deCode biobank (15) and Generation Scotland (16). There are over 123 large population-based cohorts registered in the Public Population Project in Genomics (P3G) Consortium study catalogue (17). Typically these biobanks contain data on health, environmental risk factors, nutrition, demographic, socioeconomic and lifestyle variables together with standardised bio-specimens from healthy and disease populations. While these bio-collections have tremendous value at a national level, the exchange of data and material across national legal frameworks has proved difficult due to variance in legislation and ethical issues in some countries and as a result, European biobanking activities have remained fragmented (18). There is no doubt that these currently established biobanks and biomolecular resources are a unique European strength but the ethical and legislative barriers to amalgamating these national bio-resources, which is required for statistically powered studies, has been a significant limiting factor.
If Europe is to realise the full research potential from human biobanks, there is a need for convergence, coordination and harmonisation of the biobanking and biomolecular resources infrastructure across Europe. In an effort to address this challenge, the European Commission, through Framework Programme 7 (FP7), has funded the preparatory phase of the Biobanking and Biomolecular Resources Infrastructure (BBMRI). BBMRI is being funded to establish a pan-European biobanking network through the coordination and harmonisation of the biomolecular resource infrastructure, including population-based cohorts, disease orientated cohorts, twin registries and clinical case/control studies. Networking and harmonisation of biobanking across Europe will increase the success of coordinated, large-scale biomarker discovery and validation, facilitate the identification of susceptibility genes, environment and lifestyle factors, help define aetiological pathways for multifactorial diseases and facilitate discovery of new drugs and therapies.

Molecular Medicine Ireland is actively participating in BBMRI to ensure that researchers in Ireland and Northern Ireland will have access to large international collections of bio-resources and technologies that could not possibly be achieved within Ireland and Northern Ireland alone. This will also facilitate involvement in the study of rare diseases for which we do not have sufficient bio-specimens at present. In addition, participation in BBMRI will lead to funding opportunities through subsequent European framework programmes and initiatives to which this island would not otherwise have access. These opportunities may include long-term sustainable funding for biobanking that are not currently available. As part of the implementation phase of BBMRI, a number of pilot projects will be required across Europe. GeneLibrary Ireland would serve as an ideal pilot project for such an initiative if established, since it will operate across the two jurisdictions on the island of Ireland.

The Irish Government, through the *Strategy for Science, Technology and Innovation 2006-2013*, highlighted that its strategic vision and commitment to develop Ireland as an internationally renowned centre for excellence in research can be achieved through ‘continued engagement with the EU institutions and appropriate international organisations in a co-ordinated and strategic manner with Irish input being promoted in all areas to ensure the optimum return for our research sector’. Ireland’s participation in BBMRI is key to achieving this vision for the translational research community at an all-island level. In addition, the Matrix Report on Technology Capability in Northern Ireland (undertaken by the Department of Enterprise Trade and Investment – DETI Northern Ireland Science & Industry Expert Panel) and Northern Ireland benchmarking exercise recently concluded that: “...the scientific capability and the innovation it brings is currently fragmented in Northern Ireland…and “it is the connectedness between these aspects that appears to be the most critical missing item”. GeneLibrary Ireland will aim to address this lack of “connectedness” and develop practical solutions to better “connect” the plurality of multidisciplinary expertise in Ireland and Northern Ireland. A resolution of the trans-jurisdictional issues will not only serve the objectives of GeneLibrary Ireland but will also serve as model of best practice for other initiatives.

**1.6 The Design Phase – Progress to Date**

In 2005, the HRB and R&D Office published the report of an expert group on the establishment of an all-island control biobank- *GeneLibrary Ireland: An essential new resource to underpin health research in Ireland 2005* (19). The expert group agreed that the establishment of a biobank of control material was both desirable and feasible and would add substantial value to the island’s biomedical research enterprise.

The establishment of GeneLibrary Ireland involves four distinct but linked phases incorporating the feasibility, design, implementation and operational phase as represented on Figure 1 overleaf. The feasibility phase has been completed as part of HRB and R&D Office report. In 2007 the HRB and the R&D Office issued a call to develop the design phase of GeneLibrary Ireland, which is the focus of this report. The design phase provides the elements necessary for
the implementation and operational phases of GeneLibrary Ireland. Indicative time-lines for each phase are included in Figure 1.

**Figure 1:** The four phases of GeneLibrary Ireland

Molecular Medicine Ireland, through the Irish Clinical Research Infrastructure Network (ICRIN), coordinated a successful application, led by Dr. Peter Doran, on behalf of MMI partner institutes Trinity College Dublin (TCD), Royal College of Surgeons in Ireland (RCSI), University College Dublin (UCD), National University of Ireland Galway (NUI Galway), University College Cork (UCC) and in association with Queens University Belfast (QUB) to undertake the design phase of establishing an all-island control biobank of volunteer samples and data. The University of Ulster (UU) has since joined this collaboration, ensuring that GeneLibrary Ireland is an all-island initiative involving the leading academic institutions in biomedical research and their associated hospitals. The key objective of this design phase was to develop an implementation plan for GeneLibrary Ireland, through convening expert Working Groups to examine and make recommendations on the construction of this all-island resource, in collaboration with an external Scientific Advisory Board as represented on Figure 2. This design phase was also informed by conducting site visits to similar biobanks, for example Generation Scotland and consultation with international biobanking experts.

**Figure 2:** The teams established to deliver the planning phase of GeneLibrary Ireland.
1.6.1 GeneLibrary Ireland Scientific Advisory Board

As part of the design phase a Scientific Advisory Board (SAB) comprising international experts in biobanking and genetics was established to provide a regular, independent and objective critique of the design and implementation plan for GeneLibrary Ireland. The SAB members are detailed in Table 1 below.

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<th>Name</th>
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<tr>
<td>Martin Yuille</td>
<td>Reader in Biological Resource Management Associate Coordinator for BBMRI,</td>
</tr>
<tr>
<td></td>
<td>Archive Director of UK DNA Banking Network, University of Manchester</td>
</tr>
<tr>
<td>Paul Burton</td>
<td>Professor of Genetic Epidemiology, Department of Health Sciences and</td>
</tr>
<tr>
<td></td>
<td>Department of Genetics, University of Leicester</td>
</tr>
<tr>
<td>Linda Morgan</td>
<td>Senior Lecturer/ Honorary Consultant in Clinical Chemistry University of Nottingham</td>
</tr>
<tr>
<td>David Clayton</td>
<td>Wellcome Trust/Juvenile Diabetes Trust Principal Research Fellow Cambridge University</td>
</tr>
<tr>
<td>Gerry Thomas</td>
<td>Director of Scientific Services, Wales Cancer Bank, Professor of Molecular Pathology,</td>
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<td></td>
<td>Imperial College London Hammersmith Hospital</td>
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<tr>
<td>Peter Donnelly</td>
<td>Professor of Statistical Science &amp; Fellow of St Anne’s College University of Oxford,</td>
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<td></td>
<td>Director Wellcome Trust Centre for Human Genetics</td>
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<tr>
<td>Lenna Peltonen</td>
<td>Head of Human Genetics, Wellcome Trust Sanger Institute UK</td>
</tr>
<tr>
<td>Kurt Zatloukal</td>
<td>Lead Coordinator, European Biobanking and Biomolecular Resources Research Infrastructure</td>
</tr>
<tr>
<td>Eero Vurio</td>
<td>Chancellor University of Turku, Finland and Coordinator, European Biobanking and</td>
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<td>Biomolecular Resources Research Infrastructure</td>
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Table 1: GeneLibrary Ireland Scientific Advisory Board Membership

The SAB met twice during the design phase and provided advice on;
- Overall design of the biomedical research infrastructure
- Quality, scope and relevance of the collection
- Operational performance and implementation plan

1.6.2 GeneLibrary Ireland Steering Committee

A Steering Committee to guide the design phase of GeneLibrary Ireland was established in 2008. This committee is composed of representatives of MMI, its partner institutions, QUB, UU and patient organisations. The Steering Committee is responsible for establishing the strategic priorities for the design phase and for monitoring progress against the agreed work programme. The Steering Group is also responsible for agreeing the governance and management structure for GeneLibrary Ireland along with defining the rules for access to the bio-resource and return of data. The membership of the Steering Group is detailed in Table 2 overleaf.
### Table 2: GeneLibrary Ireland Steering Group membership

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<td>Ruth Barrington</td>
<td>CEO, Molecular Medicine Ireland</td>
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<td><strong>Rapporteur:</strong></td>
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<tr>
<td>Jan Guerin</td>
<td>Programme Manager Research, Molecular Medicine Ireland</td>
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<tr>
<td>Mel Clifford</td>
<td>Director, Clifford Robbins Ltd</td>
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<td><strong>Principal Investigator</strong></td>
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<tr>
<td>Peter Doran</td>
<td>Director, University College Dublin Clinical Research Centre</td>
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<tr>
<td>Patrick Mallon</td>
<td>Lecturer in Medicine, University College Dublin and Consultant in Infectious Diseases, Mater Misericordiae University Hospital</td>
</tr>
<tr>
<td>Joe McPartlin</td>
<td>Director, Trinity Biobank Institute of Molecular Medicine, Trinity College Dublin</td>
</tr>
<tr>
<td>Louise Kenny</td>
<td>Senior Lecturer and Consultant in Obstetrics and Gynaecology, University College Hospital Galway and University College Cork</td>
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<td>Micheal Kerins</td>
<td>Professor of Surgery at University College Hospital Galway and Head of the Academic Department of Surgery at National University Ireland Galway</td>
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<tr>
<td>David Croke</td>
<td>Professor of Biochemistry, Royal College Surgeons Ireland</td>
</tr>
<tr>
<td>David Savage</td>
<td>Reader in Molecular Medicine, Centre for Public Health, Queens University Belfast</td>
</tr>
<tr>
<td>Peter Maxwell</td>
<td>Professor of Renal Medicine, Queens University Belfast Consultant Nephrologist, Belfast City Hospital</td>
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<tr>
<td>Margaret Cooney</td>
<td>ICRIN Coordinator, Molecular Medicine Ireland</td>
</tr>
<tr>
<td>Tony Bjourson</td>
<td>Director Centre for Molecular Biosciences, School of Biomedical Sciences, Ulster University of Coleraine</td>
</tr>
<tr>
<td>Eibhlin Mulroe</td>
<td>CEO, Irish Platform for Patients’ Organisations, Science and Industry (IPPOSI ) Irish Platform for Patient Organisations Science and Industry</td>
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### 1.6.3 GeneLibrary Ireland Expert Working Groups

The design phase of GeneLibrary Ireland was a multi-institutional, multidisciplinary and cross-jurisdiction undertaking. Recognising this complexity a number of expert Working Groups were established and chaired by experts from Ireland and Northern Ireland. These Working Groups informed the design phase in the following key areas as detailed on Table 3. In inviting participation to join the Working Groups for GeneLibrary Ireland an exceptionally high response rate of 92% was noted for participation across the seven institutions and patient organisations. This significant interest among stakeholders clearly demonstrated the importance of establishing this biomedical infrastructure for the island of Ireland. The Chairs of the Working Groups are listed in Table 3.
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<thead>
<tr>
<th>Name</th>
<th>Title and Organisation</th>
<th>Working Group</th>
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<tbody>
<tr>
<td>Ruth Barrington</td>
<td>CEO, Molecular Medicine Ireland</td>
<td>Governance, management and organisation</td>
</tr>
<tr>
<td>Deirdre Madden,</td>
<td>Senior Lecturer, Faculty of Law, University College Cork</td>
<td>Ethical, legal and societal issues</td>
</tr>
<tr>
<td>Avril Daly</td>
<td>Head of Public Affairs, Fighting Blindness</td>
<td>Communications Strategy</td>
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<tr>
<td>Leslie Boydell</td>
<td>Associate Medical Director for Public Health, Belfast Health and Social Care Trust</td>
<td>Participant Recruitment Strategy</td>
</tr>
<tr>
<td>Joseph McPartlin</td>
<td>Director, Trinity Biobank, Institute of Molecular Medicine, Trinity College Dublin</td>
<td>Sample and Data Collection, Sample Storage and Processing, Data Management and IT Infrastructure</td>
</tr>
<tr>
<td>Tony Bjourson</td>
<td>Director Centre for Molecular Biosciences, School of Biomedical Sciences, University of Ulster</td>
<td>Value Added Research Programme</td>
</tr>
<tr>
<td>Vincent McCabe</td>
<td>Finance Controller, Irish Heart Foundation</td>
<td>Finance and Funding</td>
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</table>

**Table 3:** The GeneLibrary Ireland Expert Working Groups.

The membership of the above mentioned Working Groups is representative of the all-island collaborative nature of this project and includes experts from all seven institutions and the patient organisations and is detailed in Appendix 1.

1.7 Conclusion

Through the establishment of the Scientific Advisory Board, Steering Committee and Working Groups, MMI with QUB and UU has prepared the design phase for GeneLibrary Ireland and the development of an implementation plan that will ensure a sustainable, relevant, internationally significant biomedical research infrastructure is established for all the people on the island of Ireland.
2.0 GeneLibrary Ireland - The Vision

2.1 Introduction

In this chapter the vision for GeneLibrary Ireland is presented and the plan for its implementation is presented in overview. The vision and plan are based on the deliberations of the expert Working Groups, the Steering Committee and the Scientific Advisory Board.

2.2 The Scientific Vision

GeneLibrary Ireland as a biomedical research infrastructure will enable and support the continued development of translational and genetic research on the island of Ireland. The biobank of 10,000 DNA and blood samples from volunteers on the island together with key phenotypic information will serve as a control population to study the genetic determinants of common diseases that significantly impact patients in Ireland and Northern Ireland. These diseases include cardiovascular disease, cancer, diabetes, arthritis, respiratory disease and cognitive disorders as well as key diseases that are over represented in the population such as coeliac disease, multiple sclerosis, cystic fibrosis and haemachromatosis. This biomedical resource will in itself also provide a valuable cohort to study the genetic background of the population on the island of Ireland.

Human genetic and molecular epidemiological studies require large standardised bio-resources with linked phenotypic data on medical, lifestyle and environmental factors. GeneLibrary Ireland will provide researchers on the island of Ireland with such a bio-resource and extended phenotypic data to investigate the roles that genes play in health and disease which, in turn, will lead to discoveries about mechanism of disease, potential new therapeutics, pharmacogenomics, biomarker discovery and personalised medicine.

Not only will GeneLibrary Ireland serve as a significant research infrastructure to support genetic research studies for academic institutions and commercial organisations in Ireland and Northern Ireland, it will also provide an important scientific output as part of its delivery. This will be achieved by conducting a whole genome wide analysis on a representative of 3000 control samples from the cohort, a number equivalent to the Wellcome Trust Case Control Consortium which has been significantly useful in defining variants associated with certain diseases (20).

The scientific output of GeneLibrary Ireland will be further enhanced by the preparation of immortalised lymphocytes on the same representative sample to facilitate genomic, metabolomic and transcriptomic studies. GeneLibrary Ireland will therefore provide the much needed control samples, with linked genotypic and phenotypic information, for case control studies for researchers on the island for example, gene association studies in type I diabetes and cancer.

Furthermore there will be significant value to be gained from having genotype information on a proportion of the population of Ireland and Northern Ireland which is not currently available. The establishment of GeneLibrary Ireland as a research infrastructure will not only provide a structured framework to support and foster large research studies to identify genetic associations of diseases of high impact in Ireland and Northern Ireland but also allow researchers on the island to share this bio-resource at a European level and internationally through participation in large, statistically powered studies.

The creation of this biomedical research infrastructure will enhance medical and genetic research in Ireland through the;
• Establishment of a carefully phenotyped control population to facilitate disease research.
• Creation of a unique, all-island resource of genetic material and health information.
• Provision of a valuable datasets for additional research into the health and genetic make-up of the population.
• Avoidance of duplication of resources and effort.
• Creation of a vibrant all-island research partnership and enhance connectedness of the biomedical research community North and South.
• Provision of a standardised format for biobanking initiatives which will support clinical research studies.
• Support to investigators in leveraging additional research funding.
• Provision of a unique opportunity for the island of Ireland to partner with international efforts in biobanking and genetics.
• Creation of this critical infrastructure which will serve to further embed the genetics and biotechnology industries in Ireland.
• Complement recent exchequer investment in health research and research infrastructure

The overall schema for the design phase of GeneLibrary Ireland consists of a number of specific elements that are highlighted in Figure 3 overleaf;
The overall schema for GeneLibrary Ireland is represented in Figure 3 below.

**Figure 3** Overall schema for GeneLibrary Ireland.
2.3 Selecting the Population
GeneLibrary Ireland aims to recruit a cohort population of all the people living on the island-of-Ireland as a whole, including immigrant populations. The target age group proposed for GeneLibrary Ireland is 30 to 60 years. It is agreed that this age-range will provide a sufficiently robust collection for provision of age-matched controls for studies of the genetic basis of the major disease burden in Ireland.

2.4 Communicating
Public participation in GeneLibrary Ireland will depend on whether or not the public is convinced that giving blood and DNA samples is a positive action. People's motivation to act will rest solely on their level of understanding and perception of GeneLibrary Ireland and associated benefits. A timely, well executed communications strategy will raise and sustain understanding and can help to create positive perceptions of this important initiative. The goal of the communications strategy will be to encourage maximum participation in GeneLibrary Ireland. The overriding objective of the communication campaign will be to provide people with a solid foundation of information on which they can make a positive decision to donate samples and to provide information. This positive decision will be driven by the fact that they have a clear understanding of the scientific and public health benefits that GeneLibrary Ireland will bring to people living on the Island of Ireland now and in future generations. In addition, participants who enrol in GeneLibrary Ireland will be offered a free health check.

2.5 Ethical, Legal and Social Issues
Recognising the complexity of GeneLibrary Ireland and the absolute requirement for the resource to be managed and used in a manner that safeguards the best interests of the cohort, it is proposed that an independent GeneLibrary Ireland Ethics Committee be established. This committee will provide continuous review of the use of the biobank and information collected to ensure that it adheres to the highest possible ethical, legal and data protection standards.

2.6 Recruiting the cohort
It is proposed that the model for sample and data collection for GeneLibrary Ireland should focus on the CRC research infrastructure in place and being developed on the island of Ireland. This will provide a recruitment model based on geographical clustering. The experience of participant recruitment to control biobanks internationally suggests a response rate of 10-20%. As the representativeness of the sample is not seen as critical for gene association studies there is no added advantage to aim for a representative sample. CRCs have already established or are under development in Cork, Galway, Dublin, Derry and Belfast. Each of these centres will be equipped and staffed with the appropriate expertise for consenting participants, performing physical and phenotypic measurements, sample and data collection and initial processing of samples. It is proposed that an external agency will be contracted to facilitate the recruitment of the population.

2.7 Phenotyping
It is proposed that a comprehensive phenotype of GeneLibrary Ireland participants will be assembled to enable investigations of genotype-phenotype interactions. This phenotyping will include;

- Baseline clinical history and examination
- Clinical chemistry and haematology
- Detailed phenotypic information relating to cardiovascular disease, respiratory disease and cognitive function

These examinations and interviews will be completed at the CRC facilities by expert staff.

2.8 Sampling
It is proposed that blood samples will be obtained from each participant in GeneLibrary Ireland. This blood sample will be used to prepare;
• Serum and plasma fraction (for measurement of proteins and storage)
• DNA
• Lymphocytes

2.9 Managing Information

A secure, reliable and user friendly centralised information management system will be developed for GeneLibrary Ireland. This information management system will be specifically designed to protect the identity of participants and ensure compliance with Data Protection Acts 1998 and 2003. Specifically, the following systems will be developed;

• Participant Information Management System
• Biobank Information Management System
• Laboratory Information Management System
• Study Information Management System

2.10 Processing Samples

Sample processing will be completed at one centralised dedicated processing centre. The centralisation of this key activity will ensure the reproducibility of processing and enhance the validity and utility of the biobank. Specifically, the following activities will be centralised;

• DNA extraction, quantification, normalisation and aliquoting
• Quality control and quality assurance

2.11 Storing Samples

It is proposed that two sample storage facilities will be used to store the GeneLibrary Ireland samples. These facilities will be designed to ensure the security and continued availability of the samples. The creation of two facilities is in line with international best practice, in terms of disaster recovery planning.

2.12 Future proofing the resource

It is anticipated that strong demand for access to GeneLibrary Ireland will put pressure on the finite DNA collected. Recognising this, it is proposed that immortalisation of lymphocytes will be completed to ensure a continued supply of DNA for use in research studies well into the future.

2.13 Genotyping the cohort

It is recommended that genotyping the control DNA samples should be completed as part of the establishment of GeneLibrary Ireland. Recognising the substantial investment required to genotype the complete library, it has been recommended that an initial 3000 samples would be genotyped using high density SNP chips. Based on this initial data set, a subsequent funding application would be submitted to finance genotyping the remainder of the cohort. Completion of this genotyping study will add substantial value to the scientific impact of GeneLibrary Ireland and will see it evolve as a dynamic resource for future genetics research.

2.14 Providing Access to the Resource and Managing Return of Data

Access to GeneLibrary Ireland resources should be open to qualified investigators from academic institutions and commercial organisations. A standard policy and procedure will be developed for GeneLibrary Ireland to define the application process for access to data and/or samples within GeneLibrary Ireland will be reviewed by both the GeneLibrary Ireland Ethics and Steering Committees. Criteria for access will include overall quality of the study, track record of the investigative team, scientific peer review, return of data to add to the bio-resource and complementarity with the all-island objectives of the library. The transfer of samples to third parties will be the exception rather than the rule as it is proposed that GeneLibrary Ireland will be commissioned by researchers to conduct the investigations on their behalf in this way the bio-
resource will remain within GeneLibrary Ireland and help to ensure the quality of the data and control of samples safe-guarded.

2.15 Interfacing with International efforts

GeneLibrary Ireland will seek to interact with international biobanking initiatives including, P3G and BBMRI. These interactions will ensure that maximum value is created and allow investigators on the island of Ireland to leverage materials from other initiatives and participate in larger, international, statistically-powered studies.

2.16 Governing and Managing

Three possible models are proposed for the governance model of GeneLibrary Ireland. Under which ever model is chosen, the Board of GeneLibrary Ireland will be responsible for the implementation of GeneLibrary Ireland as an all-island biomedical research infrastructure and subsequently, for the management and development of the infrastructure. The implementation plan for GeneLibrary Ireland will be reviewed by a recognised ethics committee to be designated in each jurisdiction. The board of management will have two committees – a Scientific Steering Committee to ensure the scientific validity of the project and an Ethics and Governance Committee to ensure the highest standards of ethics and governance. The board of management will be responsible for recruiting a Director who will be supported by a small team of staff with expertise in the areas needed to implement GeneLibrary Ireland and to manage and develop it into the future.
3.0 Ethical, Legal and Societal Issues

3.1 Introduction
As a major biomedical research infrastructure for the island of Ireland, it is vital that GeneLibrary Ireland adheres to the highest legal and ethical standards. The creation of a framework that prioritises the rights of the participants and ensures compliance with relevant law is a key determinant for the success and impact of GeneLibrary Ireland.

3.2 Ethical Oversight of GeneLibrary Ireland
Appropriate ethical oversight is necessary in the design, implementation and operational phases of GeneLibrary Ireland.

The report of the German National Ethics Council on Biobanks for Research state that ‘the involvement of an ethics committee and the need for its favourable opinion are intended to ensure that a narrowly worded consent is not exceeded, that a consent in broad terms is not inappropriately given an even wider interpretation and that exceptional situations in which consent may be waived are not illegitimately invoked’ (21).

The general functions of ethics review committees can be broadly classified as

- **Protection**: to protect the rights and welfare of human subjects of research from any physical and mental discomfort, harm and danger from research procedures; to protect the rights of a researcher to carry out legitimate investigation; and to protect the institution's reputation for research conducted and sponsored by it,
- **Advice**: to advise individual researchers on whether a project is likely to be harmful or offensive to subjects or the broader community,
- **Education**: to increase knowledge and awareness of ethical issues and regulations/directives,
- **Research Quality**: to ensure the proposed research activity is scientifically sound.

There are currently 13 Recognised Research Ethics Committees (RREC) in Ireland for the purpose of review of clinical trials on medicinal products designated by the Minister for Health and Children under the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004-2006. There are three RREC established under the Office for Research Ethics Committees in Northern Ireland for the review of all research involving NHS patients, staff and facilities including clinical trials on medicinal products.

Given the scale and ambition of GeneLibrary Ireland and the different phases involved, including the implementation and operational phases it is proposed that different levels of ethical review may be required as follows;

1. To establish GeneLibrary Ireland it is proposed that full ethics review will be undertaken by one RREC in Ireland and one in Northern Ireland and that the ethics approval granted would be recognised by all other RRECs on the island.

Once GeneLibrary Ireland is established and in its operational phase it is proposed that an independent ethics committee, the **Governance and Ethics Committee** be established to ensure that competent ethical review has been conducted for all research proposals submitted to GeneLibrary Ireland. These research study proposals may require a different level of oversight by the Governance and Ethics Committee as follows;

2. For access to samples and/or data from GeneLibrary Ireland for research studies where researchers have already received ethics approval from a RREC in Ireland and/or Northern Ireland it is proposed that the Governance and Ethics Committee will ensure that the ethics approval granted by the RREC is in conformity and that the control samples and/or data from GeneLibrary Ireland are included as part of this approval. For all-island research
collaborations clarification will need to be sought with regard to the mutual recognition of ethics approval in Ireland by a RREC in Northern Ireland and visa versa.

3. For access to samples and/or data or for re-contact of participants for research studies specifically within GeneLibrary Ireland which have not been reviewed by a REC it is proposed that the Governance and Ethics Committee would conduct a full ethics review of these proposals and ensure that these proposal conform to the overall ethics approval for GeneLibrary Ireland. Such research proposals will also be reviewed by the Scientific Steering Committee.

3.3 Ownership of Biological Samples

There are significant potential benefits to be derived from the knowledge gained from research involving human tissue and in order to realise this potential, somebody must be accorded ownership rights of the tissue. The question is whether these rights should be recognised in the source of the tissue, or the person who receives the tissue for the purposes of exploitation of its potential, or some institution deemed representative of the community and which is charged with exploitation of the potential in a way that benefits all citizens.

Tissue is arguably different from other body parts in that it is not an organ necessary for survival, it is not connected with reproduction, it is capable of therapeutic exploitation, and it may have great commercial value. As well as the inherent issues of justice that arise in the use of the tissue, there has also been an inexorable movement in health care towards a greater recognition of rights of autonomy which may also influence the way in which this issue is now considered.

There has been much academic discussion about whether the law recognises the human body as property, which is capable of being owned. Historically the human body was seen as res derelicta, a thing with no value and no ownership rights attached to it. Although there is some dispute regarding the exact provenance of this rule in the common law system, it now seems to be so enshrined in legal doctrine that it is unlikely to be overturned (22). Most jurisdictions have traditionally prohibited human bodies having a property value on the basis that it would violate the fundamental principle of respect for human dignity.

In relation to separated body parts, the law is less clear. In the United Kingdom hair, blood and urine have all been held to be property for the purposes of the criminal offence of theft. In recent years the English courts have also held that parts of a corpse are capable of being property if they have acquired different attributes by virtue of the application of skill (23). The cases do not clearly set out what must be done to a part of a body in order for it to acquire the status and nature of property. Some indicate that dissection or preservation may be sufficient, in which case the person applying the skill would have a property right in respect of it. There have been no Irish cases on this point but given the common law tradition shared by both jurisdictions, it is unlikely that an Irish court would reach a different conclusion.

The law relating to the removal and control of tissue, which has been excised from living persons for therapeutic purposes, is similarly unsatisfactory in not providing clear guidance to patients, clinicians and researchers. A number of cases in the United States have held that the person from whom tissue is excised for therapeutic purposes has no property right in that tissue. In the well-known case of Moore v Regents of the University of California John Moore had his spleen removed as part of treatment for hairy cell leukaemia (24). The treating physician discovered that Moore’s spleen cells contained potentially beneficial properties and he developed a cell line, which he eventually sold for $15 million. His research was carried out without Moore’s knowledge or consent. A legal action was initiated by Moore on a number of grounds namely conversion (the use of another’s property without their consent), breach of fiduciary duty and failure to obtain informed consent. The Californian Supreme Court rejected the property rights claim on the basis that there was no precedent on which it could be said that people had property rights over their bodies and it would be inappropriate for the law to recognise such a right as it would hinder medical research and lead to the sale of bodily parts.
In a more recent case, Washington University v Catalona the defendant worked for many years as Chief of the Division of Urologic Surgery in a private research university with a medical school (25). His research focused on prostate cancer and over many years of surgery he collected research samples from the excised cancerous tissue of his patients. The samples were stored in a biobank operated by the University and were used strictly for research purposes. Research participants were asked to sign informed consent forms, which stated that they could not assert any ownership rights in respect of the products resulting from the research. In 2003 Catalona left the university to work elsewhere and wrote to the research participants whose samples were stored at the biobank asking for their consent to have their samples released to him. A legal wrangle subsequently ensued in relation to whether the samples were owned by the University or the research participants, such that they could decide to withdraw their samples from the biobank in favour of Catalona. Under relevant legislation in Missouri, the court held that the University had satisfied the two pronged test for ownership that is exclusive possession and control. The court also considered whether the research participants had made a gift of their samples and, if so, was the gift made to the University or to Catalona. Based on the wording of the informed consent forms, the court held that they had intended to make a gift to the University.

In both of the cases cited above, the courts were concerned with the potential adverse effect on research if a property right were held to exist over excised tissue. They were also opposed to the notion that people would be able to sell their tissue to the highest bidder. There have been no Irish cases on this point but it is likely that an Irish court would have similar objections to the property model.

In addition to the question of whether the management of human tissue should be governed by property laws or another regulatory framework, biobanking raises issues about how to strike the appropriate balance between respect for persons and society’s interest in promoting research. It may be argued in this context that tissue removed in circumstances other than treatment, which is voluntarily donated, should be regarded as a gift. There is an underlying assumption that the gift will be used in good faith for the medical benefit of others and that nothing would be done that might be detrimental to the participant. It is also possible to attach conditions as to the uses to which the gift may be put.

In conclusion, individuals may intuitively feel that they ‘own’ their biological samples but this would not appear to be an accurate representation of the legal position. Although participants who make their samples available for research purposes clearly have rights to privacy and confidentiality, it is more likely that the institution / legal entity (in this case GeneLibrary Ireland) to whom the samples are given is the owner in legal terms. Although this would, strictly speaking, entitle GeneLibrary Ireland to sell or otherwise trade in the samples, it is likely that there would be less support from potential participants if this were to be the case, as studies indicate that concerns about inappropriate commercial uses of genetic material are frequently expressed by patient and research participant groups. Therefore, rather than apply an ownership model, it would be preferable explicitly to recognise GeneLibrary Ireland as custodian of the gift/samples, that is to say, that the samples are held in trust and used for the benefit of the people of the island of Ireland, with defined and transparent policies for any possible commercial exploitation which will be fully disclosed to participants and the research ethics committee.

### 3.4 Informed consent

The concept of informed consent derives from recognition of the right to self-determination and personal autonomy. Informed consent means the knowing consent of an individual or their legally authorised representative, so situated as to be able to exercise free power of choice without undue inducement or any element of force, fraud, deceit, duress or any form of restraint or coercion (26). Informed consent safeguards the participant’s autonomy, it is a requirement of justice, understood in terms of participant empowerment. It is also a central feature of the covenant relationship between healthcare professionals and the participant, expressing the professional virtue of fidelity.

Consent can usually be obtained by presenting the participant with a consent form to sign. The consent form exists to demonstrate that a process of communication has taken place during which
the participant has learned about the proposed research and use of his/her samples and reached a point where he/she can decide, on an informed basis to proceed with, restrict, or decline the proposed donation and use of the sample.

For consent to be valid
- a participant must have capacity;
- it must be voluntarily given;
- there should be no duress;
- information regarding actual donation and proposed uses of the sample must be explained;
- The participant must be able to communicate their choice as evidence of demonstrating capacity.

3.4.1 Consent regarding donations to GeneLibrary Ireland
Regulations governing genetic databases can be expressed as a set of citizenship rights regarding the use of personal genetic data (27, 28): These include:
- Right to informed consent
  - consent to participate and supply data
  - consent on the use to which personal data will be put;
- Right to confidentiality and anonymity of data;
- Right to withdraw data;
- Right of access to
  - own personal data
  - aggregate data (general public right);
- Right of ownership of data (citizen, state, industry, charity).

The application of consent to a variety of uses of personal data, which cannot be known at the point when the consent is given, raises important ethical questions (29, 30). It is both a difficult ethical and technical problem. Reflecting on the relationship between informed consent and the demands of genetic data, Baroness O’Neill observes that ‘human capacities to consent and dissent [on the use of their genetic data] are….being stretched, strained and perhaps overwhelmed by developments that arise not only from the combined revolutions in genetics and informatics, but by other developments within medicine which bring together hugely complex arrays of information and intricate regulatory systems’ (31). At present this problem is addressed largely in a negative sense by the citizen’s option of withdrawal from a biobank. Given the large unknowns in the use of genetic data once submitted, this may not be a sufficient right when measured against the reassurance it may or may not offer in the context of future research scenarios (27). GeneLibrary Ireland will make every effort to provide information to participants with regard to potential future research studies.

The model of broad consent used in a number of the international biobanks is proposed for GeneLibrary Ireland (13, 16). The following information will be provided to potential participants in written form before consent is sought:

1. Participation must be voluntary
   Participation in GeneLibrary Ireland is voluntary. At any time, a participant can withdraw consent to participate in GeneLibrary Ireland and their samples and genetic information will no longer be used.

2. The purposes, nature, extent and duration of the proposed use of data and samples.
   The aims of GeneLibrary Ireland and how participation may help the individual and his/her relatives will be explained to the participant. For some there may be no immediate benefit from participation. Circumstances that could potentially disadvantage individuals will also be mentioned such as disclosure of information under subpoena.

   The details of who is responsible for GeneLibrary Ireland, that is the names and contact details of the keeper/custodian and the organisation will be given to the participant. If this
information should change the participant will be informed. The nature of the information 
and genetic material to be collected and stored will be explained to the participant. The 
proposed duration of storage of information and genetic material will be explained to the 
participant. Consent for use of participant samples and/or data used by researchers, in 
coded or de-identified form by researchers for REC-approved research will be sought.

The guidelines for access procedures for the research use of tissue samples and genetic 
material will be explained to the participant.

3. **The possibility or otherwise of communication of research results to the participant**
The relationship of GeneLibrary staff to the participant and to the health professionals 
involved in his/her health care will be explained to the participant. GeneLibrary Ireland’s 
policy will be to provide feedback about the progress of the project and the communication 
of new research findings, which may be of interest or relevance to participants as a group, 
by web based systems or generalised information leaflets. The participant’s views on 
feedback will be sought through focus groups. GeneLibrary Ireland will indicate to 
participants that individual results of genetic studies would not be given to participants as 
these are research based studies.

The participant will be asked to specify what may be done with his/her identified information 
and stored genetic material after death, and his/her wishes will be recorded.

The participant will be asked to consent to being approached by GeneLibrary Ireland staff 
with an invitation to participate in future research studies.

4. **The extent of and conditions for, the possible transfer of samples and data.**
The scientific potential of samples and data can often be fully exploited only if their use is 
not confined to individual research projects specifiable in advance. Participants will be 
asked to give generalised consent to the use of their samples and data for the purposes of 
medical, including genetic research. The same applies to consent relating to the duration of 
storage and utilisation of samples and data. Participants will be able to consent to the use 
of their samples and data for an indefinite period. Modern research is dependent on 
national and international cooperation and networks. For this reason, participants will also 
be able to consent to the transfer of samples and data from GeneLibrary Ireland to third 
parties for the purposes of medical research. However, except in circumstances prescribed 
by law, the transfer must take place only in anonymised or coded form, with the recipient in 
the latter case having no access to the code. Should the recipients’ research require an 
association with personalised data, this may be provided only by an official of the 
GeneLibrary Ireland to which the participants originally entrusted their samples and data. 
All transfers of samples and data to third parties will be fully documented for future 
reference. The transfer of samples to third parties will be the exception rather than the rule 
as it is proposed that GeneLibrary Ireland will be commissioned by researchers to conduct 
the investigations on their behalf that way the bio-resource will remain within GeneLibrary 
Ireland and help to ensure the quality of the data and control of samples. Researchers who 
are provided with samples and data from GeneLibrary Ireland will agree to no further 
transfer of these materials to a fourth party other than through publication.

5. **The use of data**
Participants will be informed that they will determine to whom information about them may, 
and may not, be given.
   - The participant will be asked to consent to disclosure of his/her information in a 
coded format to, and access to his/her genetic material by researchers whose 
research has been approved by an REC.
   - GeneLibrary Ireland staff will ensure that no identified information and/or genetic 
material will be disclosed on a GeneLibrary Ireland participant, without written 
informed consent.
   - Participants will be informed of the GeneLibrary Ireland’s policy on disclosure of 
information and the giving of genetic material in a coded, de-identified format.
Participants will be made aware that GeneLibrary Ireland staff may be required to disclose information about them, and/or release their genetic material, to a court or persons/organisations to who disclosure is authorised or required by law.

6. The right to withdraw consent
Participants will have the right to withdraw their consent to the use of their samples and data at any time. It will not be possible to waive this right. Participants will be advised that it is not possible to withdraw data that has already been accrued and analysed on him/her but that no new data will be generated and his/her samples will no longer be used within GeneLibrary Ireland. Participants will be informed about the fate of samples and data if consent is withdrawn and if GeneLibrary Ireland closes down.

7. Possible commercialisation of the proposed research (including the possibility of filing patent applications on the results).
GeneLibrary Ireland information and associated genetic material may be used, after REC approval, for research which, in time, may result in the development of a product of benefit to those with the disorder. For example, genetic material and information from GeneLibrary Ireland may contribute to discovery of the gene responsible for a disorder, followed by the patenting of a genetic test based on that discovery. The development of such a product is likely to occur in the private sector and may have commercial potential, but participants will not receive any financial benefit from the use of their information and material for the research.

A draft Patient Information Leaflet (Appendix 2) and Consent Form (Appendix 3) have been produced for GeneLibrary Ireland.

3.5 Data Protection Acts
The Data Protection Acts 1988 and 2003 (Ireland) and the Data Protection Act 1998 (UK) are applicable to ‘personal data’ which is defined as data relating to a living individual who is or can be identified either from the data or from the data in association with other information that is in, or is likely to come into, the possession of the data controller (32). Unless it can be definitely stated that the data are not identifiable (this is a complex argument), the principles of the Acts will apply. As medical data/information is being collected, this data will be classed as sensitive personal data. Secondary use of data is permissible, but only with sufficient safeguards and ensuring that harm is not caused to data subjects.

3.5.1 Principles of Data Protection
The Data Protection Commissioner in Ireland has laid out eight principles in the Guide For Data Controllers with regard to those who control personal data (data controllers) (33). These state that the data controller must:
1. Obtain and process information fairly (data processor must ensure, so far as practicable, that the following information be provided to the data subject: (a) the identity of the data controller (b) if he or she has nominated a representative for the purposes of this Act, the identity of the representative (c) the purpose or purposes for which the data are intended to be processed, and (d) any other information which is necessary, having regard to specific circumstances in which the data are or are to be processed)
2. Keep it only for one or more specified, explicit and lawful purposes
3. Use and disclose it only in ways compatible with these purposes
4. Keep it safe and secure
5. Keep it accurate, complete and up-to-date as far as resources allow
6. Ensure that it is adequate, relevant and not excessive
7. Retain it for no longer than is necessary for the purpose or purposes
8. Give a copy of his/her personal data to that individual, on request
3.5.2 Provision of Information and Explicit Consent

In addition to the above, the processing of sensitive personal data will be permissible once the data subject gives his/her explicit consent. Whilst there is no definitive formula for this, the provision of information to the data subject is an essential feature of data protection compliance. The Office of the Data Protection Commissioner (Data Protection Acts 1988 and 2003: A Guide For Data Controllers) states that to ensure fair processing of sensitive data it must be ensured that: “the data subject has given explicit consent…to the processing, i.e. the data subject has been informed of the purpose/s in processing the data and has supplied his/her data with that understanding…”

In relation to information to be given to participants in a gene bank, The UK Human Genetics Commission in its 2002 Report, Inside Information, recommends (34):

“We believe that it is good practice that in the obtaining of consent, as a minimum the following information should be given to prospective participants:

- The purpose of the research envisaged
  - The aims of the research and its scope should be explained. For the reason given above, it will usually not be possible to give details of all the research projects which may utilise the information or the samples.

- The procedures involved
  - Any physical procedures (such as taking a blood sample or a medical history) must be fully explained.

- The storage arrangements for the information
  - Participants should be informed how samples and genetic information are to be stored and for what period (if this is known).

- Confidentiality issues
  - It should be explained to participants how access to the database will be controlled.

- Implications for the participants
  - Participants should be informed of any implications or risks which the giving of a sample may have for them. It should be made clear whether or not there is to be any feedback, and what form this will take. If information might be accessed for any other purpose, this should be explained.

- Commercial use
  - The commercial use of genetic databases is discussed in section 3.4.1. It should be made clear to prospective participants if access is to be granted to commercial companies and that participants will not benefit from such use.

A Health Research Board Discussion Document on the Data Protection Acts 1988 and 2003 (32) also comments that:

“Thus, for the processing of prospective identifiable health research data for medical research (Step 1) data must be processed fairly (kept for specific purpose/s and ensure provision of information); and (Steps 2 and 3) the consent sought at Step 2 should be explicit. The obtaining of explicit consent for prospective health research data for medical research will provide the best protection for individuals. In this regard, consent forms for research and data processing could be devised which envisage future secondary uses and options. These options could be:
(i) Permitting the current research and processing of identifiable data for this research only
(ii) Permitting the current research and processing of identifiable data and for that data to then be anonymised and used for future purposes
(iii) Refusing processing of the identifiable data for the current research and for anonymisation for processing of data for any future research (complete refusal)
(iv) permitting processing of identifiable data for any study relating to the condition for which the data was originally collected, provided they are contacted and their consent is obtained...”
Consent and the provision of information are essential in satisfying the obligations of the Data Protection Acts. The provision of information will be incorporated into the consent process (as part of the information leaflets, websites and consent forms). The Acts oblige collected data to be secured, to ensure this the GeneLibrary Ireland data management system will be planned, documented, implemented and monitored to ensure confidentiality and privacy of data. In addition, by virtue of the Data Protection Act 1988 (section 16(1)) Regulations 2007 those processing genetic data must register with the Data Protection Commissioner in Ireland. This regulation refers only to those “who processes genetic data within the meaning of section 41 of the Disability Act 2005.” Section 41 refers only to processing of genetic data in relation to employment, insurance, pensions, mortgages. Clarification will be sought with regard to whether GeneLibrary Ireland will require registration in both Ireland and Northern Ireland. Full transparency with the Data Protection Commissioners in Ireland and/or Information Commissioner in the UK will be sought. As part of this process full documentation outlining the data protection strategy for GeneLibrary Ireland will be prepared.

3.6 Human Tissue Act (UK)

A number of European countries including Estonia, Norway, Sweden, Latvia, France, the UK and Spain have enacted legislation to regulate the taking, storage and use of human tissue. Biobanking in Northern Ireland is governed by the Human Tissue Act (HTA), 2004 (35). There is no comparable legislation governing the collection, storage and use of human tissue in Ireland, although the Department of Health and Children has undertaken a consultation process on the content of legislation arising from the recommendations of the Madden report on Post Mortem Practices and Procedures (2006). Present indications are that proposed legislation will cover biological material from deceased persons and from living persons for research purposes.

The Human Tissue Act in Northern Ireland makes consent the fundamental principle underpinning the lawful taking, storage and use of human tissue. The Act sets out the requirements to obtain appropriate consent for the removal, storage and use of human material (organs, tissues and cells, other than gametes, embryos, hair, nails) from living people. It provides for penalties for those who carry out activities covered by the Act without proper consent. The Act established the Human Tissue Authority to regulate the storage of human material for education, training and research purposes in England, Wales and Northern Ireland. No person in Northern Ireland can store or use human material as defined under the Act without a license from the Human Tissue Authority. The authority conferred by a license extends to the designated individual named in the license. The person designated in the license is responsible for ensuring that the other persons to whom the license applies are suitable people, that suitable practices are used and that the conditions of the license are met. The premises in which biological material covered by the Act is stored must also be licensed. The Human Tissue Authority may lay down standards expected in relation to consent and prepare codes of practice on the storage and use of human tissue.

Human tissue is referred to in the HTA as ‘relevant material’ and includes any materials that come from a human body that includes human cells from living people. The proposed samples to be
stored within GeneLibrary Ireland include DNA, serum, plasma and immortalised cells therefore it is likely that this bio-resource will need to comply with the HTA. Clarification will be sought from the HTA (UK) as to whether GeneLibrary Ireland will come within the scope of the HTA UK and if a license will be required (36).

3.7 Coding of Participant Sample and Data
The HRB and R&D Office feasibility report indicated that all participant samples and data would be irreversibly anonymised (19). However, since this report was published experience from international biobanks and the scientific advice of the SAB would strongly support the coding of participants samples and data and the inclusion of the possibility of re-contact within the design of GeneLibrary Ireland. There are some ethical concerns around the issue of re-contacting participants in certain circumstances which will be further considered in the implementation phase of GeneLibrary Ireland. All genetic research proposals which involve re-contact of GeneLibrary Ireland participants will require ethical oversight by the Governance and Ethics Committee.

3.8 Conclusion
In conclusion all components of GeneLibrary Ireland will be completed with the protection of participants and compliance with relevant law as their cornerstone. The establishment of the independent Governance and Ethics Committee will ensure that GeneLibrary Ireland is developed and operates to the highest ethical, legal and data protection standards.
4.0 Communicating the Vision

4.1 Introduction
An effective communications strategy is key to ensuring the success of GeneLibrary Ireland. Public participation is dependent on convincing the public that donating samples is a positive action. People’s motivation to act will rest on their level of understanding and perception of GeneLibrary Ireland and the associated benefits. A timely, well executed communications strategy will raise and sustain this understanding and create positive perceptions of this important initiative. The key objective of this campaign will be to provide people with a solid foundation of clear information on which they can make a positive decision to participate. This positive decision will be driven by the fact that they have a clear understanding of the scientific and public health benefits that GeneLibrary Ireland will bring to people living on the Island of Ireland now and in future generations.

4.2 Current public awareness and understanding of biobanking
Many studies have shown that there is a public willingness to donate samples for medical research. For example, Lindblad et al, 2006 found that 86% of the Swedish public would be willing to donate a blood sample for research and 78% would agree to donation and storage (37). A UK MRC and Wellcome Trust focus group study revealed that participants would be willing to donate samples providing the research was ethical.

For GeneLibrary Ireland to succeed, people need to turn positive intent into action. Cousin et al conducted a survey in Ireland about public perception of biomedical research showing that the Irish public is positively disposed towards medical research (38).

In order to engage people and ensure they participate, it is important to understand what they think about the concept, what would motivate people to participate in GeneLibrary Ireland or what might put them off. It is recommended that focus groups be convened as a mechanism to gauge this understanding.

Using focus groups it is possible to:

- Gauge people’s level of awareness and understanding about biobanking
- Find out any underlying perceptions or preconceptions about biobanking
- Elicit any concerns they may have
- Establish a list of common questions that they would have about participation

Understanding this information will determine the type and level of content to be developed as part of the communications portfolio for GeneLibrary Ireland.

It is also possible to establish:

- Who the public respect/admire/listen to
- Who the public would take advice from

This will help determine channels that could be used to get positive messages across or a network of champions and identify trusted groups (e.g. GPs, public health nurse). In this way a celebrity champion(s) may be identified to lead by example and provide the first sample.

Using Focus Groups GeneLibrary Ireland will aim to identify:

- What media, if any, the public read, watch, listen to and their views on different media
- Where the public search for information about health issues
- Levels of concentration for particular show cards (this could be material developed by the group for testing purposes)
- Media or communications outlets that the public DO NOT trust or listen to

The results of such focus groups will help shape which media, education channels and mechanisms will be the most effective to deliver the GeneLibrary Ireland message.
Considering the all-island dimension of GeneLibrary Ireland, it will be important to conduct at least 18 focus group meetings across the target groups identified and across urban and city locations north and south.

4.3 Communications Strategy

The communications strategy for GeneLibrary Ireland will be centered on creating public awareness in a manner that engages the enthusiasm of the whole island of Ireland. The public in Ireland and Northern Ireland is positively inclined towards medical research (36). This study also established that ongoing public education is necessary to ensure continued dialogue between the essential stakeholders – public, professionals and policy makers. One of the main objectives of the communications strategy will be to educate and build understanding. The strategy will be an attempt to provide people with positive attitudes and opinions on genetic research and to consider the long-term benefits of biobanking in general.

Print, online and broadcast media reach an extensive audience on a daily basis and a tailored, coherent message is essential when engaging the media and press and the use of simple language in all general releases will ensure public understanding and interest.

GeneLibrary Ireland will also provide accurate, impartial and up to date information for all stakeholders. This will be delivered via a dedicated Communications Officer whose role will be to ensure only accurate, appropriate information is circulated, limiting the need to correct or contradict inaccurate information.

Information on GeneLibrary Ireland will also consider the language needs of new populations in Ireland and Northern Ireland, and those with sensory limitations, as well as being sensitive to situations involving cross-border differences. GeneLibrary Ireland staff, such as research nurses, will be closely involved in developing the literature as their extensive experience in communicating and developing relationships with patients and participants will be important in ensuring the information provided is comprehensive and appropriate. The National Adult Literacy Agency provides a consultancy service on creating documents using simple, everyday language. GeneLibrary Ireland will involve them in the production of any publicly available information.

4.3.1 GeneLibrary Ireland Branding and Advertising Campaign

Once the core message of GeneLibrary Ireland is developed and approved, the brand identity of GeneLibrary Ireland will be creatively designed and delivered in a consistent and transparent fashion. The core message and brand identity must be emphasised at all times during a strategic advertising campaign. The campaign will be delivered across local and national media including radio, television and press as well as online media. All audio-visual media advertising will be strongly supported by web and/or printed information leaflets. A well-planned and well-promoted launch of GeneLibrary Ireland will be the single most important event to generate momentum behind the advertising campaign and to establish contact with the public and press.

4.3.2 GeneLibrary Ireland Website

The influence of the internet on the targeted population (30-60 years old) in Ireland and Northern Ireland should not be underestimated. According to the Amarach study, 40% of Irish Internet users are between 25 and 44 years of age. 16% are between 45 and 54 and 27% are over 55 years of age (39). It appears that the older public now expects an interactive online presence and this strategy will be central to the GeneLibrary Ireland communications strategy.

Web-based communication for other biobanking initiatives has traditionally been one-directional – using the website as a form of “digital broadcasting” focused solely on public understanding of biobanking and has generally resulted in a relatively passive public engagement. There is a real opportunity for GeneLibrary Ireland to take advantage of elements of the “participatory web” (Web 2.0), in order to promote more active public engagement practices which could lead to a shift in the Irish public’s participation in similar scientific projects. An interactive GeneLibrary Ireland website could have components to the site that people click on and discover and learn about biobanking in
an engaging and entertaining way. Examples of platforms, which could be used to create more active public engagement, include a GeneLibrary Ireland YouTube channel and blog.

An important component of the GeneLibrary Ireland website will be a comprehensive frequently Asked Questions (FAQ) section, a draft selection of possible FAQ for GeneLibrary Ireland is included in Appendix 4.

4.3.3 GeneLibrary Ireland Written Material

All written materials, especially recruitment material (leaflets, consent forms, questionnaires) will be open, transparent and should reflect the core message of GeneLibrary Ireland. Recognisable GeneLibrary Ireland brand identity and web and telephone contact information is a prerequisite for all written material. Informational posters, leaflets and newsletters will be targeted to hospital, CRCs, GP waiting rooms, library stands, etc. All printable material will also be available for download through the website.

4.3.4 Engagement with Media and Press

To ensure transparency, press members should have access to a dedicated communications officer to deal with press inquiries. The traditional methods of interaction with the written media in the form of press releases, press conferences – local and national – will be supported by the following initiatives:

*Human interest pieces and public champions* will provide a valuable source of “feel-good factor” towards GeneLibrary Ireland, which the press is typically quick to pick up on. This method has been used by UK Biobank where several celebrities and national charities have endorsed the project.

*Exercises for maintaining the relationship with the written media* such as letters to the editor, organising meetings with editorial boards, responding quickly to comments/articles and correcting factual inaccuracies in the media.

4.4 Engagement and Education

A major objective of the communications strategy of GeneLibrary Ireland is to educate and build understanding - to attempt to establish positive attitudes to genetic research and to consider the long-term benefits of biobanking in general in the population in Ireland and Northern Ireland. Emphasis will be placed on public engagement rather than just public understanding. Engaging the support of the following people will be essential to ‘swell the tide’ and act as an informed source and positive influence around GeneLibrary Ireland:

(a) People who hold positions of influence in the community

(b) CRC and GeneLibrary Ireland staff

(c) The research community

From a communication’s perspective these groups are key messengers. They must be identified, informed, educated and supported to deliver a united message. It should be emphasised that engagement and education programmes should be tailored to the stage of the project outlined in the following sections

4.4.1 Prior to Implementation of GeneLibrary Ireland

*Identify Public Ambassadors and Champions*

The communications officer will construct an all-island network of people who not only can be called upon to make positive statements to the media, but who are ambassadors of the project from the beginning. All ambassadors must understand the importance of this project and the potential benefits to future generations on the island, and should be informed and educated as part of the communications strategy. As GeneLibrary Ireland will recruit participants based on
geographical clustering around the CRCs it will be a priority to identify local ambassadors and champions who would be more effective in establishing credibility in the community around each CRC.

*Stakeholder Engagement*

All primary stakeholders will be approached as well as agencies or individuals representing them. CRC staff, as part of their training for the implementation of GeneLibrary Ireland, will be actively encouraged to become ambassadors for the project. Any identified representative group will be encouraged to pass on the message to their members and to place the recruitment message on internal websites. It should be noted that this list will include appropriate channels as an all-island initiative. These stakeholders are detailed in Table 4 below.

<table>
<thead>
<tr>
<th>Group</th>
<th>Reason</th>
<th>Channels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nursing community</td>
<td>Front line project staff</td>
<td>The support of the key nursing agencies both north and south will be key here</td>
</tr>
<tr>
<td>CRC Staff, GPs Medical Professionals</td>
<td>CRC and GPs staff will need to be specifically trained as ambassadors.</td>
<td>Use established medical networks to recruit appropriate clinical professionals.</td>
</tr>
<tr>
<td>Patient Support Groups</td>
<td>Extremely useful for promoting awareness and providing information to target special interest populations.</td>
<td>Medical Research Charities Group (MRCG) Genetic and Rare Disorders Organisation (GRDO) Irish Platform for Patient Organisations Science and Industry (IPPOSI) Genetic Interest Group in NI</td>
</tr>
<tr>
<td>Research community</td>
<td>Research scientists are generally viewed as trustworthy in public opinion.</td>
<td>Use established networks of researchers to recruit appropriate scientists. Molecular Medicine Ireland (MMI)</td>
</tr>
<tr>
<td>Industry groups</td>
<td>Could encourage voluntary employee participation by including the details in staff newsletters and on internal websites.</td>
<td>Irish Pharmaceutical Healthcare Association Irish Medical Devices Association Major and Local Trade Unions Large Corporations</td>
</tr>
<tr>
<td>Sporting Figures</td>
<td>Members of the sporting community are more likely to be motivated by health issues.</td>
<td>e.g. Gary O’Toole, orthopaedic surgeon and former Olympian</td>
</tr>
<tr>
<td>Celebrities</td>
<td>Appropriate public figures from the world of entertainment and politics should be approached.</td>
<td>e.g. Aoibhinn Ni Shulleabhain, science graduate and former Rose of Tralee</td>
</tr>
<tr>
<td>Participants</td>
<td>Any member of the public who donates is a potential ambassador</td>
<td>All participants should leave the CRC with a positive experience and a wealth of information to distribute among their local community.</td>
</tr>
</tbody>
</table>

*Table 4: List of potential GeneLibrary Ireland stakeholders*
The education of ambassadors

Prior to the implementation of GeneLibrary Ireland, a simple and effective central message for the project must be agreed. Informing and educating ambassadors and stakeholders of this central core message will be vital in order for them to deliver a consistent message to the public with regard to GeneLibrary Ireland.

Education workshops will be held for all ambassadors at which a communications pack (handbook, contact list, public information etc.) will be distributed to ensure all ambassadors are confident in delivering the key message. The strategy of tailored messaging to different groups will be emphasised at this stage, with possibly different and more comprehensive education packs being distributed among stakeholders (those working within the programme). In this regard, GeneLibrary Ireland staff coming into contact with participants will be fully aware of the public information which has been distributed, including letters of invitation to identified targets. Every member of GeneLibrary Ireland who will represent the project in the media will also be fully aware of the information which has been issued to the public and participants.

4.4.2 During and Post-GeneLibrary Ireland

Community education and outreach

A principal aim of GeneLibrary Ireland will be to keep participants and the wider public at a local and an all-island level, educated and informed about the project. The objective will be to strive to build a relationship of trust and credibility, and ultimately to convince the general public that contributing to GeneLibrary Ireland is a worthwhile venture. Using feedback obtained from the initial focus groups a community outreach programme will be designed with a combination of some or all of the following elements:

- Public forum informational evenings
- Participation in local radio news programmes or public interest broadcasts
- Schools debating competition
- Local press conferences and news bulletins
- Newsletter to all participants, thanking them for volunteering and reiterating the importance of their contribution.

Research findings arising from GeneLibrary Ireland

At the time of publication of the first tranche of research findings from GeneLibrary Ireland, a press briefing and press release will be delivered. Using a tailored message to suit different groups, press releases will go out to news programmes across all media, both local and national. Science / health / medical correspondents and journalists who express an interest in the launch of GeneLibrary Ireland will be specifically targeted. All identified research community ambassador(s) will be encouraged to relay a consistent message at this stage. Using the tailored approach, a scientific / specialist research focus aimed at niche publications, medical journals will be taken. A human interest angle, ‘colour’ pieces for the general public, personal testimonies reflecting on the positive outcomes would be a very effective combination for the general public. Popular TV shows (e.g. afternoon shows, breakfast TV, Nationwide) will also be considered in addition to news programmes.

In the future a travelling road show of the research findings will be organised with an engaging exhibition presenting the information in simple layman’s terms, avoiding professional jargon. All research publications should be accessible on the homepage of the GeneLibrary Ireland website to ensure transparency.
**Internal communications**

Effective internal communications to ensure consistent messages and a positive disposition towards the project will be a high priority. Consistency and frequency at this level of communication will ensure those involved in the project, i.e. GeneLibrary Ireland board members and management team, staff, nurses and clinical investigators, are communicating a coherent and unified message in a way that will be understandable to the general public. Any amendments to the key messages or updates will be distributed in a timely fashion.

4.5 Conclusion

The integrated communications strategy designed to ensure GeneLibrary Ireland's success will include:

**Trust and Transparency**

Engagement is key to the success of GeneLibrary Ireland. Trust and transparency are vital to the decision to engage and their importance will be guiding principles.

**Dedicated Communications Professional**

A dedicated GeneLibrary Ireland communications professional will be recruited to facilitate the implementation of the communications strategy from the outset.

**Focus Groups**

The use of focus groups will allow GeneLibrary Ireland to gauge public opinion on biobanking and also facilitate the views of the public on the development of materials for participants.

**A tailored message**

A communications strategy of tailored messaging based largely on the results of Focus Groups will be implemented to ensure that all stakeholder groups understand the core message of GeneLibrary Ireland.

**Precedence/Partnership**

GeneLibrary Ireland is in a unique position – it has the opportunity to create a best-in-class biobanking communications strategy from the learnings and insights of other international biobank initiatives.

**Use of Champions**

Champions and ambassadors will be used as effective methods to influence public opinion to participate in GeneLibrary Ireland.

**Reporting of Research Findings**

All research findings from GeneLibrary Ireland will be clearly reported in plain language through the general media. Website updates and Newsletters to participants will help to foster feelings of ownership of the project and will generate a positive feeling of achievement and being part of something important to the people of the island. In turn this goodwill will encourage greater participation as the project continues.
5.0 Recruiting Participants

5.1 Introduction
To enable the development of GeneLibrary Ireland as a biomedical research infrastructure to support ongoing translational research, a robust strategy for participant recruitment has been developed to ensure the 10,000 participant target will be realised.

5.2 Sample Population
GeneLibrary Ireland will be inclusive of the population of people living in Ireland as a whole, including immigrant populations. From the 2006 census 12% of residents in Ireland identified themselves as 'non-Irish', it is therefore likely that at least 10% of the participants recruited to GeneLibrary Ireland will be 'non Irish' (40). It may be argued that the inclusion of ethnic minorities could have certain disadvantages for GeneLibrary Ireland including:

- Confounding of genetic case-control differences as these groups are genetically distinct from the majority population on the island
- Gene-gene interactions specific to an ethnic minority cannot be excluded
- Reduction of power since minorities may be excluded from the main analysis

However, as GeneLibrary Ireland is being established as a biomedical research infrastructure to study genes associated with the common diseases that affect and will affect the population of Ireland and Northern Ireland as a whole, it is important to be all-inclusive. The majority of the control population recruited to GeneLibrary Ireland will have an Irish genotype and thus serve as strong controls for common disease cases. It must be noted that there is already an inherent variability within the Irish genotype whereby some allele frequencies can differ by up to 10% between East and West coast communities with some diseases showing different incidence (41). It must also be recognised that there are some diseases in Ireland, for example HIV where a significant proportion of cases are 'non-Irish' as observed in the Dublin City HIV cohort. This is a longitudinal study of patients with HIV infection funded by the HRB and led by Prof William Powderly. Moreover any decrease in power of GeneLibrary Ireland, that arises through collecting samples from immigrant participants can be readily addressed by increasing the sample size of the biobank if necessary. This is easily achievable and fits with the longer term vision of GeneLibrary Ireland as a sustainable resource for health research on the island. The collections within GeneLibrary Ireland will also be used in wider international studies, for example through the P3G Consortium and BBMRI which will also utilise the “non-Irish” in larger statistically powered studies.

GeneLibrary Ireland will ensure that the ethnic origin of each participant will be determined as precisely as possible at enrolment as part of the baseline questionnaire and be recorded so that researchers can request samples and data representing the population of interest for their investigations.

5.3 Sample Size
It is recommended that a sample size of 10,000 is appropriate for GeneLibrary Ireland and will provide a suitably powered control sample for cases representative of the common diseases and those overrepresented for the population of Ireland and Northern Ireland. For whole genome association studies, greater sample sizes provide better confidence about risks of the top few most strongly associated SNPs, and also provide information regarding a much greater number of risk SNPs, allowing identification of those which contribute more modest risks of disease. For common disorders with multi-factorial contributions, the larger the sample size the better, with estimates of suitable sample sizes lying in the tens of thousands (42). The size of this sample to function as a control for many case collections is therefore limited more by the practicality of collecting very large case collections in Ireland. 10,000 samples represents a reasonable estimate of feasible study population sizes over the next few years: while much larger sample sizes will be more informative for really understanding the genetic basis of multi-factorial disease, these sample sizes will be
most likely achieved through collaboration in international consortia. The presence of this control sample will reduce costs of Irish participation in such consortia.

Ten thousand is considered a minimum sample size to look at gene association studies for disease (43). This will also provide a reasonable sample size for GeneLibrary Ireland to participate in large statistically powered international collaborative studies. In addition, the catalogue of biobanks held by the P3G Observatory includes only those biobanks with a minimum sample size of 10,000 thereby facilitating the inclusion of GeneLibrary Ireland (17).

5.4 Target Age Group

A broad spectrum of population-based biobanks for biomedical research has been established or is being planned in Europe, Asia and in the Americas. Within Europe, large population-based biobanks exist in the UK, the Nordic countries as well as in Austria, Estonia, France, Germany, Italy, the Netherlands, Portugal and Spain. Several other countries have studies in the preparatory phase. The existing European biobanks are quite diverse with respect to the populations included, the nature and size of the biological specimens held and the clinical and anthropomorphic data available. A number of these biobanks, including some from outside Europe, are summarised with respect to size, age range, and whether the focus is on understanding the links between gene environment and chronic diseases, in the Table 5 below.

<table>
<thead>
<tr>
<th>Name</th>
<th>Approximate Size</th>
<th>Age range (years)</th>
<th>Chronic Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK Biobank</td>
<td>500,000+</td>
<td>40-69</td>
<td>Yes</td>
</tr>
<tr>
<td>Estonian Genome Project</td>
<td>100,000 initially</td>
<td>Adults</td>
<td>Yes</td>
</tr>
<tr>
<td>Icelandic decode Biobank</td>
<td>10,000 (pilot)</td>
<td>16+</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>250,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kadoorle Study of chronic disease in China</td>
<td>500,000</td>
<td>35-74</td>
<td>Yes</td>
</tr>
<tr>
<td>The Gambian National DNA Bank</td>
<td>57,000</td>
<td>Not available</td>
<td>No</td>
</tr>
<tr>
<td>The Mexico City Prospective study</td>
<td>160,000</td>
<td>35+</td>
<td>Yes</td>
</tr>
<tr>
<td>The Indian National Biobank</td>
<td>2-3 million</td>
<td>18+</td>
<td>Yes</td>
</tr>
<tr>
<td>CARTaGENE, Quebec Canada</td>
<td>65,000</td>
<td>25-74</td>
<td>Yes</td>
</tr>
<tr>
<td>German National Genome Research Network</td>
<td>Multiple studies</td>
<td>All ages</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>With approx.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20,000 per study</td>
<td>(pilot stage)</td>
<td></td>
</tr>
<tr>
<td>Norwegian Mother &amp; Child study</td>
<td>100,000 pregnant</td>
<td>Adults and</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>women; 100,000</td>
<td>children &amp; 70,000</td>
<td></td>
</tr>
<tr>
<td></td>
<td>children</td>
<td>fathers</td>
<td></td>
</tr>
</tbody>
</table>

Table 5: Summary of biobanks internationally
These selected studies tend to focus on adults (the Norwegian study representing a notable exception). The inclusion criteria with respect to volunteer age, differs somewhat across the studies – with several studies including young adults from 16 or 18 years and over. In considering the age range for inclusion, the study objectives are clearly relevant. The rational provided for the choice made for the UK Biobank study (40-69 years) states:

“This age range allows investigation of the common causes of morbidity and premature mortality, and also allows ascertainment of events at an age where such cause-specific outcomes are generally well recorded, with less co-morbidity (and competing causes of mortality) than outcomes at older ages”

The target age group agreed for GeneLibrary Ireland is 30 to 60 years. While this age group differs from that proposed in the HRB and R&D Office feasibility report which was 25-74 years, it is considered that the younger age group represented a migratory group and would be more difficult to enroll and that the older age group will be partly represented in the Irish Longitudinal Study on Ageing (TILDA) which has a target age group of 55-70 years (19, 44). The inclusion of the 30 year old age group will provide a younger population with a phenotype and genotype that is not confounded by such factors as medication usage or chronic disease presentation. This age group is also slightly wider than the UK study limits, but the lower age limit reflects the choice in several other biobanks. This age distribution will also allow GeneLibrary Ireland to be complementary to other studies currently ongoing or underway in Ireland for example, TILDA.

5.5 Recruitment Model

The model for sample and data collection for GeneLibrary Ireland will focus on the CRC research infrastructure. This will provide a recruitment model based on geographical clustering. The experience of participant recruitment to control biobanks internationally suggests a response rate of 10-20%. As the representativeness of the sample is not seen as critical for gene association studies there is no added advantage to aim for a representative sample. Currently there are CRCs already established or under development in Cork, Galway, Dublin, Derry and Belfast. Each of these centres will be fully equipped and staffed with the appropriate expertise for consenting participants, performing physical and phenotypic measurements, sample and data collection and initial processing of samples. This approach provides the following key advantages,

- The closeness of potential participants to the centres should enhance response rates
- There would be no need for mobile data collection units with associated costs
- Targeted and local advertising is easier in a clustered situation
- The approach capitalises on the research expertise and infrastructure that has already been developed

The population of the cities included is as follows (45, 46)

- Greater Belfast City – 580,000
- Cork City and county – 481,295
- Greater Derry Council – c90,000
- Dublin city and counties – 1.187 million
- Galway city and county – 231,670

The following sample numbers are therefore proposed based on the population size and inclusive nature of this all-island initiative:

- Belfast – 2500
- Cork – 1500
- Derry – 1000
- Dublin – 4000
- Galway – 1000
The above participant numbers proposed per CRC will serve as a guide and will be used flexibly and reviewed regularly once recruitment has commenced.

5.6 Sampling Frames

As GeneLibrary Ireland will not be recruiting a representative sample of the overall population but rather a geographically clustered sample, a number of sampling frames can be used to recruit the target population. These include the GEO Directory in Ireland, and the Land and Property Service Agency’s Address Database and GP Registry in Northern Ireland. All these sampling models have been used successfully for a number of studies as outlined in the following sections and will allow the opportunity to access a wide target base. It is proposed that participant recruitment through these sampling frames will be sub-contracted to a third party that has significant experience in this area. This will be done through a competitive tender process. This agency will generate household lists in the vicinity of the CRCs from the sampling frames and will issue a letter of invitation and accompanying project information developed by the Communications Officer to participate in GeneLibrary Ireland.

5.6.1 Ireland: GeoDirectory

The GeoDirectory is a listing of all addresses in Ireland, compiled by the Economic and Social Research Institute (ESRI). It contains separate lists of commercial and residential addresses. The ESRI’s RANSAM programme generates probability samples where each dwelling has a known probability of selection. A random selection of sampling points based on aggregates of townlands, using a minimum population criterion, is generated. These form the Primary Sampling Units (PSUs) or clusters. This method has been successfully used to recruit the sample of over 10,000 participants in SLÁN 2007 (47). One of the features of the GeoDirectory is that non-eligible addresses (e.g. vacant, derelict) cannot be fully excluded. For example, the GeoDirectory identifies 2.7% of residential addresses as vacant, compared to an estimate of 15% by Census 2006. This means that a percentage of addresses in a sample based on the GeoDirectory will not be identifiable as ineligible. Sampling for GeneLibrary Ireland will need to adjust for these non-eligible addresses. In addition the use of the Geo Directory will make this data broadly comparable with the SLÁN data from urban centres and thereby allow a reasonable judgement on the representativeness of the sample for GeneLibrary Ireland.

5.6.2 Northern Ireland: Land and Property Service Agency’s Database

In Northern Ireland the Land and Property Service Agency’s (LPSA) Address Database can be used in a similar way to the GeoDirectory in the South of Ireland. The Northern Ireland Health and Social Wellbeing Survey (the latest version was completed in 2005/6), was based on a systematic random sample of 5,000 addresses drawn from the LPSA Address Database (48). The LPSA addresses were sorted by district council and ward, in this way the sample was effectively stratified geographically. Fieldwork for the 2005 survey was carried out from February 2005 to March 2006. Interviews were sought of all adult members (those aged 16 and over) of eligible addresses to yield a representative sample across Northern Ireland. Completed sample size was 4,245 (4,145 aged 18+ years). The Northern Ireland Health and Social Wellbeing Survey was also run in 2001 and 1997 with the overall sample size for the 1997 survey being 3520 people. The overall response rates range from 66% in 2005 to 75% in 1997. The 1997 Northern Ireland Health and Social Wellbeing Survey also included a blood sample, which indicates that 53% of the effective sample provided physical measurements for the survey, 85% of which also gave a blood sample (49). Overall the response rate for participants who provided a blood sample was 45% of the effective sample for the survey.

5.6.3 Northern Ireland: GP patient register

An alternative approach available in Northern Ireland is to use the central list of people registered with general practitioners. This list is comprehensive in coverage with virtually everyone living in Northern Ireland included (1.8 million people on the list). Demographic data on the list includes the person’s address, date of birth, and their doctor. The register would better target the initial
invitation letter as it would be addressed to a named individual within the required age-range. The use of the named invitation letter would require ethical consideration, and the initial letter would need to be delivered through the Central Services Agency in Northern Ireland – the Agency who manages the central register. The disadvantage of this approach is that it would lead to different sampling methods being used in both jurisdictions. However as GeneLibrary Ireland is not aiming for a representative sample this should not be an issue but rather provide an effective way to recruit participants to the study in Northern Ireland. Unfortunately a similar system is not available in Ireland.

5.7 Conclusions

In conclusion, the recruitment of the GeneLibrary Ireland sample will be based on:

- Recruitment of 10,000 participants to provide sufficient power for research studies envisaged
- Sample population will be clustered around CRC facilities
- Participants from all ethnic backgrounds will be invited to participate
- Target age-range of participants will be 30-60 years
- An external agency will be contracted to recruit the sample based on
  - GeoDirectory
  - Land and Property Service Agency’s Database
  - GP patient register
6.0 Managing Information

6.1 Introduction

The creation of a knowledge-based, integrated, secure, compliant data management platform to support GeneLibrary Ireland is a major goal to ensure the realisation of this all island research infrastructure. This system will be based on an expansion of the research information system currently being developed at participating CRCs. GeneLibrary Ireland requires an overall Information Management System to include the following:

- Participant Information Management System;
- Biobank Information Management System;
- Laboratory Information Management System;
- Governance & Study Information Management System.

The exact nature of these systems will depend on a number of factors including the study design, conditions attached to ethics approval, and data protection legislation. A schematic of a possible Information Management System solution is shown in Figure 4 below. This is loosely modelled on the IMS used in Generation Scotland which was presented to the Data Management Expert Group by the IT experts from Generation Scotland as part of an interactive information sharing workshop which was conducted as part of the design phase to inform this group. This solution will provide uniformity of standards across all sites.

### Figure 4
A schematic of a possible Information Management System solution for GeneLibrary Ireland.

6.2 Participant Information Management System (PIMS)

As previously described, GeneLibrary Ireland participants will be recruited through an external agency using GeoDirectory, GP registers etc. GeneLibrary Ireland will develop an IT system to provide participant invitation and appointment management. In addition, management of consent status and agreement for re-contact will be managed through this system. The PIMS will ensure
participants present themselves at the appropriate CRC, register and provide consent to the study and personal details. The CRC will store consent forms, personal information and paper back-ups of phenotypic and physical measurements for their participants only. The CRC will provide the participant with a unique CRC research number, e.g. GLI0001. This number will be one of two numbers used to trace the participant’s de-identified (coded) research and sample data in all subsequent systems. Software at the CRC will contact the central Biobank Information Management System for a unique GeneLibrary Ireland study number. The CRC and GeneLibrary Ireland will exchange a unique CRC research number and GeneLibrary Ireland study number – therefore both systems will have two pieces of unique information for coded participant tracking. Software at the CRC will also contact the Laboratory Information Management System to initiate sample tracking and bar coding. The participant will engage in a number of activities, including a self administered questionnaire, physical measurements, a structured interview and provision of blood samples. Software will be required to capture and collect data from these activities and perform basic data checking. Data collected will be encrypted and uploaded to a central research database via a secure method. This data would contain no participant identifiable information at this stage. Samples will be bar coded and shipped to the central LIMS.

6.3 Biobank Information Management System (BIMS)

The Biobank Information Management System is the central research information system for GeneLibrary Ireland. The system provides data storage and management; an interface to the LIMS sample management system and sample processing systems (to extract appropriate genotype, biochemistry and *omics data); an interface to a Governance and Study Information Management System to facilitate quality assurance; and interfaces for researchers seeking to analyse the data or obtain data or aliquot samples for additional research. Coded data for each participant will be uploaded into the system from each of the CRC’s. The BIMS will maintain a unique GLI and CRC number for each participant. The BIMS will include sophisticated activity monitoring and logging to ensure that all activity on the system will be logged.

6.4 Laboratory Information Management System (LIMS)

It is proposed that a single central laboratory be used for all processing, considerably simplifying the need to build and design a heterogeneous LIMS. The LIMS will interface with all laboratory equipment used to store and analyse samples, in particular, a sample management system that will provide facilities for sample shipment, storage, aliquoting, and DNA extraction. The LIMS will also include facilities to link to genotype, biochemistry and ‘omics’ data as required. This data will be fed into the BIMS. The LIMS will use the GeneLibrary Ireland and CRC unique participant numbers and 2D bar coding to track participant samples. The barcode system will need to be capable of handling required freezer temperatures of -80°C. The LIMS will include sophisticated activity monitoring and logging.

6.5 Governance & Study Information Management System (GSIMS)

The Governance and Study Information Management System will provide an interface to monitor continually the BIMS and LIMS (via the BIMS) and produce periodic reports for quality assurance, error logging, access etc. The system can also be used for general project management system by the GeneLibrary Ireland governing committee to provide SOP's for GeneLibrary Ireland staff, to inform researchers of corrected data fields and to provide an application procedure for researchers wishing to gain access to the BIMS.

6.6 Interface Research Institutes and other bodies

The GeneLibrary Ireland project is designed to collect data for research purposes, therefore the systems must facilitate access to the greatest possible extent while always ensuring adherence to ethical and legislative criteria. Researchers will gain access to the system via an application to the GSIMS. In general, researchers can be divided into two categories; users who wish to perform statistical analysis; users who wish to perform more specific analysis and additional sample analysis. Following approval from the GeneLibrary Ireland Scientific Steering Committee, the
researcher will gain access to the BIMS data analysis engine via a secure web connection, or access to a subset of data and aliquoted samples. The BIMS may need facilities to store results produced by additional analysis of samples. It will be important that all procedures and equipment across research sites are standardised to ensure the integrity of the data.

6.7 Data interface at an International level

Appropriate systems for making data available to international studies will be considered in particular GeneLibrary Ireland will seek to ensure harmonisation wherever possible with such systems that may be developed by BBMRI to ensure that the data generated will be used to its full potential. The European Genotyping Archive is the only such system available internationally at present for this purpose and this resource is for genotyping data. GeneLibrary Ireland will seek to interact with and deposit data to this archive to ensure that the widest possible impact of GeneLibrary Ireland is realised on an international basis.

6.8 Data Security

Security in the GLIIMS will be multi-tiered whereby an exploit / failure of one security system will not allow the integrity of the overall system to be compromised. The exact level of security required will depend on work flows, data specifications, etc.

- Extensive SOP's and training will be required to ensure that staff at GeneLibrary Ireland, and the CRC's, and researchers with access to data subsets, do not accidentally (or maliciously) expose the systems or system data. No user should gain access to any of the IT systems without undergoing training and signing appropriate agreements. A dual level login system (where the user has to authenticate using two methods, e.g. username/password & biometrics) should be considered to prevent unauthorised access in the case of a user losing their username / password. A policy of full activity logging should be pursued to enable tracing of all activity on the various systems.
- All data collected will be stored in encrypted format. All data communication channels should be encrypted.
- Databases will not contain personal identifiable information and coded research data.
- Databases storing personal identifiable data will be maintained on the CRC's hospital systems. The CRC's are experienced in ensuring patient confidentiality. These databases will not be attached to a public network.
- Database staging may be used to prevent full access to a coded database in the event of a systems exploit.
- All systems will be capable of passing an IT audit. Systems will be in an appropriate, physically secure, hosting environment, managed by staff trained to handle systems containing data registered for data protection.
- Each IT system will be mirrored and backed up at a remote site for disaster recovery purposes.
- Systems development will be handled by an IT manager and the or through a bespoke build or additional customisation via outsourcing.

6.9 Conclusion

In conclusion, an integrated, planned, centralised information management system will be developed for GeneLibrary Ireland, as a core enabling technology. Specifically, it is proposed to

- Develop IT infrastructure in consultation with all stakeholders to ensure user friendliness and utility.
- Ensure compliance with data protection legislation and international best practice.
- Deploy a Participant Information Management System.
- Deploy a Biobank Information Management System.
- Deploy a Laboratory Information Management System.
- Deploy a Governance & Study Information Management System.
- Recruit an IT Manager to oversee the information system development and use.
7.0 Phenotyping and Sampling

7.1 Introduction

The central element of GeneLibrary Ireland is the participant contact stage. The sampling and clinical phenotyping component of GeneLibrary Ireland will be centred around the CRC research infrastructure. Currently, centres for patient contact visits are available for GeneLibrary Ireland at:

- Altnagelvin Hospital, Derry
- Beaumont Hospital, Dublin
- Belfast City Hospital, Belfast
- Cork University Hospital, Cork
- Mater Misericordiae University Hospital, Dublin
- St. James University Hospital, Dublin
- St. Vincent's University Hospital, Dublin
- University College Hospital, Galway

The structuring of the GeneLibrary Ireland patient visits around the CRCs is a key to success as it

- Reassures the participant of the professionalism of the team.
- Provides access to significant research nursing experience and expertise.
- Provides a research centric environment for patient visits
- Gives access to state-of-the-art infrastructure.
- Provides indemnity cover to GeneLibrary Ireland participants under the clinical Indemnity Scheme.

All aspects of this workflow are designed for harmonisation with international procedures and guidelines to maximise the potential benefits to be gained from cooperating with comparable collections internationally. Towards this end numerous guideline and collection protocol documents available on the P3G Website Observatory have been considered (17).

7.2 Phenotypic Information

The purpose of GeneLibrary Ireland is to serve as a control population to study the genetic determinants of common diseases which significantly impact patients in Ireland and Northern Ireland including cardiovascular disease, cancer, diabetes, arthritis, respiratory disease and cognitive disorders, along with key less common diseases which are more prevalent in the Irish population such as coeliac disease, multiple sclerosis, cystic fibrosis and haemachromatosis.

Phenotypic data will be collected through the use of clinic questionnaires, post-visit questionnaires and clinic physical assessments. The phenotypic questionnaires and assessments that will be performed at baseline have been chosen to maximise the value of the collection.

In addition some of the measures provide useful clinical information. The results of the comprehensive cardiovascular assessment will be provided to participants and to their general practitioners. This will serve the dual purpose of health promotion and encouragement of participation in GeneLibrary Ireland.

7.2.1 Personal, Lifestyle and Medical Data

General information regarding the health, medical and lifestyle of GeneLibrary Ireland participants will be collected as part of the questionnaires. The information to be collected in this way includes:

- Personal Details
- Personal and Family Health
- Medications
- Family History
The data collected in this questionnaire will provide important information regarding the overall health and wellbeing of GeneLibrary Ireland participants. While it was proposed in the HRB and R&D Office feasibility report that GeneLibrary Ireland would conduct a baseline health evaluation study of the population of the island of Ireland, it was agreed that this would require a different study design. This is particularly true considering that GeneLibrary Ireland will not be a representative sample of the population of island of Ireland based on a response rate of 10-20% experienced from international control biobanks. Since the publication of the HRB and R&D Office feasibility report the SLAN 2007 report has been published, which has conducted a health evaluation study for the population of Ireland (19, 47).

The following sections provide the scientific justification for collecting detailed phenotypic information concerning cardiovascular risk and disease, cognitive function and mental health.

7.2.2 Cardiovascular phenotypic measures

Atherothrombotic events, myocardial infarction and stroke, are responsible for approximately 40% of total mortality in the western world, and are leading causes of morbidity burden world-wide. Both atherosclerosis and thrombosis are complex disorders - both environmental factors and genetic factors contribute to their pathogenesis. Furthermore three of the six key cardiovascular risk factors, hypertension (elevated blood pressure), hyperglycaemia (diabetes), dyslipidaemia (high cholesterol and triglycerides) are themselves complex disorders – the contribution of genes to their pathogenesis is estimated to be considerable. Age, male gender and smoking are the other major risk factors for atherothrombotic events. Hence GeneLibrary Ireland will collect robust measures of blood pressure (clinic blood pressure measurement), glycaemia (glycosylated haemoglobin), and lipids (full lipid profile).

Blood pressure (BP) measurement:

Sub-optimal control of blood pressure (BP) is responsible for over half of all strokes and heart attacks worldwide. Family studies into the influence of genetic factors underlying high BP have shown that overall heritability of essential hypertension ranges from 20% to 55% (50; 51). A number of recent scans of the human genome have provided compelling evidence for existence of several chromosom al regions that are linked to BP. These genomic fragments, known as BP quantitative trait loci (BP-QTLs) are present on almost all human chromosomes (52, 53). Candidate gene studies have shown that elevated BP may be associated with genetic variants in the genes that encode components of the renin-angiotensin-aldosterone system, beta-adrenergic signalling, sodium homeostasis system, intracellular signaling, vasoactive molecules such as endothelins and nitric oxide, growth factors, molecules of oxidative stress and inflammatory response (54).

It is proposed to measure clinic BP. The measurement of ambulatory BP has also been considered, because of its considerably greater precision and reproducibility, and also its avoidance of the white coat effect. However it has been agreed that in a biobanking context this may not be practical or feasible for 10,000 participants. The measurement of ambulatory BP would be a valuable sub-study for consideration within GeneLibrary Ireland in particular as, ambulatory pressures, particularly night-time values, have recently been confirmed to more powerfully predict cardiovascular mortality than clinic pressures amongst hypertensive patients (55). GeneLibrary Ireland will have unparalleled phenotypic information to use in both candidate gene and genome wide approaches concerning elevated BP. It is expected that identification of genetic signatures of essential hypertension will have significant impact on clinical practice. Those at high risk of hypertension will be identified early, as will those at increased risk of hypertension associated target organ damage. Genetic markers of response to antihypertensive treatment will help to
genetically tailor the most suitable BP-lowering therapy, and minimize the risk of adverse effects with a potential to improve compliance and the overall control of BP.

**Common carotid atherosclerosis:**
Common carotid artery intima-media thickness (CC-IMT), measured with precision and reproducibility using B-mode ultrasound, is a well established measure of sub-clinical atherosclerosis (56, 57). Increased CC-IMT is seen with all known risk factors for atherothrombosis (age, male sex, smoking, obesity, hypertension, dyslipidaemia, hyperglycaemia, homocystinuria, inflammation and oxidant stress). It is an independent predictor of cardiovascular events (58, 59) Carotid IMT is highly heritable. Data from the Framingham study and from other researchers suggest that up to 60% of the variation can be explained by inheritance (60-62).

Candidate gene studies over the last five years have identified a number of variants that are associated with increased CC-IMT. The majority of these studies have examined variants in genes with influence on established atherothrombotic risk factors such as blood pressure, dyslipidaemia, and glycaemia. Associations have also been noted between carotid arterial wall thickening and polymorphisms in genes involved in processes more recently implicated in the pathogenesis of atherosclerosis, namely inflammation, response to infection, oxidant stress, thrombosis, and matrix remodeling. While CC-IMT would be an exciting measure to include as part of the phenotypic measures for GeneLibrary Ireland it is recognised that it would not be practical to perform on 10,000 participants from both training and funding perspective therefore it will be a measure for consideration as a sub-study within GeneLibrary Ireland.

### 7.2.3 Diabetes, hyperglycaemia and lipids
Diabetes and hyperglycaemia are amongst the greatest public health challenges that the world faces this century. Close to 5% of the Irish population are currently diabetic, and with the continuing rise in the prevalence of overweight and obesity, this figure is expected to increase to at least 7% over the next decade (63). Diabetes is a condition not only of hyperglycaemia but also insulin resistance, dyslipidaemia and hypertension. This combination of risk factors certainly contributes to the three-fold greater cardiovascular morbidity and mortality in patients with diabetes, compared to subjects without diabetes. The pathogenesis of diabetes is complex. Both impaired pancreatic insulin secretion, and insulin resistance in peripheral tissues such as muscle, liver and adipose tissue, play important roles. Environmental factors such as nutrition, obesity and physical inactivity certainly interplay with genetic determinants.

Whilst it would be ideal to acquire a fasting measure of glucose and lipids, it would be impractical to ask all volunteers to come fasting to the clinic. This would restrict the time periods during which the clinical assessment could occur to early morning, and thereby markedly slow the progress of the project. Fortunately, glycosylated haemoglobin reflects plasma glucose levels over the previous 10 weeks, and is completely uninfluenced by recent eating. The full lipid profile that is to be performed includes measurement of total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, and triglycerides. Total cholesterol, HDL cholesterol are little influenced by recent meals. Triglycerides are influenced by proximity to eating, but this lipid is of considerably less importance as a risk factor for cardiovascular events that the other three lipid fractions.

### 7.2.4 Obesity
The prevalence of obesity has risen dramatically over the last 20 years and continues to rise in Ireland and Northern Ireland and throughout the world. It is of major concern because it is associated with very significant morbidity and mortality, increasing the risk of type 2 diabetes, hypertension, coronary artery disease, degenerative arthritis, and cancer at a number of sites. Any investigation of the relative role of genetic and lifestyle factors (and gene-environment interactions) as contributors to chronic disease should therefore include a measurement of obesity, and this variable should be considered in the overall statistical analysis of results. GeneLibrary Ireland therefore proposes to measure obesity in all participants.
Obesity is typically measured as body mass index (BMI), defined as the weight in kilograms divided by the square of the height in metres. This provides a measure of general adiposity, however it gives no indication of body fat distribution. Abdominal fat deposition is considered to be a key component of obesity, with recent evidence suggesting that abdominal obesity (measured as waist circumference; or waist-to-hip ratio) may in fact be a more useful measure of obesity than BMI. Abdominal obesity is strongly associated with cardiovascular disease risk factors (such as adverse lipoprotein concentrations) and may be a better predictor than BMI of the future risk of metabolic complications, chronic disease and all-cause mortality. One investigation (64) of over 20,000 U.S adults who were participants in two examinations of the National Health and Nutrition Examination Survey (NHANES) showed that both measures of obesity were highly correlated with each other. Obesity as measured by either parameter, but especially abdominal obesity (waist circumference), showed a rapid increase between NHANES III (1988 to 1994) and 1999/2000. Another study from the US concluded that abdominal obesity (as assessed by waist circumference) was associated with increased total health care charges and was a better predictor of health care costs than the more widely used BMI; however the relatively small sample size (n=424) may have limited the interpretation of these results (65). Most notably, a paper recently published (66) examined the association of BMI, waist circumference and waist-to-hip ratio with the risk of death among 359,387 participants from nine European countries in the European Prospective Investigation into Cancer and Nutrition (EPIC). The findings showed that both general adiposity (as measured by BMI) and abdominal obesity (as measured by waist circumference) were strongly associated with the risk of death, and supported the use of including both measures in assessing the risk of death across the entire range of adiposity values. Waist-to-hip ratio was found to be less strongly related to BMI, and is generally considered more difficult to measure and to interpret than waist circumference. Based on this evidence, particularly the recent data of Pischon et al (66), it is proposed to measure waist circumference, in addition to the more traditional measure of obesity - BMI, in the proposed study.

7.2.5 Chronic Obstructive Pulmonary Disease Respiratory Function

Chronic Obstructive Pulmonary Disease (COPD) is the fourth leading cause of death in the western world and the only one of the six leading causes of death that is increasing steadily since 1970 (67). Whereas mortality from coronary artery disease and stroke has decreased by 60% since 1965, mortality from COPD has increased by 163% (68). The results from epidemiological and family studies provide evidence for genetic factors as contributors to chronic obstructive airways disease susceptibility (66). Cigarette smoking is by far the most important environmental risk factor for COPD, but less than half of all heavy smokers develop COPD. This indicates a genetic contribution to the individual disease susceptibility. It is therefore important to measure phenotypes and to perform genome-wide scans of COPD patients in order to unravel the contribution of the COPD susceptibility genes. While genetic studies to date appear to have focused on candidate genes implicated in the pathogenesis of the disease the performance of large genome-wide association studies will allow the identification of new genes involved in COPD.

Alpha-1 antitrypsin deficiency (AATD) is the only known genetic risk factor for the development of COPD. Alpha-1 antitrypsin deficiency is caused by mutations within the AAT gene. Recent Irish studies indicate that AATD may be twice as prevalent as previously estimated, with one of the highest incidences in Europe (70). Large studies with extensive coverage of candidate genes have identified genetic variants that may contribute to the disease (71). The GeneLibrary Ireland collection provides the opportunity of combining data with similar collections to achieve statistical power for genome-wide association studies that offer the prospect of identifying new genes involved in COPD susceptibility and genetic modifiers of disease phenotypes. Spirometry will be used to test for pulmonary function.

7.2.6 Cognitive function, mental health and neuropsychiatric disorders

GeneLibrary Ireland proposes measures in three related domains: Cognitive, Mental Health, and Neuropsychiatric disorders. All measures are well validated, widely used, and have established population norms and are all known to have substantial genetic components.

Cognitive function
General and specific aspects of cognitive performance are highly heritable across the span of life (72). A potentially distinguishing feature of GeneLibrary Ireland would be the capture of detailed cognitive phenotype information on a large cohort. Core measures proposed will overlap with the Generation Scotland project. GeneLibrary Ireland will include more comprehensive data than larger studies such as UK Biobank. With access to high-throughput genotype data (for example 1 million SNP data), this could address questions such as:

1. Whether sequence or structural genomic variation has subtle phenotypic effects on normal cognitive function
2. What are the general population effects of genes implicated in abnormal cognitive function?
3. What is the role of cognitive genes in modifying risk for mental health and other disorders or general health outcomes?
4. What genetic pathways are involved in social cognition (which may be relevant to rarer disorders such as autism?)

Measures of cognitive function that will be administered during the visit to the clinic are:

- General cognitive ability (IQ) using the Wechsler Adult Reading test, and Raven’s matrices, a non verbal abilities test.
- Memory, using the logical memory task from the Wechler memory scale.
- Executive function, using the Letter Numbers Sequencing task from the Wechler memory scale and the Verbal Fluency Task.
- Social cognition, using the eyes of the mind task.

**Personality and mental health traits**

There is a substantial genetic and neuroimaging literature on the heritability and biological basis of personality and quantitative mental health traits. These traits contribute to risk of major psychiatric disorder and correlate highly with functional performance, quality of life, relationships, and general health outcomes. From a stress vulnerability perspective psychological characteristics (for example, Type A personality) are highly predictive of increased risk for a variety of psychological and physical health problems (for example Cardio-vascular disease, Cancer, Depression).

The following measures will be administered as part of the questionnaires;

- Eysenck Personality Questionnaire–revised: The Eysenck Personality Questionnaire-Revised (EPQ-R) provides a measure of three dimensions of personality and is the most recent in the series of measures developed by the Eysneck HJ and Eysneck SBG. The main advance is the revision of the third major dimension-Tough-Mindedness which includes the addition of six items to clarify this scale. This revised scale deals with normal behaviours which become pathological only in extreme cases and the term ‘tough-minded’ is suggested in use with non-pathological samples. The traits measured are P-Psychoticism or Tough-Mindedness, E-Extraverssion, N-Neuroticism or Emotionality and L-Lie. (73)
- Schizotypy assessment: Attenuated psychotic experiences are even more common in the general population (74). These may overlap genetically with more severe forms and have an uncertain clinical course. The Community Assessment of Psychic Experiences (CAPE) (75) is a 42-item self-report questionnaire which is used to measure attenuated psychotic experiences.

**Neuropsychiatric disorders**

Mental disorders including schizophrenia, bipolar affective disorder, recurrent major depression and substance abuse have a substantial impact on global disease burden and are significantly heritable (76). In terms of Disability Adjusted Life Years (DALY’s) unipolar depression accounted for 10 million DALY’s, number one on the list and accounting for 8.2% of the total disease burden for developed countries. Also in the top 10 are Alzheimer’s and other dementias (number 4), and alcohol use disorders (number 5). The major psychotic disorders (schizophrenia and bipolar disorder) are a substantial public health concern. These are substantially heritable, have a complex genetic aetiology and a combined population prevalence of ~2%.

Approximately one in 10 people in Ireland will have a lifetime major depressive episode and national rates of alcohol consumption and problem drinking are among the highest in Europe (77).
Major depression, alcohol and nicotine dependence are sufficiently common to justify investigation as primary phenotypes proposed for GeneLibrary Ireland but are also important risk factors for other mental and physical morbidity. A project of this nature offers an opportunity to investigate complex relationships between mental and physical disorders and genetic and environmental risk factors for common disease. The diagnosis of life-time major depressive disorder, problem drinking/alcohol dependence and nicotine dependence can be established using reliable diagnostic instruments (e.g. screening using the Structured Clinical Interview for DSM-IV (SCID) (78). Information on these disorders is available in other biobank resources (e.g. Generation Scotland, UK BioBank). The ability to re-contact participants would add substantially to the value of this information in GeneLibrary Ireland. In particular, this would allow assessment of the relationship between genetic risk factors and illness development, course and treatment response as well as formal testing of risk prediction.

The following neuropsychiatric disorder screening tool will be administered as a part of the questionnaires.

- **General Health Questionnaire (GHQ):** The most common assessment of mental well-being is the GHQ. Developed as a screening tool to detect those likely to have or be at risk of developing psychiatric disorders, it is a measure of the common mental health problems/domains of depression, anxiety, somatic symptoms and social withdrawal. Available in a variety of versions using 12, 28, 30 or 60 items, the 28-item version is used most widely. This is not only because of time considerations but also because the GHQ28 has been used most widely in other working populations, allowing for more valid comparisons (79).

- **Depression:** The SCID-I/NP instrument is used in studies in which the subjects are not identified as psychiatric patients (for example, community surveys, family studies, research in primary care) and therefore would form a valuable tool to examine depression in participants within GeneLibrary Ireland.

### 7.3 Participant Contact & Appointment

As previously discussed the generation of GeneLibrary Ireland cohort lists and initial contact with potential participants will be facilitated through a third party, specifically retained for this project. Details of participants who express an initial interest in becoming part of the study will be passed to the nearest CRC, where the dedicated research team will engage with the participant. As part of this initial contact the participant will be sent a pack of information to include

- GeneLibrary Ireland Information booklet
- Participant information leaflet
- Details of the medical assessment that they will undergo
- Consent form
- Information on questionnaires
- Contact details of research team to arrange an appointment

Through this pack of materials participants will have the opportunity to consider the project in detail and if still interested in participating will contact with the research team in the CRC to arrange an appointment.

### 7.4 Questionnaires

GeneLibrary Ireland proposes to collect extended phenotypic measures which will facilitate genotype-phenotype studies. To enable the collection of this phenotypic information and to reduce both the burden on participants and the time required for the clinic visit, the questionnaires will be delivered in two formats, one as part of the clinic visit and a second post visit questionnaire. The post-visit questionnaire will be followed up with a telephone call from the research nurse to ensure that the participant has completed the questionnaire and to assist the participant with any difficulties. This telephone call will facilitate the completion and return of the post visit questionnaire to the CRC. This questionnaire has been developed based on that from Generation...
Scotland and GeneLibrary Ireland has received approval from the Generation Scotland’s Executive Committee for its use. This questionnaire has also been correlated closely with the Data-SHaper tool developed by the P3G Consortium to ensure international harmonisation. This will facilitate the comparability of data with other international collections and maximize its potential use. The cognitive function, mental illness and neuropsychiatric disorder questionnaires are international validated tools and GeneLibrary Ireland proposed to use these in their original format, with permission from the originators, to ensure that the data collected will be directly comparable to other international studies (73-75, 78, 79).

The information to be collected as part of these questionnaires includes the following:

- **Clinic-visit questionnaire**
  - A. Personal Details
  - B. Personal and Family Health
  - C. Family History
  - D. Smoking History and Exposure to Tobacco Smoke
  - E. Alcohol
  - F. Personality and Mental Health trait measures – Community Assessment of Psychic Experience.

2. **Post-visit questionnaire**
   - H. Medication
   - I. Educational and Occupational History
   - J. Siblings
   - K. Household
   - L. Income
   - M. Personality and Mental Health trait measures
   - N. Neuropsychiatric Disorder Screening tools

The proposed GeneLibrary Ireland questionnaires are detailed in Appendix 5.

7.5 **Visit to CRC**

The visit to the CRC is the core element of GeneLibrary Ireland.

This visit will be key to:
- Ensure participants have all necessary information about the project
- Obtain informed consent
- Describe and explain the touch screen and post-visit questionnaires
- Perform the medical examination
- Collect blood samples

Recognising the fact that participants are giving freely of their time to support this project, it will be GeneLibrary Ireland policy that waiting time is kept to an absolute minimum (less than 10 minutes) and that total visit time is less than two hours, where practicable. The CRC visit will be composed of the following key stages;

7.5.1 **Overview of the Project**

The research nurse will take the time to describe GeneLibrary Ireland and answer any questions that the participant may have. Information materials developed by the communication officer will form the basis of this description, to ensure consistency of message.

7.5.2 **Consent**

The research nurse will discuss the participant information leaflet and consent form with the participants. All sections of the forms will be discussed in detail and any concerns of the participant will be answered, prior to the consent form being signed. A copy of the consent form will be given to the participant for their own records. The use of the CRC infrastructure for GeneLibrary Ireland
will ensure that all the research nurses involved in delivering this project have significant experience in the informed consent process.

7.5.3 Review of questionnaires
The research nurse will assist the participant with the visit questionnaire as required and check for accuracy and consistency on completion. The post-visit questionnaire will be explained to the participant. Specifically, any components of the questionnaire, which the participant needs guidance on, will be explained and discussed in depth. Following completion of the questionnaire, it will be uploaded automatically to the participant information management system.

7.5.4 Medical History & Examination
The research nurse will record the participant’s medical history as part of a structured interview. This will be recorded using standard approaches and data collected will be entered on the study specific clinical research form (CRF).

Medical examination will include:
- Vital Signs
- Biometrics
- Symptomatic
- Vision
- Hearing
- Autonomic Function
- Resting ECG
- Spirometry
- Blood Pressure

As a key part of the GeneLibrary Ireland policy any finding in the clinical examination that requires immediate attention, will immediately be escalated to the CRC Clinical Director for advice on how to proceed.

7.5.5 Sample collection
Having completed the initial medical examination the research nurse will proceed to draw blood samples from the participants. As with all elements of the clinic visit approved, harmonised SOPs will be used during sample collection. The CRC research nurses have significant experience in blood collection. An overview of the sampling is shown in Figure 5 overleaf.
The following samples types will be collected from each participant as outlined in the Table 6 below.

<table>
<thead>
<tr>
<th>Type of sample</th>
<th>Volume collected (ml)</th>
<th>Assay</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDTA</td>
<td>6ml x 3</td>
<td>DNA</td>
</tr>
<tr>
<td>EDTA</td>
<td>6ml x 1</td>
<td>Chemistry</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HbA1c</td>
</tr>
<tr>
<td>EDTA</td>
<td>6ml x 1</td>
<td>FBC</td>
</tr>
<tr>
<td>ACD</td>
<td>6ml x 1</td>
<td>Lymphocytes</td>
</tr>
<tr>
<td>Serum /EDTA P100</td>
<td>6ml</td>
<td>Proteomics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metabolomics</td>
</tr>
</tbody>
</table>

Table 6: The sample types to be collected from GeneLibrary Ireland participants

7.5.6 Clinical Analyses
GeneLibrary Ireland considered the option of processing all clinical samples in a centralised laboratory to facilitate reproducibility and lack of variability of results. However it has been agreed
that the hospital laboratories located in the vicinity of the CRCs involved in GeneLibrary Ireland have well established quality assurance schemes in operation, have or are in the process of acquiring accreditation to CPA and/or ISO 15189 standards and therefore the variability in the results of the analytes listed below are not be considered significant. In addition the proximity of the local hospitals to the CRCs will ensure that the results of the clinical analysis are likely to be returned to the CRCs on the same day to facilitate a more efficient feedback of these results to participants. This will also save on courier costs for same day transfer of samples for analysis to the central laboratory. It is proposed that the following will be assayed as part of GeneLibrary Ireland:
  - FBC
  - Total cholesterol and HDL cholesterol
  - Urea & Electrolytes
  - Liver function tests
  - Triglycerides
  - HBA1c

7.5.7 Biosampling for GeneLibrary Ireland
In addition to sampling for immediate clinical analysis, as outlined above, additional samples will be collected for use in GeneLibrary Ireland. These include samples for lymphocyte preparation, DNA extraction and serum and plasma storage. Samples will be barcode labeled at the CRC and transferred to the central processing laboratory.

The processing of these samples is detailed in chapter 8.

7.6 Completion of Participant record
Once completed all information pertaining to the participant will be uploaded onto the participant management information system. Results of clinical analyses will be uploaded once received from the hospital laboratory. In addition this information will be used to produce a standardised report for return to the participant and / or their GP once complete.

7.7 Visit close Off
Following conclusion of the clinical visit, the research nurse will thank the participant for giving generously of their time to enable the project. Before leaving the CRC participants will specifically be
  - Asked to confirm whether they would like to be kept up to date on the GeneLibrary Ireland through newsletters etc.
  - Asked to confirm if they would like their health assessment results to be forwarded to their general practitioner.
  - Given answers to any outstanding questions.
  - Given the contact details of the nurse who completed their visit should they have any follow up questions.
  - Provision of a lunch voucher for the local hospital restaurant.
  - Asked to agree a date and time to receive a telephone call from the research nurse to discuss and complete the post-visit questionnaire.

7.8 Conclusion
The contact with participants, from initial identification to visit close off will be delivered through the network of CRCs. The embedding of GeneLibrary Ireland within this state-of-the-art clinical and translational research infrastructure will ensure that the participant experience is positive and that the data and samples collected are of the highest quality. The phenotypic measurements proposed will provide a comprehensive picture of the health status of each participant and will ensure the utility of the collection across a host of investigational domains.
8.0 Sample Processing and Management

8.1 Introduction

The collection of an integrated, harmonised bio-resource is the major objective of GeneLibrary Ireland. This resource will be constructed in a uniform manner across all sites. A comprehensive picture of the mechanism for storage and processing of the biological samples collected has been developed. It is recommended that a single central sample processing facility should be developed for GeneLibrary Ireland to ensure standardisation of sample handling. In addition two independent, identical storage facilities are created to store the samples. This splitting of stored material across two independent provides a backup for disaster recovery. All aspects of the sample collection and processing will be piloted extensively and centralised training of CRC research nurses on all requirements for GeneLibrary Ireland will be conducted prior to initiation.

In defining the procedures for sample processing and management international best practice guidelines such as ISBER and OECD guidelines and those available through the P3G Consortium will be used to ensure international harmonisation (80, 81).

8.2 Sample Management

As previously discussed a central element of GeneLibrary Ireland is the development of a comprehensive, integrated data management system. A key element of this system will be the interface between the coded participant record and the sample. Specific components of the biobank information management system described in section 6.3 and detailed further below.

Bar code labels will be printed with a linear barcode that includes human readable indication of contents. Each specimen will have a label that tightly adheres under all projected storage conditions. Labels which are resistant to all common laboratory solvents will be used. The BIMS will ensure specimens can be tracked effectively from the site at which they are collected through their arrival and subsequent shipment from the central laboratory. An inventory system will be in place that tracks the location and status of every sample in GeneLibrary Ireland. GeneLibrary Ireland will ensure that the time of sample collection and the critical steps of the processing and freezing procedures will be documented.

This inventory system must;

1. Track sample identifiers such as sample ID, barcode ID, date of collection and sample type.
2. Include information on the availability, volume and concentration of aliquots.
3. Include information as to the history of sample movement, sample thaws (as appropriate), and shipment to and from external sites.

8.3 Immediate Processing at Collection Site

Processing of blood samples at the collection centres will be minimal. After collection of a complete set of vacutainers, the unique bar-code on each one will be scanned into the Collection centre IT system that links each vacutainer with the unique participant identifier number. This is important to link the participant data from the CRC with the start of the laboratory data structure in the central Laboratory Information Management System (LIMS).

CRC processing will include

- Serum Preparation
- Plasma Preparation
- Transfer of serum and plasma to new containers
- Addition of DMSO to ACD tube for subsequent lymphocyte immortalization (82)

8.4 Sample Shipping

Following collection and initial processing at local CRC sites, samples will be shipped to the central laboratory. SOPs governing the packaging and shipping of samples will be put in place and
harmonised across all centres. To reduce courier costs it is envisaged that samples from each centre will be sent to the central laboratory in batches.

The following Samples will be shipped to the central facility;
- EDTA
- Serum
- Plasma
- ACD

Recognising the importance of careful control of sample handling and transporting the following will be implemented for GeneLibrary Ireland.

**Transport Log**
Each centre will maintain a Transport Log to record shipments to the central laboratory. This log will be included in the functionality of the BIMS described above. Each transport entry will be given a unique transport number. The Log will track the following elements:
- Transport Number
- Recipient/Source
- Date received or shipped
- Courier
- Sample description
- Number of samples received or sent
- CRC details

### 8.5 Central Laboratory Standard Operation Procedures Manual
It is envisaged that the central processing laboratory will work towards ISO9001 certification. GeneLibrary Ireland will develop written policies and procedures in a standardised format incorporated into a Standard Operating Procedures (SOP) Manual. These SOPs shall state policies and define and describe in detail, all procedures to ensure that all samples are received, handled, processed, stored and disseminated for subsequent research and other uses in a standardised manner. The National Cancer Institute has published guidelines on ‘Best Practice for Biospecimen Resources’ which proposes policies and procedures for inclusion in an SOP manual some of which are included in the list below to ensure international harmonisation (83).

- Specimen handling policies and procedures including supplies, methods and equipment.
- Laboratory procedures for sample processing and tests performed in-house and any specimen aliquoting or other specimen processing.
- Policies and procedures for shipping and receiving specimens.
- Records management policies.
- Quality assurance and quality control policies and procedures for supplies, equipment, instruments, reagents, labels, and processes employed in sample retrieval and processing.
- Policies regarding safety programmes.
- Emergency and safety policies and procedures, including reporting of staff injuries and exposure to potential blood-borne pathogens.
- Policies and procedures for the investigation, documentation and reporting of accidents, errors, complaints and adverse outcomes.
- Policies and procedures and schedules for equipment inspection, maintenance, repair and calibration for the purpose of maintaining equipment.
- Procedures for disposal of medical waste and other hazardous waste.
Policies and procedures describing requirements of training programmes for all staff.

8.6 Processing at Central Laboratory
It is anticipated that over a two year period approximately 40 participant sample sets daily will arrive at the central laboratory for processing, (based on 5-day week, 50 weeks/year). When the participant samples arrive at the central laboratory they are logged into the Laboratory Information Management System (LIMS). The samples in the transport containers must match the sample identifiers expected from the collection centre. The vacutainers will then be processed using automated systems, with times and temperatures of all operations and operator identifiers logged in the LIMS. Processing of samples at the required throughput and quality will be efficiently carried out and monitored by trained personnel.

8.6.1 DNA Extraction
DNA extraction will be performed using an automated system an example of which includes the AutoPure system purifies DNA from blood samples as large as 10 mL using Puregene chemistry and results in a large quantity of high quality nucleic acids. The Puregene DNA chemistry is based on a modified salt precipitation method. Ten mL of whole blood typically yields 350ug of high molecular weight DNA that is 100-200 kb in size (84).

8.6.2 Sample Storage
It is recommended that two separate storage facilities for GeneLibrary Ireland biological materials be developed. It is anticipated that one storage facility will be located in each jurisdiction. Samples from each participant will be stored in two geographically separate locations in order to protect the resource from loss. One location will house the “working” archive that will typically be used first for any research project. The other location will house an identical liquid archive that will be used when samples in the working archive have been exhausted. All regulations and standard operation procedures of the biobank will apply to the operation of the back-up storage sites.

All samples will be stored in manual liquid nitrogen archives, with the exception of two aliquots each of plasma and serum held at -80°C in separate freezers, as well as four aliquots of purified DNA held at -20°C.

Fractions and aliquots of blood samples stored for each participant are represented in table 7 below.

<table>
<thead>
<tr>
<th>Vacutainer Tube</th>
<th>Fractions</th>
<th>Number of Aliquots</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Liq N2</td>
</tr>
<tr>
<td>EDTA X 3</td>
<td>DNA extraction</td>
<td>4 (-20°C)</td>
</tr>
<tr>
<td>EDTA</td>
<td>Plasma</td>
<td>4</td>
</tr>
<tr>
<td>ACD</td>
<td>Lymphocytes</td>
<td>1</td>
</tr>
<tr>
<td>Serum Tube</td>
<td>serum</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 7: Fractions and aliquots of blood samples stored for each GeneLibrary Ireland participant.
8.7 Specimen Retrieval

The procedures recommended below assume retrieval of frozen specimens from freezers for distribution, but are applicable to other storage conditions and equipment.

Retrieval of specimens for shipment or analysis requires strict adherence to protocols for proper specimen inventory and tracking, as well as adherence to established safety standards in working with freezers and other storage equipment.

Locating Specimens in Storage
Specimens to be retrieved must be located in the appropriate specimen inventory system and will be verified against their unique identification coding. A specimen requisition will be generated according to procedures applicable to the LIMS tracking and inventory system. The requisition will be checked for accuracy before transmission to the biobank, according to established SOPs and QC standards.

Specimen Retrieval
At the central laboratory specimens will be located and retrieved as documented on the specimen requisition and in accordance with SOPs.

Documentation of Retrieval
The specimen retrieval process will be documented and include the steps taken to confirm completeness of the process, to document shipment, and to conduct quality checks according to the SOP.

Principles for international specimen exchanges
Many countries have adopted safeguard mechanisms and regulations to ensure the security of specimens and associated personal data as well as to protect the right of ownership and intellectual property that may stem from research conducted using biospecimens collected on their national territory. An international compilation of human subject protection has been compiled by the Office for Human Research Protections of the US Department of Health and Human Services (http://www.hhs.gov/ohrp/international/HSPCompilation.pdf). In addition, reference will be made to the OECD global biological resource centre networks (85). These principles will also be considered in the context of BBMRI so it will be important that GeneLibrary Ireland ensures that its policy for international exchange of samples will be compatible with these guidelines. In several instances, however, these measures may tend to impose restrictions on international specimen exchanges, thus having a detrimental effect on developing large, multi-centric studies. It is therefore important to develop international procedures to facilitate and oversee human specimen exchanges that respect the principles of national and international regulations on human subject research protections. Under such procedures, studies that meet a number of conditions may be granted a waiver of restrictions on specimen exchanges.

8.8 Representative cohort of cell lines
As part of the GeneLibrary Ireland planning process, significant consultation was made with investigators both in Ireland and abroad to gauge opinions on optimal study design. A recurrent theme of these discussions was the need to future-proof the bioresource to ensure continued availability of DNA from the cohort. For example, it has been noted that techniques involving epigenetic analysis require significant amounts of DNA, and thus will provide a significant draw on the library. It is anticipated that there will be a very strong demand for GeneLibrary Ireland samples from researchers in Ireland and Northern Ireland along with international investigators. In this context it has been recommended to lay down lymphocyte cell lines from each participant. This will allow GeneLibrary Ireland to meet future demand for significant draws on the resource, by providing a collection of cell lines which will subsequently be available for immortalisation. Epstein-Barr virus (EBV) is able to immortalize human B-lymphocytes with high efficiency, and thus can be used as a strategy to produce immortalised cell lines to provide a continued supply of DNA (86).
It is recommended that lymphocytes on a subset of participant samples laid down as part of the sampling phase, be immortalised using EBV. This activity can be outsourced to external agencies such as Health Protection Agency Culture Collections (HPACC) in the UK. Once a cell line has been successfully established, a bank of four ampoules is generated and stored in the ECACC Cryostorage facility. Sample progress is tracked using a purpose built Laboratory Information Management system, linked to electronic inventory management software. As part of routine quality assurance, all cell banks are screened for freedom from mycoplasma, and a proportion of every batch is tested for sterility, cell count and viability and authenticity against source material (blood spot card prepared at receipt) using STR-PCR profiling. The process takes approximately five to six weeks to complete.

It is proposed that initially 3,000 cell lines would be generated in this way. This would add substantial value to GeneLibrary Ireland by providing a long term sustainable source of DNA for the research community. Additional funding for immortalisation of the other 7,000 lymphocyte preparations would be sought from other sources in the future.

8.9 Conclusion

The key processes have been defined to ensure that GeneLibrary Ireland remains a useful resource for the biomedical research community. Specifically the policies and procedure detailed herein will provide for the creation of a bio-resource, which can be seamlessly integrated, with established and ongoing international bio-collections.
9.0 Impact of GeneLibrary Ireland on Ireland’s Biomedical Research Landscape

9.1 Introduction
The creation of this landmark biomedical research infrastructure will add significant value to the all-island research enterprise and afford all stakeholders the opportunity to heighten the impact of ongoing clinical and translational research. This bio-resource can be further developed to enhance its impact on the research landscape, in both the all-island and international context.

9.2 Genetic Analysis of GeneLibrary Ireland

9.2.1 Control sample genotypes
The Wellcome Trust Case Control Consortium genotyped 3,000 samples taken from different regions of Britain and used as shared controls to map variants associated with seven common diseases (20). The Consortium serves as a prototypic study. An important output of GeneLibrary Ireland will be to furnish a cohort of genotyped controls from Ireland and Northern Ireland which may then be compared in subsequent studies to case collections sampled outside this project. A large control sample is also desirable as this may compensate somewhat in study power for limited case numbers (as is often the case in rarer diseases). Furthermore a large sample is helpful as there is known genetic structure on the island of Ireland itself (some allele frequencies can differ by up to 10% between East and West coast communities and some diseases show different incidence) (41). The 10,000 control sample will afford the opportunity to subsample controls in order to match geography and/or genetic background within case collections from the island.

9.2.2 Genotyping GeneLibrary
Ideally the genotyping of the control DNA library should be completed as part of this study, to maximise the scientific impact of this infrastructure. GeneLibrary Ireland should at a minimum use a standard genome wide SNP genotyping panel to map associations to interesting traits collected from sample volunteers. The current state of art is to use a 0.5 or 1 million SNP genotyping chip with allied detection of copy number variation (CNV). The amount of SNP markers are unlikely to increase beyond the present number in the near future as current numbers more than sufficiently cover the genome. SNP markers may be fully integrated with second generation sequencing applications should and when their use becomes cost effective. Improved CNV content has already been added to the current versions of chips. This data will be co-analysed with phenotypic data to identify novel gene-trait associations. One approach would be to subsample the whole population sample for cases and controls for each trait of interest. However, a simpler strategy would be to genotype all 10,000 samples to facilitate the same data being used as a control reference population. Genotyping of the GeneLibrary Ireland sample set could be completed within three month time lag of the collection and processing of DNA samples. Recognising the substantial investment required to genotype the complete library, it has suggested that an initial 3000 samples would be genotyped using high density SNP chips equivalent to the state of the art technology at this time. This sample size will be equivalent to that genotyped by the Wellcome Trust Case Control Consortium. Based on this initial data set, a subsequent funding application would be submitted to finance the genotyping the remainder of the cohort.

9.2.3 Defining Genetic Composition of the population of the island of Ireland
The generation of a minimum level of genotype data will give a scientific output which is integral to GeneLibrary Ireland, rather than having its focus solely as a resource generation for subsequent work. The typing and analysis of data will have utility in three important ways. First, it will allow a linkage between the interesting and medically important traits recorded in the sample collection and genotype. Second, it will provide a large control sample for genotype-phenotype association studies carried out in linked studies. Third, it will contribute to population genetic studies which co-analyse Irish genetic variation with data emerging from other European populations and make novel inference about the past biology of the island’s population.
The balance of effort in the scientific community has shifted radically in recent years from generation of genotypes towards standardised collection and accurate phenotyping of samples. This is because of the availability of relatively inexpensive, high-throughput genotyping technologies, which are capable of calling SNPs throughout the genome at a density sufficient for genome wide association studies. Genotyping is now relatively cheap, whereas sampling and analysis are expensive. In the last 18 months there have been many quality publications which have pinpointed genes with effects on complex human traits; for example being type 2 diabetes the number of susceptibility loci robustly identified has climbed from two to 20 in this period (87). This methodology is now routine.

9.2.4. Inferring the past

An indirect output of a baseline genotyping of the sample collection will be data which may be used in conjunction with genome wide SNP data from other European populations to make novel inference about the migrations and other features of past demography on the Atlantic façade of Europe. First generation studies of the genetic diversity of Ireland have been performed with some interesting inferences emerging (88). However, the advent of new technologies will enable a deeper examination of the historic forces that have shaped the genomes of this island. For example, it should be possible to better model the timings and natures of past migrations to our shores. Also, it will afford an opportunity to detect population genetic signatures of selection around particular genes that is to infer at which loci variation existed that was a matter of life and death for our ancestors. Importantly, the genetics of the Irish population is interesting because of our peripheral location and will have relevance to broader genetic geographical issues when placed in the broader context of these islands and Western Europe.

9.3 Underpinning Health Research in Ireland and Northern Ireland

The establishment of GeneLibrary Ireland will have a transformative effect on the biomedical research landscape at an all-island level. Specifically this landmark project will:

- Provide an unprecedented bank of control material for disease gene association studies.
- Enhance fundamental expertise in biobanking.
- Establish a framework for all-island collaborative genetic research.

Over the last number of years, researchers in Ireland and Northern Ireland have contributed to world class research in identifying genes that play a key role in disease susceptibility and risk (6-11). Some of these genetic research studies include the identification of genes associated with the Irish schizophrenia population (6), the expression of an airway epithelial gene in the diagnostic evaluation of smokers with suspect lung cancer (7), the demonstration of a role for the DNA repair genes, XRCC3, XRCC4, XRCC5 in the aetiology of myeloma (8), the recognition of seven new genes associated with coeliac disease (9), the detection of mutations in the gene encoding filaggrin that cause ichthyosis vulgaris and predispose to eczema and secondary allergic diseases (10) and the identification of a role for the gene NET1 in the development and progression of gastric cancer (11). The establishment of GeneLibrary Ireland will add substantial value to ongoing genetic research in Ireland.

A number of investigators in Ireland and Northern Ireland conducting genetic research studies expressed interest in using the GeneLibrary Ireland bio-resource once established. In addition, industry groupings are extremely supportive of the establishment of GeneLibrary Ireland and believe that it will be particularly useful in the area of research and development, for example in pharmacogenetics and pharmacogenomics.

9.4 Enabling Additional Research

As previously discussed, the questionnaires that participants will complete will collect detailed information on health and lifestyle. These data will serve to underpin ongoing health and social sciences research in Ireland by providing a comprehensive dataset, linked to clinical and genetic information.
The World Health Organisation has reported that, on a global scale in the period up to 2030, there will be a dramatic shift in the distribution of deaths from younger to older people and from communicable to non-communicable diseases, with the leading causes of death likely to be ischaemic heart disease, cerebrovascular disease, HIV infection and COPD (89). Most of these diseases are complex, reflecting the interaction between genetic and environmental influences. Central to understanding environmental factors is an understanding of the effect of lifestyle, including diet and physical activity on the evolution of disease.

9.5 Conclusion

The creation of GeneLibrary Ireland will transform the all-island research agenda through;

- Defining the genetic composition of the population on the island of Ireland
- Underpinning genetic research
- Inferring the genetic history of the population of the island
- Defining genes associated with common diseases that impact patients in Ireland and Northern Ireland which in turn will lead to improved understanding of disease mechanisms, therapeutic discovery and advances in personalised medicine
- Facilitating collaborative on the island and internationally
10.0 Economic and Social Benefits

10.1 Introduction

Through the creation of this unique all-island collaborative resource, GeneLibrary Ireland will deliver substantial value to the biomedical research community in Ireland and Northern Ireland.

Specifically GeneLibrary Ireland will;

- **Embed** all-island, trans-institutional partnership in the research landscape.
- **Build** on the collaborative research networks being established by ICRIN and NICRIN.
- **Drive** Ireland and Northern Ireland’s involvement in landmark EU wide research programmes.
- **Strengthen** ongoing research endeavours within the island.
- **Provide** a snapshot of the genetic composition of the population of Ireland and Northern Ireland.
- **Support** delivery of Ireland’s aims under the strategy for science, technology and innovation.
- **Develop** a key research infrastructure as delivered in FORFAS research infrastructure report.
- **Implement** the transformation objectives of the health research board’s strategy – making knowledge work for health.
- **Underpin** the development of Ireland’s knowledge economy.

The benefits from GeneLibrary Ireland will contribute to the transformation of the research landscape and enable the island’s ambition to be a world leader in biomedical research.

10.2 All-Island Research

Gene Library Ireland presents a unique opportunity to shape the research landscape in Ireland and Northern Ireland and influence research strategy for long term growth and sustainability. We emphasise that the establishment of GeneLibrary Ireland will send a positive signal to the research community at an all-island level and internationally regarding our research ambition and focus. The GeneLibrary Ireland initiative has already added significant value by bringing together a multidisciplinary group from across the Island of Ireland. MMI has united representatives from seven institutions across two jurisdictions together with the patient representatives all of which are key clinical, academic, and patient stakeholders. It is clear that significant capacity and capability in terms of infrastructure and skills for undertaking a diversity of population genomics and personalised medicine research already exists in Ireland and Northern Ireland. However, a weakness that exists is that the key players are generally not well “connected” across the island as a whole.

The Matrix Report on Technology Capability in Northern Ireland (undertaken by the Department of Enterprise Trade & Investment – DETI Northern Ireland Science & Industry Expert Panel) and Northern Ireland benchmarking exercise recently concluded that:

“...the scientific capability and the innovation it brings is currently fragmented in Northern Ireland…and “it is the connectedness between these aspects that appears to be the most critical missing item”.

It also stated that:

“NI is trailing the rest of Western Europe, the USA and Eastern Countries in terms of the overall technology innovation performance. However, the basic building blocks necessary to build a platform for rapid improvement are already in place in terms of extensive highly competitive capability in R&D, excellent schooling and overall intellectual infrastructure.”
On an all-island basis this lack of connectedness is further compounded by the practicalities of navigating two separate legislative frameworks that relate to healthcare, ethics, patient records, etc. that are perceived as additional obstacles to undertaking population-based research. Therefore a key objective of GeneLibrary Ireland will be to address this lack of connectedness and develop practical solutions to better connect the plurality of embedded multidisciplinary expertise. Such a resolution of the trans-jurisdictional issues will not only serve the objectives of GeneLibrary Ireland but also serve as model of best practice for other initiatives.

GeneLibrary Ireland as a biomedical infrastructure at an all-island level will better connect the research community and associated stakeholders, with the primary objective of identifying the key genetic determinants of common disease in both jurisdictions. This would provide a multidisciplinary critical mass that could drive Irish participation and involvement in other European and international biobanking initiatives, for example the Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) and the Public Population Project in Genomics (P3G) Consortium which will be discussed in more detail in section 10.8. Such an all-island biomedical infrastructure, will act as a key driver for international harmonisation generally, and ensure that Ireland is strategically positioned to participate in future international genomic studies and attract significant additional funding.

10.3 Public perception / education

Participation in GeneLibrary Ireland will depend on whether or not the public is convinced that giving blood and DNA samples along with detailed clinical and medical information is a positive action. People’s motivation to act will depend on their level of understanding and perception of GeneLibrary Ireland and the associated benefits. GeneLibrary Ireland will develop and deliver a timely, well executed communications strategy which will raise and sustain public understanding and create positive perceptions around biobanking and the benefits of conducting genetic research studies aimed at understanding disease process and developing new therapies and tests. GeneLibrary Ireland will ensure that a major part of the communications strategy is to educate and build understanding. This will be addressed through the development of an interactive, informative and functional GeneLibrary Ireland website which will include a section specifically for the public along with the results of research studies conducted in group format, the design of information pamphlets, a local media and radio campaign and a community outreach programme. Engagement with the public will also afford the opportunity for ‘healthy’ people to participate and contribute positively to research studies as part of GeneLibrary Ireland as it may be perceived that only patients can participate in research studies.

10.4 Impacting Healthcare

Biomedically-relevant, quality-assessed samples and data are essential if clinical, academic and commercially-driven research are to treat and prevent common and rare human diseases. The advancement of biomedical research is dependent upon exploiting the opportunities arising from developments in genetic knowledge and technology. The availability of the complete sequence of the human genome, annotated with a comprehensive catalogue of genes and sites of sequence variation (polymorphisms) coupled with the development of new tools for studying DNA, opens up new possibilities for discovering genetic effects on human health (19). The sequencing of the human genome allows researchers to integrate new data on genetic risk factors with demographic and lifestyle data. Researchers are therefore in a prime position for understanding the causes of illness and disease by merging large volumes of molecular genetic data with clinical, environmental and epidemiological factors. A key objective is to discover how genetic variation influences disease susceptibility. This is because discovering an effect of variation in a gene upon disease susceptibility establishes an unequivocal causal relationship between the gene product (a protein) and the disease or distinction under study. Genetic information, although valuable in itself, does not inform us about the effects of genetic variation on disease risk or traits of importance to human health. To study such effects, access to collections of human biological samples and clinical data is required. It is therefore possible to now begin to explore the important role that genes play in disease and in health, across a whole range of diseases, from Alzheimer’s to coronary heart disease, from diabetes to cancer. Such studies advance understanding of the
molecular basis of disease susceptibility and open up possibilities for developing new preventive or therapeutic approaches, by developing drugs that target the gene product or pathways. In addition, there are certain diseases that are over-represented in Ireland for example coeliac disease and cystic fibrosis which provide a unique opportunity to define the genetic associations with risk and susceptibility to these diseases in the Irish population.

The creation of GeneLibrary Ireland will provide an invaluable collection of samples along with well-annotated clinical and medical data on the population of Ireland and Northern Ireland. This bio-resource will provide the control group to conduct genetic association studies for common diseases that affect the patients on the island of Ireland. Creating an all-island biobanking infrastructure is an important opportunity to add value to existing health research and to avoid duplication of scarce resources.

10.5 Impacting National Strategy

Significant investment has been committed by both the Irish and UK government to the construction and implementation of CRCs in Dublin, Belfast, Cork, Galway and Derry which will be networked via ICRIN in Ireland and NICRIN in Northern Ireland. This in turn will establish a harmonised and world-class clinical research infrastructure that will allow Ireland and Northern Ireland to be competitive in the era of personalised medicine. There is also a collaborative trans-institutional consorted effort to develop specialised disease cohorts, to rapidly adapt clinical measures in response to new knowledge and therapeutics and to deliver high-quality well-identified samples. All such collections need to be undertaken in a manner allowing them to be linked with other similar collections at an all island level where increased sample size is required. GeneLibrary Ireland will not only provide the control bio-resource for these disease networks but also provide a standardised framework for biobanking activities across the island and ensure harmonisation internationally. In addition, the Irish government through the National Cancer Strategy has recognised that biobanks are essential to the advancement of cancer research and has established an Expert Group of the Minister for Health and Children to deliver a report on the establishment of a National Cancer Biobank for Ireland as part of the Cancer Control Programme. GeneLibrary Ireland will work to ensure it is aligned and harmonised as far as possible with such national biobanking initiatives.

GeneLibrary Ireland as an all-island bio-resource infrastructure, will position itself at the centre of translational research activity by developing strong partnerships with all stakeholders involved in healthcare, from the public, healthcare providers, researchers to industry partners. It is key that GeneLibrary Ireland is complementary and linked to current research programmes funded and currently ongoing in Ireland, for example the Irish Longitudinal Study on Ageing (TILDA) and THE Survey of Health and Retirement in Europe (SHARE).

The establishment of GeneLibrary Ireland as a biomedical research infrastructure will provide a benchmark for standardising and harmonising all biobanking activities for the island of Ireland which is currently not in place throughout the island. Furthermore, researchers will not need to secure additional funding from the Agencies to develop individual control groups for each research study funded.

10.6 Underpinning the knowledge economy

The Irish Government, through the Strategy for Science, Technology and Innovation 2006-2013, has recognised the need to ‘upgrade existing infrastructure and develop new facilities to support research’ and has invested significantly towards the establishment of a world class research infrastructure for Ireland through the creation of CRCs, funding biobanking facilities and attracting high quality clinical and translational researchers. The government has highlighted how its strategic vision and commitment to develop Ireland as an internationally renowned centre for excellence in research can be achieved through ‘continued engagement with the EU institutions and appropriate international organisations in a co-ordinated and strategic manner with Irish input being promoted in all areas to ensure the optimum return for our research sector’. In addition, the Advisory Council for Science, Technology and Innovation. Towards Better Health: Achieving a
Forfás report 2006 noted the need to ‘fully exploit the potential for international networking and leveraging funding for health research under the EU’s Seventh Framework programme for Research, 2007-2013’. Participation in international biomedical research infrastructures including BBMRI is fundamental to achieving this vision for the translation of Irish research on the island to an international level. In addition the HRB corporate strategy for 2006 has identified biobanking as a priority for Ireland. In May of 2007 Enterprise Ireland commissioned the CIRCA group to deliver a set of views and recommendations on infrastructural and other initiatives that would improve the environment for creation of economic activity from the expertise and Research and Technology Development activities in the Irish healthcare system. This report identified biobanks as a ‘fundamental requirement for effective healthcare research and for validation of many pharmaceuticals and devices’.

The establishment of GeneLibrary Ireland as a research infrastructure will not only provide a strong framework to support and foster large research studies to identify genetic associations with common diseases in Ireland and Northern Ireland but also allow our researchers to share this bioresource internationally through participation in large statistically powered studies. This bioresource will also provide significant research opportunities to increase the critical mass of PhDs as part of delivering the knowledge economy.

10.7 Addressing industry requirements

As part of the design phase of GeneLibrary Ireland the views of industry groupings including pharmaceutical, medical devices and biotechnology companies were sought to ascertain the value of this biomedical infrastructure for Ireland and Northern Ireland and its impact for indigenous industry. From this consultation it appears that industry is extremely supportive of the establishment of GeneLibrary Ireland and is confident of the value added for the island of Ireland in particular in the area of research and development, for example in the development of pharmacogenetics and pharmacogenomics. This is further supported in the Higher Education Authority (HEA) and Forfás commissioned report ‘Research Infrastructure in Ireland – Building for Tomorrow 2007’ has recognised that ‘genebanks and biobanks’ are a specific research infrastructure requirement for the instrument and medical devices industry in Ireland.

10.8 Driving Ireland’s Engagement in European Research

10.8.1 Biobanking and Biomolecular Resources Research Infrastructure

The Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) is funded by European Framework Programme 7 (FP7) to develop a pan-European biobanking network comprising population-based cohorts, population isolates cohorts, twin registries, clinical case/control studies and will include blood, urine, DNA, tumour tissue samples along with different types of biomolecular resources. In addition to biological materials and related data, BBMRI will facilitate access to detailed and internationally standardised data sets of sample donors (clinical data, lifestyle and environmental exposure) as well as data generated by analysis of samples using standardised analysis platforms. In addition, BBMRI will include a broad spectrum of high-end analysis platforms (high-throughput sequencing, genotyping, gene expression profiling technologies, proteomics and metabolomics platforms, tissue microarray technology etc.) which will be available to members. These platforms will guarantee that the analysis of biological materials is performed with the latest technologies and under standardised conditions, which enables sharing of data generated within the scientific community. This is seen as an important measure to achieve the most efficient use of non-renewable biological materials, which are a limited resource, and at the same time to avoid redundant analyses. Furthermore this will provide the best opportunity to define and correlate healthy, pre-clinical and clinical profiles, and will strongly boost the integrated study of biological and genetic disease mechanisms, improve the delineation of clinical phenotypes and establish biomarker spectra for disease prognosis and therapy monitoring. BBMRI will integrate several ongoing national, European and global projects and initiatives, including research projects funded under FP5 and FP6 as well as new projects under FP7, public/private partnerships which are directly related to the needs of BBMRI. BBMRI will work with the P3G consortium on biobank harmonisation; the strategic research agenda of the
Innovative Medicines Initiatives and the OECD initiative on a global network of Biological Resource Centers. In order to avoid duplication of efforts and to ensure further development and integration of these activities BBMRI has included representation from these projects and initiatives in the work packages and as members on various boards of BBMRI or as external experts. BBMRI has included global leaders of the scientific community and industry from non–European countries on its Advisory Board to ensure that this pan-European research infrastructure will have global relevance and integration.

Biomedically relevant, quality-assessed samples and data as well as associated biomolecular resources, are essential for clinical, academic and commercially-driven research to treat and prevent common and rare human diseases, including cancer, diabetes, cardiovascular disease. Although currently established biobanks and biomolecular resources are a unique European strength, valuable and irreplaceable national collections typically suffer from fragmentation of the European biobanking-related research community. This hampers the collation of biological samples and data from different biobanks that is required to achieve sufficient statistical power. Moreover, it results in duplication of effort and jeopardises sustainability because of the lack of long-term comprehensive funding approaches.

Currently Ireland is an active member of BBMRI through Molecular Medicine Ireland and the HRB both of which are participating in Work package 7, Funding and Financing. In addition Michael Griffith the former CEO of Fighting Blindness has been appointed as Chair of the Stakeholders Group for BBMRI ensuring that Ireland will act as a key player in this European infrastructure. Participation in BBMRI will ensure that GeneLibrary Ireland as an all-island biomedical research infrastructure will be established and harmonised in line with international best practice. In addition researchers in Ireland and Northern Ireland would be able to access large international collections of bio-resources and technologies to facilitate biomarker discovery, drug development, understanding the complex nature of genetic disease which will in turn lead to better understanding of disease pathogenesis and improved health care for the people of Ireland. Furthermore as part of its implementation phase, BBMRI will be looking for pilot projects to build a prototype of the pan-European infrastructure and to demonstrate its feasibility. GeneLibrary Ireland could serve as a key pilot project.

10.8.2 Public Population Project in Genomics (P3G) Consortium

The Public Population Project in Genomics (P3G) is an international consortium for the development and management of an infrastructure to support population genomic studies. The three founding member of the P3G Consortium include CARTaGENE, the Estonian Genome Project and the GenomEUtwin study. The P3G Consortium seeks to foster collaboration, optimise design, promote harmonisation of biobanks and facilitate transfer of knowledge. The P3G Consortium has developed an observatory, which is a central internet repository of scientific information and tools aimed at facilitating the development, realisation and harmonisation of research projects. It includes a series of catalogues documenting large population-based biobanks worldwide and allows the rapid overview of the similarities and differences along with potential for harmonisation between participant biobanks. The consortium has developed the DataSHaPER, which is a series of tools aimed at facilitating harmonization and at supporting biobanks to design questionnaires, and other data-collection devices. This consortium provides a significant resource to the biobanking community globally. In addition the P3G Consortium creates a network in population genomics comprising over 3 million participants for epidemiological studies and thereby provides the statistical power for analysing complex genetic and environmental determinants of health and disease. GeneLibrary Ireland will aim to be harmonised with the P3G consortium and seek membership in the implementation phase to allow this biomedical research infrastructure to be used to its full potential.

10.8.3 European framework programmes

European framework programmes are particularly important for building networks of European partners in academia and in industry to realise multi-disciplinary large-scale research activities and to develop coordinated initiatives to facilitate the translation of research into better diagnostics and treatments for patients. European initiatives funded through FP7 include the European Clinical
Research Infrastructure Network (ECRIN) and BBMRI both of which Ireland participate in through MMI. Ireland’s participation in European framework programmes has allowed researchers on the island to contribute and participate in significant international collaborations including, Nano2Life, the first European Network of Excellence in the area of nanobiotechnology, LIPGENE a large European study on the metabolic syndrome aimed at understanding the interactions between genetics and diet and BLOODOMICS a European collaboration of scientific and medical expertise to identify genetic markers in coronary artery disease. The involvement of Ireland and Northern Ireland in strong international collaborations will afford funding opportunities through subsequent European framework programmes and initiatives to which as an island we would not otherwise have access. GeneLibrary through participation in BBMRI will seek to collaborate on funding opportunities through subsequent European Framework Programmes.

10.9 Measuring the Impact

While it is clear that GeneLibrary Ireland will add great value to the biomedical research landscape on the island it is important to include a number of measures to evaluate its social, economic, healthcare and research impact in the short and long term for Ireland and Northern Ireland. The following elements will be included in the impact evaluation for GeneLibrary Ireland.

1. The level of funding leveraged by research projects involving GeneLibrary Ireland
2. The number of academic and industry applications received to use the biomedical research infrastructure
3. The number of research programmes, both clinical and translation that the biobanking infrastructure provided by GeneLibrary Ireland will support
4. The number of publications, both public interest and peer-review involving this biomedical research infrastructure
5. Internationalisation
   a. To secure GeneLibrary Ireland as a pilot project for the implementation phase of BBMRI
   b. To partake in collaborative applications for funding through FP7 and other European initiatives
   c. Participation in international biobanking networks, including BBMRI and P3G Consortium
6. Innovation
   a. The contribution of the GeneLibrary Ireland bio-resource to indigenous R&D development on the island
   b. The number of patents filed by researchers using the GeneLibrary Ireland resource
   c. The number of licenses associated with research facilitated through GeneLibrary Ireland
   d. The contribution of GeneLibrary Ireland to the development and/or support of spin out companies
   e. The contribution of GeneLibrary Ireland to the development of the biomedical research landscape to support foreign direct investment
7. International recognition of GeneLibrary Ireland through peer review publication and participation in pan-European biobanking collaborative initiatives
8. To evaluate GeneLibrary Ireland’s contribution to public awareness of biobanking and understanding of science

GeneLibrary Ireland as a biomedical research infrastructure will capitalise on investment in the research landscape to date and will provide a strong foundation for future growth in disease research in Ireland and Northern Ireland. The creation of this infrastructure will add significant value to ongoing efforts to position Ireland as an ideal location for clinical and translational research and help to ensure our competitiveness into the future along with fostering strong collaborations between researchers within the island.
11.0 Governance and Management of GeneLibrary Ireland

GeneLibrary Ireland must be well governed if it is to establish scientific credibility and maintain and honour public trust. There exists a large body of common elements for biobanks to use when creating a governance framework which are publicly available on the P3G Consortium website resource (17). These may be classified to include:

- Relevant legislation, regulations and standards

A biobank must adhere to existing legislation, regulations and standards including those dealing with the taking, storage and use of human tissue; human rights; confidentiality and data protection; health and safety and the protection of humans involved in research.

- Scientific and ethical evaluation through professional and institutional guidelines

Proper scientific and ethical evaluation ensures that the scientific project is necessary, has scientific merit, is an appropriate and potentially beneficial use of funds, that the researchers that wish to conduct it are qualified and capable, and that the research has been designed and will be carried out in a credible and ethical manner.

To secure this credibility the governance of biobanks usually includes several committees: for instance, a sample and data access committee ensures that the data and materials are used for scientifically valid and ethical research; a scientific advisory committee determines scientific goals and how they can be reached; a financial committee, and so on.

- Public legitimacy

Public legitimacy of the project is necessary to recruit healthy volunteers to participate as distinct from involving patients in traditional clinical investigations related to their diseases. The GeneLibrary Ireland model does not allow potential participants to be informed of all research purposes for which their donation will be used. Therefore, enough trust must be engendered in GeneLibrary Ireland for the public to give broad consent to unspecified future uses of their material and data. Participants must have also had sufficient trust that the biobank will exercise complete confidentiality in the use of donors’ samples and data during all phases of the project. In addition, public legitimacy will be further enhanced through independent ethical oversight of the establishment of the biobank and future research studies.

GeneLibrary Ireland requires the support of the target population and the population at large. The tax payer wants to know how public money for these projects is being spent. They want to know that it is being properly conducted and under what conditions, and how the results of research will affect them. Public approval in turn affects the Government’s commitment to fund the project. Public legitimacy requires a governance structure that is competent, transparent, and representative of the key stakeholders and that takes account of the different legal requirements in the two jurisdictions.

From the Comparative Guide in P3G, it would appear that to protect and promote the public legitimacy of biobanks, most countries rely on a combination of conformity with legislation, the implementation of codes of good practice, and crucially an investment in a programme of public communication and legitimisation.

The governance arrangements for GeneLibrary Ireland must meet the criteria under each of the headings above. The governance arrangements are complicated by different legal requirements in the two jurisdictions of Ireland and Northern Ireland.

The HRB and R&D Office feasibility report sets out the following parameters for the governance of
GeneLibrary Ireland will have a Board of Management, a scientific steering committee and an executive subcommittee responsible for day-to-day management.

Custodianship of GeneLibrary Ireland and control of the use of the samples will rest with a Board of Management that is representative of all interested parties, with an independent chair and a number of independent members, with no vested interest or conflict of interest.

The Board will be responsible for GeneLibrary Ireland’s central administration and for storage arrangements for the data and the biological samples. The Board will establish a scientific steering committee to develop policy and to oversee applications from researchers wishing to use the resource. This management structure will be developed and implemented by the HRB and the RDO in consultation with interested parties and individuals.

The steering committee of researchers would decide GeneLibrary Ireland’s strategic direction and prepare a detailed protocol; a smaller, executive sub-committee would be responsible for day-to-day management.

GeneLibrary Ireland - An essential new resource to underpin health research in Ireland, HRB/R&D Office, 2005

11.1 Legislation, Regulations and Standards

A number of countries (Estonia, Norway, Sweden, Latvia, France, the UK and Spain) have enacted legislation to regulate the taking, storage and use of human tissue. The storage of relevant biological material in Northern Ireland is governed by the Human Tissue Act, 2004, the provisions of which are detailed in chapter 3. The Department of Health and Children in Ireland has consulted about proposed legislation on human tissue and it is likely that this legislation will cover biological material from living persons for research purposes together with material from deceased persons. When passed GeneLibrary Ireland will need to comply with this legislation.

In the absence of legislation in Ireland, the recommendations of report of the Irish Council of Bioethics, Human Biological Material: Recommendations for Collection, Use and Storage in Research (2005) provide useful guidance on best governance practice in relation to biobanking in Ireland (90). The Report distils the guidelines of international organizations such as HUGO, UNESCO, the Declaration of Helsinki and the Council of Europe related to biobanking activity and locates them in an Irish context. The recommendations of the report are helpful in defining the appropriate governance structures for GeneLibrary Ireland.

This report emphasises the importance of consent of the individual to donate his or her biological material for the purposes of research. This donation is given as a gift on the assumption that it will be used in good faith for the medical benefit of others. Intellectual property rights arising from human biological material donated for research may be sold or licensed and potential participants should be alerted to this possibility at the time consent is obtained. Researchers and sponsors of research using the donated material should consider sharing commercial benefits arising from research amongst the wider community from which the research participants were drawn. The report draws attention to the importance of respect for confidentiality in maintaining trust between researchers and participants and to the duty of confidentiality and privacy to research participants as is required under the Data Protection Acts.

The report suggests that for human tissue in biobanks, the important consideration is not legal ownership of the biological material but who has the right to control the use of the donated material (90).
The concept of ‘custodianship’ is useful in this context. The custodian of the biological material has responsibility for the ethical preservation, use and disposal of both biological material and data, without having rights of property to the material. The custodian who manages the biological material on a day-to-day basis ... should be a named person who is employed by the institution in which the material resides. However, formal responsibility for custodianship should rest with institutions rather than individuals. This ensures the continued maintenance of material when there are changes in personnel as a result of retirement, death or change of employment.

The custodian should be responsible for developing transparent procedures for dealing with access to the material by the research community. Best practice suggests that access to archival material should be subject to scientific peer review and the agreement of a management committee.

The European Directive on Data Protection applies to both jurisdictions and the provisions of its implementing Acts are detailed in chapter 3.

It appears that the principles underpinning biobanking in the Human Tissue Act and the Report of the Bioethics Council are similar– the intrinsic value of human material, the contribution of human tissue to research to improve the treatment of disease, the importance of informed consent of participants, the need for ethical and scientific approval, the significance of the license holder or custodian in the management of the biobank and the contribution of international and national standards and codes of practice to maintain quality of biobanking. Both jurisdictions are governed by the principles set out in the EU Directive on Data Protection, although the Directive has been transposed in different ways in the two jurisdictions.

The body acting as the custodian of GeneLibrary Ireland should have a legal status commensurate with its responsibilities to establish and maintain a biobank to the highest international standards, to ensure the biobanks scientific credibility and to ensure public legitimacy. This means that the body responsible for GeneLibrary Ireland should be established as a legal entity on a not for profit basis across the two jurisdictions for the purpose of commissioning and maintaining an all-island biobank.

11.2 GeneLibrary Ireland as a Legal entity – Proposed Models

There are three models that may be used for the governance of GeneLibrary Ireland, a consortium of interested partners, the establishment of a new, not-for-profit company limited by guarantee or the extension of an existing not for profit company such as Molecular Medicine Ireland.

11.2.1 Consortium Model

GeneLibrary Ireland could be established by a legal agreement between the participating institutions in both jurisdictions setting up a consortium to establish and manage GeneLibrary Ireland. A model for such an agreement is the consortium agreement establishing and maintaining the Screening for Pregnancy Endpoints (SCOPE project). SCOPE is an international collaboration to develop a pregnancy biobank involving 10,000 women and their partners with a view to identifying biomarkers for screening and diagnosing adverse pregnancy outcomes such as preeclampsia, preterm birth and foetal growth restriction. The parties to the consortium are the University of Adelaide, Uniservices (New Zealand), King’s College London, the University of Manchester and University College Cork. The original agreement dates from 2006 and is for five years.
Example

The SCOPE Consortium agreement commits the parties to establishing a formal framework for the parties to work co-operatively to exchange skills, knowledge and material to enable research collaboration. The primary intent in forming the consortium is to recruit patients and establish and expand a biobank to discover and evaluate potential screening and diagnostic markers for pre-eclampsia, pre-term birth and foetal growth restriction and to conduct collaborative research projects in the field, including research projects with their parties and to share data, information and resources of relevance to an agreed schedule of research projects. The consortium agreement provides for a Scientific Steering Committee, with a representative of each party, to undertake the co-ordination and consultation to agree the research projects to be undertaken each year. It is the responsibility of the Scientific Steering Committee to ensure that all clinical studies are conducted according to study protocols, standard operating procedures and good laboratory practice and to review proposed public disclosures of research conducted. Other matters covered by the consortium agreement include intellectual property, the variation and termination of the agreement, public disclosure, and confidential information, the appointment of agents to act on behalf of the Consortium, indemnities and dispute resolution. In relation to intellectual property, the parties have agreed that the revenue generated from any intellectual property generated from research using the biobank will be shared equally between all the partners. The parties to the Consortium agree that the agreement will be construed and governed by English law.

While the SCOPE Consortium provides a model for the governance of GeneLibrary Ireland across borders, there are significant differences in the nature of the SCOPE biobank and GeneLibrary Ireland that have implications for governance. The main difference is that the SCOPE biobank is being built from samples from consenting women who are accessing maternity services because of pregnancy. The samples are collected by midwives employed by the hospital/university and stored in the hospital/university in which they are collected. They are not centrally processed. Each participating hospital/university remains responsible for the samples once collected. The Consortium does not employ any people as all contracts are with the participating hospitals/universities. Whether GeneLibrary Ireland could be built and managed on the basis only of a Consortium Agreement between the participating institutions on the island of Ireland needs careful consideration.

11.2.2 New Not-for-Profit Company Model

GeneLibrary Ireland could be governed and managed by a new body established as a charitable company, limited by guarantee with a board of directors representative of key stakeholders. The company could be established by the partner institutions charged with responsibility for developing GeneLibrary Ireland. The company could be registered in Ireland and in Northern Ireland or it could be registered in one jurisdiction and operate in both. The memorandum and articles of association could commit the company to establish and maintain GeneLibrary Ireland as an all-island biomedical research infrastructure to the highest international standards. The objects could permit access to the resources of GeneLibrary Ireland by any researcher with the agreement of the company’s scientific committee, ethical review from a recognised research ethics committee and funding to conduct the research. The UK Biobank, described below, provides a model of such a company in action. The purpose of UK Biobank is to provide a resource to help scientists tackle the painful, disabling and life threatening diseases of middle and old age such as cancer, heart disease, diabetes, dementia, depression, arthritis and osteoporosis. The aim is to collect blood and urine samples and health information from 500,000 volunteers and to follow them for the next 30 years.
UK Biobank is a charitable company limited by guarantee. It was incorporated in England and Wales on 28 November 2003 and registered a charity in England and Wales on 30 December 2003. The two members of the Charity are the Medical Research Council and the Wellcome Trust Limited (as trustee of the Wellcome Trust). The charity is established under a Memorandum of Association setting out its objects and powers and is governed under its Memorandum and Articles of Association.

Under its Articles, Directors may be appointed either by the Members, or by the Board with the agreement of the Members. Under the terms of a contract entered into by the charity, the Members are entitled to appoint one Director each and they are jointly entitled to appoint additional Directors. The Secretary of State for Health, the Scottish Ministers and the University of Manchester (which hosts the charity) are entitled to appoint one Director each. There are currently eight directors.

The day to day running of the charity is delegated to the Chief Executive/Principal Investigator who is supported by a management team appointed by the Board. About 30 staff members are employed and expenditure in the financial year 2006-7 was £6m.

The UK Biobank Steering committee (chaired by the CEO/PI) provides scientific advice. An Ethics and Governance Council acts as guardian of the ethics and governance framework devised for UK Biobank. UK Biobank is funded by the Wellcome Trust, the Medical Research Council, the Department of Health (London) and the Scottish Executive (13).

A new, charitable company could fit the requirements of establishing an all-island biomedical research infrastructure with central processing of samples and storage facilities on two sites. One in each jurisdiction. A choice would have to be made between a company established by the funders, who would have the right to nominate members of the Board or one established by the partners delivering on the GeneLibrary project. In the latter case, the lines of accountability to the funders would have to be clearly set out. The Board of the company would be responsible for the samples and information collected and could employ staff to deliver on the project. A prerequisite for this model is the agreement of the funders or the university partners to establish a new body for the purposes of GeneLibrary Ireland. In the current financial climate, such agreement may not be forthcoming. If the company registers in the two jurisdictions – which is desirable for reasons of public legitimacy reasons, there is added expense and bureaucracy.

11.2.3 Extension of existing not for profit company such as Molecular Medicine Ireland

The governance and management of GeneLibrary Ireland could be entrusted to an existing charitable company such as Molecular Medicine Ireland (MMI). Molecular Medicine Ireland was established in 2008 by its five academic members to build capacity in Ireland for research into the molecular bases of health and disease, for translational and clinical research and for related graduate education and training. Its current members are NUI Galway, Royal College of Surgeons in Ireland, Trinity College Dublin, University College Cork and University College Dublin. In 2007, Queen’s University Ireland joined with MMI to respond to the HRB and R&D Office call to develop the design phase of GeneLibrary Ireland. The University of Ulster subsequently joined the initiative.
If MMI were chosen as the governance and management structure for GeneLibrary Ireland, it would desirable that QUB and/or UU join as members or at least establish a formal relationship with the company for the purposes of establishing and managing GeneLibrary Ireland. Considering that MMI is already in existence and involves five of the seven partner institutions, the Steering Group suggest that this could serve as the most appropriate model for the legal entity for GeneLibrary Ireland. In addition, the seven partner institutions in association with MMI have demonstrated the ability to work together in the preparation of the design phase for GeneLibrary Ireland.

It would be possible to establish GeneLibrary Ireland as a discreet business unit of MMI, with its own board of Management. The Chair of the GeneLibrary Ireland board of Management would have to be an independent person with no vested interest or conflict of interest, as would other members of the board of Management.

Before assuming responsibility for developing GeneLibrary Ireland, the partner institutions would need to be assured that sufficient funding will be available to deliver this biomedical research infrastructure.

### 11.3 Organisational Structure of GeneLibrary Ireland

The Board of GeneLibrary Ireland, whether of a consortium, a new, not for profit company or an extension of Molecular Medicine Ireland, will consist of about 10 members, representative of the
participating academic institutions and of patient groups. The chair will be independent of any of participating institutions and should a person of standing on the island or Ireland or internationally. (If GeneLibrary Ireland is established under an extended Molecular Medicine Ireland, the chair would be a member of the Board of MMI). No member of the board of management will have any commercial interest that would conflict with the objectives of establishing the biobank. The board of management will be responsible for the implementation of GeneLibrary Ireland as an all-island biomedical research infrastructure under the terms of any contract awarded by the HRB and R&D Office; for the on-going operation, development and funding of GeneLibrary Ireland when established; for the appointment of a Director and staff to implement and run GeneLibrary Ireland; for ensuring the scientific validity of the project and that it operates to the highest ethical and governance standards.

The need for ethical review of the construction of a biobank is noted in the document *International Declaration on Human Genetic Data* (2003) published by The International Bioethics Committee (IBC) of UNESCO (91).

GeneLibrary Ireland, in the implementation phase, will require ethical approval in both jurisdictions, for the standards, regulations and guidelines to be adopted for the collection, processing, use and storage of human genetic data, human proteomic data and biological samples. One recognized ethics committee in each jurisdiction should be designated for this purpose by the respective Ministers of Health or by the HRB and the R&D Office. The board of management will submit its proposal for GeneLibrary Ireland at implementation stage for ethical approval to these two committees.

The board of management will have two committees – a Scientific Steering Committee and an Ethics and Governance Committee. Each committee will be chaired by a member of the board of management and will include external members with appropriate expertise. The Ethics and Governance Committee will be responsible to the board of management for the following:

- Ensuring that applications to access GeneLibrary Ireland as a control biobank have appropriate approval from a research ethics committee;
- Review of all applications from researchers for access to GeneLibrary Ireland as a primary research resource;
- The preservation and protection of confidential personal information;
- Regular independent ethics audit of the project’s procedures and activities;
- Adherence of project to all relevant legislation, guidelines and standards;
- Protecting intellectual property generated by GeneLibrary Ireland and promoting the concept of benefit-sharing in the community.

The Scientific Steering Committee will be responsible for

- Ensuring the utility of the project for the advancement of science and for the benefit of society;
- Regular independent scientific audit of project’s procedures and activities;
- Scientific review of applications for access to GeneLibrary Ireland as a primary resource;
- Ensuring that applications to access GeneLibrary Ireland as a primary research resource are scientifically valid.

The Director, who will have a strong scientific and management background, will be responsible to the board of management for the implementation of GeneLibrary Ireland and when, established, for its overall management and operation.

The Director will be supported, in the implementation phase, by a team of people reporting to
him/her with expertise in and responsibility for operations, communications, recruitment, laboratory processing/storage, data management and finance. The role of communications and recruitment will be reviewed when the target of 10,000 volunteers is achieved. As far as possible, operational tasks will be contracted out to ensure that the core team is as small as possible.

The diagram below outlines the probable organisational structure of GeneLibrary Ireland, whether established by a consortium agreement, a new not for profit company or as part of an existing not for profit company.

**Organisational Structure for GeneLibrary Ireland**

![](image)

*During the implementation phase, GeneLibrary Ireland will need a dedicated resource for communications and for recruitment. These resources could be reviewed when GeneLibrary Ireland is established.*

**11.4 Access to Bio-resources and Return of Data**

As previously discussed, there are a number of internationally competitive genetics research groups across the island and international partners who have expressed a strong interest in accessing the bio-resource of GeneLibrary Ireland. It is anticipated that significant demand for access to GeneLibrary Ireland samples and data will emerge from project inception of the project. The appropriate mechanism for access to samples and further expansion of the GeneLibrary Ireland dataset needs to be defined. The following key constituents are expected to use this resource;

- Investigators within the seven partner institutions
- Investigators from other academic centres on the island of Ireland
- International academic research groups
- Multi-national collaborative teams
- Pharmaceutical and Biotechnology industry

Prior to bio-resources being made available, it is essential that there are clear and transparent rules that govern how the samples and data may be used. GeneLibrary Ireland will adopt a policy
for defining rules of access to, and return of data from research studies to the bio-resource along with the publication of data from GeneLibrary Ireland resources. GeneLibrary Ireland will ensure that all applications for access to the bio-resource are in keeping with its core objectives and overall ethics approval. A standard procedure will be defined for all investigators, both academic and commercial, who wish to access the bio-resources and data of GeneLibrary Ireland with applications undergoing scientific peer review and ethical review as appropriate which will be overseen by the Scientific Steering Committee and Governance and Ethics Committee. A fee will be charged for access to data and bio-resources towards the costs of sample and/or data retrieval, preparation, analysis and to assist with the ongoing maintenance costs of GeneLibrary Ireland. It is likely that the fee structure will be higher for commercial use of the bio-resource. Special consideration will be given to researchers associated with small and spin out companies from partner institutions. It will be a requirement for all researchers both academic and commercial to return a copy of the final dataset used in their analysis, along with derived variables and descriptions of these variables after a period of twelve months from the signing a data or material transfer agreement with GeneLibrary Ireland and allowing for publication and protection of intellectual property (IP). This will ensure that the GeneLibrary Ireland is a living and up-to-date bio-resource for the population of Ireland and Northern Ireland, while also enhancing the value of the collection for future research studies.

The key components of the agreement between research investigators and GeneLibrary Ireland regarding access to samples include

1) Scientific review of the proposed project to ensure the quality of the research
2) Ethical review of the project to ensure compatibility of project with GeneLibrary Ireland consent and ethical framework
3) Agreement regarding recovery of costs, to contribute towards the ongoing maintenance and development of GeneLibrary Ireland
4) Formal protocol for sample transfer
5) Formal protocol for the return of unused samples to the library
6) Mechanism for return of data generated (following publication) to the main GeneLibrary Ireland databank
7) Agreement that all data generated using GeneLibrary Ireland will be deposited in international, publicly available genotyping databanks
8) Agreement by the research group to provide updates to GeneLibrary Ireland regarding the progress of the project for annual reports etc.
9) Agreement regarding acknowledgement of GeneLibrary Ireland resource in publications

11.5 Professional Recognition of GeneLibrary Ireland

Professional recognition of the efforts of long-term quality biobanking is essential to justify not only the input of the biobank personnel but also that of the participants, users and especially the funders. The taxpayer needs to be sure that the major investment is justified and has an impact on health at society level. The development of a quantitative parameter to measure the value of a biobank would address many of these issues. Unfortunately there is no standardised way to recognise the contribution of biobanks to the complex chain of activity leading to new diagnostic measures and/or therapeutics for clinical use. In terms of recognition a biobank and its investigators may or may not be included in the first paper that described the resource in the reference section. Cambon-Thompson has proposed establishing a Biobank Impact Factor (BIF) to quantify the use, and hence the value, of a biobank (92). The BIF would be a quantitative measure, comparable to the Science Citation Index (SCI), of the impact of the research resulting from the biobanks use and would recognise those who established and maintained the resource. It is proposed that authors would cite the biobank for example GeneLibrary Ireland in the references
section of their paper so that the Institute for Scientific Information could track this information. In this way the BIF would become a more objective measure, similar to the SCI, of the impact of the biobanking activities and contribution to health. Recognition of biobanking as a scientific research activity would boost the recognition and quality of GeneLibrary Ireland leading to increased use of this biomedical research infrastructure and leverage funding opportunities. Such a measure would allow participants, investigators and funders alike to trace uses and research results from GeneLibrary Ireland. In the absence of a recognised quantitative measure GeneLibrary Ireland will ensure that the use of its bio-resources will be acknowledged in all publications. However for publications where GeneLibrary Ireland bio-resources are used as a primary research resource rather than as a control group it will be important that appropriate GeneLibrary Ireland principal investigator(s) will be involved in this research and also be included as a co-author(s) in the publication. This will allow GeneLibrary Ireland to build on its scientific profile which in turn will allow it to grow and develop and attract additional funding for its long-term sustainability.

11.6 Intellectual Property (IP)

As a research infrastructure funded by public money, GeneLibrary Ireland will not in itself be interested in developing IP from the bio-resource or in its commercialization. However GeneLibrary Ireland will work to ensure that the principal investigators and their institutions involved protect any IP generated from research using GeneLibrary Ireland bio-resources. It will be the responsibility of the individual institutions involved and/or commercial organisations to develop agreements as part of their research collaborations to ensure that an IP agreement is in place. In the event that any commercial benefit arises from research using GeneLibrary Ireland resources, participants will be advised that they will not receive any direct benefit and that any benefits will be for the health of the population on the island of Ireland. It may be useful to consider the Funding Agency Requirements & Guidelines for Managing Research-Generated Intellectual Property published by the Commercialisation Steering Group, in 2006 to define IP agreements between collaborators.
12.0 Conclusion

The creation of GeneLibrary Ireland, on the basis of the design outlined in this report will serve the research enterprise on the island of Ireland and add tremendous value to ongoing research efforts. Recognising the need for GeneLibrary Ireland to be built on a strong organisational foundation, a detailed strategy and proposed implementation plan has been presented in this report.

The design phase to date has ensured the buy-in of all key stakeholders and has drawn on a wealth of expertise. Specifically the design process for GeneLibrary Ireland, as an all-island biomedical research infrastructure has;

- **Established** and initiated the GeneLibrary Ireland Steering Committee and Scientific Advisory Board
- **Engaged** an unprecedented panel of experts who have created a framework for the delivery of the project.
- **Secured** the support of all participant institutions and their research centres.
- **Agreed** GeneLibrary Ireland’s coordination and management policies and procedures.
- **Addressed** the ethical, legal and social issues that confront the establishment of this biomedical research infrastructure.
- **Provided** a comprehensive communication strategy for interaction and communication with all key stakeholders with trust and transparency at its core to enlist public engagement and participation in GeneLibrary Ireland.
- **Developed** a robust participant recruitment strategy centred around the CRCs based on a geographical clustering model using the GEO Directory in Ireland and the Land and Property Service Agency’s Address Database and GP Registry in Northern Ireland.
- **Agreed** the phenotypic information to be collected from all participants in GeneLibrary Ireland.
- **Prepared** key Standard Operating Procedures (SOPs) that will be used to deliver the research programme.
- **Proposed how** GeneLibrary Ireland will be delivered in line with international best practice.
- **Integrated** the GeneLibrary Ireland vision with other ongoing international biobanking initiatives.
- **Articulated how** maximum value for money will be returned from GeneLibrary Ireland

GeneLibrary Ireland represents a major infrastructural development for the research community on the island of Ireland. Its establishment will enhance the impact of research in Ireland and Northern Ireland and will also send a clear signal to the international community about the commitment of this island to research and development.
References

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44. www.tilda.ie


91. International Declaration on Human Genetic Data (2003). The International Bioethics Committee of UNESCO.

### ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>AATD</td>
<td>Alpha-1 antitrypsin deficiency</td>
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<tr>
<td>BBMRI</td>
<td>Biobanking and Biomolecular Resources Research Infrastructure</td>
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<tr>
<td>BDI-II</td>
<td>Beck Depression Inventory</td>
</tr>
<tr>
<td>BIMS</td>
<td>Biobank Information Management System</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>BP</td>
<td>Blood Pressure</td>
</tr>
<tr>
<td>BP-QTLs</td>
<td>Blood Pressure - Quantitative Trait Loci</td>
</tr>
<tr>
<td>CAPE</td>
<td>Community Assessment of Psychic Experiences</td>
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<tr>
<td>CC-IMT</td>
<td>Common Carotid Artery Intima-media Thickness</td>
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<tr>
<td>CEO</td>
<td>Chief Executive Officer</td>
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<tr>
<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
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<td>CRC</td>
<td>Clinical Research Centre</td>
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<tr>
<td>CRF</td>
<td>Clinical Research Form</td>
</tr>
<tr>
<td>DALY</td>
<td>Disability Adjusted Life Years</td>
</tr>
<tr>
<td>DETIN</td>
<td>Department of Enterprise Trade and Investment Northern Ireland</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
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<tr>
<td>EBV</td>
<td>Epstein-Barr virus</td>
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<tr>
<td>ECACC</td>
<td>European Collection of Cell Cultures</td>
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<td>ECRIN</td>
<td>European Clinical Research Infrastructure Network</td>
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<td>EDTA</td>
<td>Ethylenediaminetetraacetic acid</td>
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<tr>
<td>EPIC</td>
<td>European Prospective Investigation into Cancer and Nutrition</td>
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<td>EPQ-R</td>
<td>Eysenck Personality Questionnaire-Revised</td>
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<td>ESRI</td>
<td>Economic and Social Research Institute</td>
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<td>EU</td>
<td>European Union</td>
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<tr>
<td>FAQ</td>
<td>Frequently Asked Questions</td>
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<tr>
<td>FBC</td>
<td>Full Blood Count</td>
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<td>FEV1</td>
<td>Forced expiratory volume</td>
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<tr>
<td>FFQ</td>
<td>Food Frequency Questionnaire</td>
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<td>FORFAS</td>
<td>Ireland National Advisory Body for Enterprise and Science</td>
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<td>FP7</td>
<td>Framework Programme 7</td>
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<td>FVC</td>
<td>Forced Vital Capacity</td>
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<td>GEO Directory</td>
<td>Geography Directory of address in Ireland</td>
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<td>GHQ</td>
<td>General Health Questionnaire</td>
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<td>GIS</td>
<td>Geographical Information System</td>
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<td>GLIIMS</td>
<td>GeneLibrary Ireland Laboratory Information Management Systems</td>
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<td>GP</td>
<td>General Practitioner</td>
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<td>GRDO</td>
<td>Genetic and Rare Disorders Organisation</td>
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<td>GSIMS</td>
<td>Governance &amp; Study Information Management System</td>
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<tr>
<td>HDL</td>
<td>High-density lipoprotein</td>
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<tr>
<td>HEA</td>
<td>Higher Education Authority</td>
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<td>HIV</td>
<td>Human immunodeficiency virus</td>
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<td>HPACC</td>
<td>Health Protection Agency Culture Collections</td>
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<td>Health Research Board</td>
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<td>HTA</td>
<td>Human Tissue Act</td>
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<tr>
<td>IATA</td>
<td>International Air Transport Association</td>
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<tr>
<td>IBC</td>
<td>International Bioethics Committee</td>
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<td>ICRIN</td>
<td>Irish Clinical Research Infrastructure Network</td>
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<td>IDA</td>
<td>Irish Development Authority</td>
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<tr>
<td>IMDA</td>
<td>Irish Medical Devices Association</td>
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<tr>
<td>IMI</td>
<td>Innovative Medicines Initiative</td>
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<tr>
<td>IPAQ</td>
<td>International physical activity questionnaire</td>
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<td>IPHA</td>
<td>Irish Pharmaceutical Healthcare Association</td>
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<td>IPPOSI</td>
<td>Irish Platform for Patient Organisations Science and Industry</td>
</tr>
<tr>
<td>Acronym</td>
<td>Definition</td>
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<tr>
<td>ISBER</td>
<td>International Society for Biological and Environmental Repositories</td>
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<tr>
<td>LDL</td>
<td>Low-density lipoprotein</td>
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<tr>
<td>LIMS</td>
<td>Laboratory Information Management System</td>
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<tr>
<td>LPSA</td>
<td>Land and Property Service Agency's</td>
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<tr>
<td>MMI</td>
<td>Molecular Medicine Ireland</td>
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<tr>
<td>MRCG</td>
<td>Medical Research Charities Group</td>
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<td>NHANES</td>
<td>National Health and Nutrition Examination Survey</td>
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<tr>
<td>NICRIN</td>
<td>Northern Ireland Clinical Research Infrastructure Network</td>
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<td>NUIG</td>
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<tr>
<td>OECD</td>
<td>Organisation for Economic Co-operation and Development</td>
</tr>
<tr>
<td>PBMC</td>
<td>Peripheral Blood Mononuclear Cell</td>
</tr>
<tr>
<td>PRTLI</td>
<td>Programme for Research in Third-Level Institutions</td>
</tr>
<tr>
<td>PSU</td>
<td>Primary Sampling Units</td>
</tr>
<tr>
<td>QUB</td>
<td>Queens University Belfast</td>
</tr>
<tr>
<td>R&amp;D</td>
<td>Research &amp; Development</td>
</tr>
<tr>
<td>RCSI</td>
<td>Royal College Surgeons in Ireland</td>
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<tr>
<td>REC</td>
<td>Research Ethics Committee</td>
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<tr>
<td>SAB</td>
<td>Scientific Advisory Board</td>
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<tr>
<td>SCID-I/NP</td>
<td>Structured Clinical Interview for Depression –</td>
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<td>SCOPE</td>
<td>Screening for Pregnancy Endpoints</td>
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<td>SHARE</td>
<td>Survey of Health and Retirement</td>
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<tr>
<td>SLÁN</td>
<td>Survey of Lifestyle attitudes and Nutrition</td>
</tr>
<tr>
<td>SME</td>
<td>Small and Medium-sized Enterprises</td>
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<tr>
<td>SNP</td>
<td>Single Nucleotide Polymorphism</td>
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<td>SOP</td>
<td>Standard Operating Procedures</td>
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<tr>
<td>STA</td>
<td>Specimen Transfer Agreement</td>
</tr>
<tr>
<td>TCD</td>
<td>Trinity College Dublin</td>
</tr>
<tr>
<td>TILDA</td>
<td>Irish Longitudinal Study on Ageing</td>
</tr>
<tr>
<td>U &amp; E:</td>
<td>Urea and Electrolyte</td>
</tr>
<tr>
<td>UCC</td>
<td>University College Cork</td>
</tr>
<tr>
<td>UCD</td>
<td>University College Dublin</td>
</tr>
<tr>
<td>UK</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>UNESCO</td>
<td>United Nations Educational and Scientific Cultural Organisation</td>
</tr>
<tr>
<td>UU</td>
<td>University of Ulster</td>
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</table>
Appendix 1 GeneLibrary Ireland Expert Group Membership
### GeneLibrary Ireland Project Team

<table>
<thead>
<tr>
<th>Name</th>
<th>Title and Organisation</th>
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<tbody>
<tr>
<td>Dr Ruth Barrington</td>
<td>CEO Molecular Medicine Ireland</td>
</tr>
<tr>
<td>Peter Doran</td>
<td>Principal Investigator and Director of Clinical Research Centre, University College Dublin</td>
</tr>
<tr>
<td>Joseph McPartlin</td>
<td>Director, Trinity Biobank, Institute of Molecular Medicine, Trinity College Dublin</td>
</tr>
<tr>
<td>Jan Guerin</td>
<td>Programme Manager Research, Molecular Medicine Ireland</td>
</tr>
<tr>
<td>Paul Barry</td>
<td>Finance and Operations Manager, Molecular Medicine Ireland</td>
</tr>
<tr>
<td>Mel Clifford</td>
<td>Director CliffordRobbins Ltd., Consultancy and Project Management</td>
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### GeneLibrary Ireland Working Group 1 Ethical, legal and societal issues

<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Chair:</strong></td>
<td></td>
</tr>
<tr>
<td>Deirdre Madden,</td>
<td>Senior Lecturer, Faculty of Law, University College Cork</td>
</tr>
<tr>
<td><strong>Rapporteur:</strong></td>
<td></td>
</tr>
<tr>
<td>Jan Guerin</td>
<td>Programme Manager for Research, Molecular Medicine Ireland</td>
</tr>
<tr>
<td>Mel Clifford</td>
<td>Director, Clifford Robbins Ltd</td>
</tr>
<tr>
<td>Asim Sheikh,</td>
<td>Barrister-at-Law and</td>
</tr>
<tr>
<td></td>
<td>Lecturer in Forensic and Legal Medicine, University College Dublin</td>
</tr>
<tr>
<td>Harry Comber</td>
<td>Statutory Lecturer in Epidemiology, University College Cork</td>
</tr>
<tr>
<td></td>
<td>and Director of the National Cancer Registry</td>
</tr>
<tr>
<td>William Watson</td>
<td>Senior Lecturer, College of Life Sciences, School of Medicine &amp; Medical Science University College Dublin</td>
</tr>
<tr>
<td>Suzanne Norris</td>
<td>Consultant Hepatologist, St James’ Hospital</td>
</tr>
<tr>
<td>Siobhan McGrath</td>
<td>Manager of the Office for Research Ethics Committees, Northern Ireland</td>
</tr>
<tr>
<td>Andrew Greene,</td>
<td>Professor of Medical Genetics, School of Medicine and Medical Science, University College Dublin and National Centre for Medical Genetics</td>
</tr>
<tr>
<td>David Smith</td>
<td>Ethicist, Epidemiology Department, Royal College Surgeons Ireland</td>
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**GeneLibrary Ireland Working Group 2 Communications Strategy**

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<tbody>
<tr>
<td><strong>Chair:</strong> Avril Daly</td>
<td>Head of Public Affairs, Fighting Blindness</td>
</tr>
<tr>
<td><strong>Rapporteur:</strong></td>
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<tr>
<td>Jan Guerin</td>
<td>Programme Manager for Research, Molecular Medicine Ireland</td>
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<tr>
<td>Mel Clifford</td>
<td>Director, Clifford Robbins Ltd</td>
</tr>
<tr>
<td>Sally-AnneFisher,</td>
<td>Communications Officer, Trinity College Dublin</td>
</tr>
<tr>
<td>Eilis O’Brien</td>
<td>Director of Communications, University College Dublin</td>
</tr>
<tr>
<td>Gillian Markey</td>
<td>Communications Manager, Health Research Board</td>
</tr>
<tr>
<td>Denise Cremins</td>
<td>Medical Research Charity Group</td>
</tr>
<tr>
<td>Anne Madden</td>
<td>Director of Research, Advocacy and Primary Prevention, Northern Ireland Chest Heart &amp; Stroke</td>
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<tr>
<td>Derek Mitchell</td>
<td>Communications Officer, REMEDI, National University Ireland Galway</td>
</tr>
<tr>
<td>Valerie McKelvey-Martin</td>
<td>School of Biomedical Sciences, University of Ulster, Public Understanding of Science, Northern Ireland</td>
</tr>
<tr>
<td>Claire Percy</td>
<td>University College Dublin</td>
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## GeneLibrary Ireland Working Group 3 Participant Recruitment Strategy

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<tr>
<td><strong>Chair:</strong> Leslie Boydell</td>
<td>Associate Medical Director for Public Health Belfast Health and Social Care Trust</td>
</tr>
<tr>
<td>Rapporteur:</td>
<td>Programme Manager for Research, Molecular Medicine Ireland Director, Clifford Robbins Ltd</td>
</tr>
<tr>
<td>Jan Guerin</td>
<td>Programme Manager for Research, Molecular Medicine Ireland Director, Clifford Robbins Ltd</td>
</tr>
<tr>
<td>Mel Clifford</td>
<td>Programme Manager for Research, Molecular Medicine Ireland Director, Clifford Robbins Ltd</td>
</tr>
<tr>
<td>Peter Maxwell</td>
<td>Professor of Renal Medicine Queens University Belfast, Consultant Nephrologist, Belfast City Hospital</td>
</tr>
<tr>
<td>Eibhlin Mulroe</td>
<td>CEO, IPPOSI</td>
</tr>
<tr>
<td>Leslie Daly</td>
<td>School of Public Health and Population Science, University College Dublin</td>
</tr>
<tr>
<td>Rose Ann Kenny</td>
<td>Department of Medical Gerontology, Trinity College Dublin and St. James's Hospital</td>
</tr>
<tr>
<td>Alan Kelly</td>
<td>Senior Lecturer in Biostatistics, Dept of Public Health &amp; Primary Care, Trinity College Dublin</td>
</tr>
<tr>
<td>Hannah McGee</td>
<td>Head Division of Population Health Sciences, Royal College Surgeons Ireland</td>
</tr>
<tr>
<td>Cecily Kelleher</td>
<td>School of Public Health and Population Sciences, University College Dublin</td>
</tr>
<tr>
<td>David Marshall</td>
<td>Central Survey Unit Northern Ireland and Statistics Research Agency, McMauley House, 2-14 Castle Street, Belfast BT1 1SA</td>
</tr>
<tr>
<td>Ivan Perry</td>
<td>Professor of Public Health, Department of Epidemiology and Public Health, University College Cork</td>
</tr>
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# GeneLibrary Ireland Working Group 4

## Sample and Data Collection, Sample Storage and Processing, Data Management and IT Infrastructure

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<tbody>
<tr>
<td><strong>Chair</strong></td>
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</tr>
<tr>
<td>Joe McPartlin</td>
<td>Director, Trinity BioBank Institute of Molecular Medicine, TCD</td>
</tr>
<tr>
<td><strong>Rapporteur:</strong></td>
<td></td>
</tr>
<tr>
<td>Jan Guerin</td>
<td>Programme Manager for Research, Molecular Medicine Ireland</td>
</tr>
<tr>
<td>Mel Clifford</td>
<td>Director, Clifford Robbins Ltd</td>
</tr>
<tr>
<td>Jane Grimson</td>
<td>Director of Health Information with the HIQA and Chair of the Centre for Health Informatics at Trinity College Dublin</td>
</tr>
<tr>
<td>Peter Doran</td>
<td>Director, University College Dublin Mater Clinical Research Centre</td>
</tr>
<tr>
<td>Brendan Buckley</td>
<td>University College Cork Dept of Pharmacology &amp; Therapeutics</td>
</tr>
<tr>
<td>Helene McNulty</td>
<td>School of Biomedical Sciences, University of Ulster, Coleraine</td>
</tr>
<tr>
<td>Alice Stanton</td>
<td>Senior Lecturer in Pharmacology, Royal College Surgeons Ireland</td>
</tr>
<tr>
<td>David Savage</td>
<td>Reader in Molecular Medicine, Centre for Public Health, Queens University Belfast</td>
</tr>
<tr>
<td>Jackie Breiden</td>
<td>Clinical Research Coordinator, University College Dublin Mater Clinical Research Centre</td>
</tr>
<tr>
<td>Michael Connolly</td>
<td>Director of Network Services, Mater Misericordiae University Hospital</td>
</tr>
<tr>
<td>Denis Shields</td>
<td>Professor of Clinical Bioinformatics, Conway Institute, University College Dublin</td>
</tr>
<tr>
<td>Sean Strain</td>
<td>Director, Norther Ireland Centre for Food and Health (NICHE), School of Biomedical Sciences, Ulster University</td>
</tr>
<tr>
<td>Michael Gill</td>
<td>Departments of Psychiatry and Genetics, Trinity Institute for Neurosciences, Trinity College Dublin</td>
</tr>
<tr>
<td>Geoff Bradley</td>
<td>Trinity Centre for High Performance Computing</td>
</tr>
<tr>
<td>Elaine Kay</td>
<td>Beaumont Hospital Dublin</td>
</tr>
<tr>
<td>Anne Molloy</td>
<td>Research Senior Lecturer, Trinity College Dublin</td>
</tr>
<tr>
<td>Mary McGrath</td>
<td>University College Dublin</td>
</tr>
<tr>
<td>Michael Keane</td>
<td>Professor of Medicine and Therapeutics, School of Medicine &amp; Medical Science. University College Dublin</td>
</tr>
<tr>
<td>Martin Molloy</td>
<td>Director IT, UCHG</td>
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<tr>
<td>Name</td>
<td>Organisation</td>
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<tr>
<td>Frank Barry</td>
<td>Scientific Director, REMEDI, National University Ireland Galway</td>
</tr>
<tr>
<td>Ailbhe Cullen</td>
<td>Royal College Surgeons Ireland</td>
</tr>
<tr>
<td>Andrew Murphy</td>
<td>Department of General Practice, National University Ireland Galway</td>
</tr>
<tr>
<td>Sean Ennis</td>
<td>School of Medicine and Medical Science, University College Dublin and National Centre for Medical Genetics</td>
</tr>
<tr>
<td>David Toomey</td>
<td>Molecular and Cellular Therapeutics, Royal College Surgeons Ireland</td>
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### GeneLibrary Ireland Working Group 5 Value Added Research Programme

<table>
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<tr>
<td><strong>Chair:</strong></td>
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</tr>
<tr>
<td><strong>Tony Bjourson</strong></td>
<td>Director Centre for Molecular Biosciences, School of Biomedical Sciences, University of Ulster</td>
</tr>
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<td><strong>Rapporteur:</strong></td>
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<tr>
<td><strong>Jan Guerin</strong></td>
<td>Programme Manager for Research, Molecular Medicine Ireland</td>
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<tr>
<td><strong>Mel Clifford</strong></td>
<td>Director, Clifford Robbins Ltd</td>
</tr>
<tr>
<td><strong>Colm Harmon</strong></td>
<td>Director of the Geary Institute and a Professor of Economics, University College Dublin</td>
</tr>
<tr>
<td><strong>Daniel Bradley</strong></td>
<td>Smurfit Institute of Genetics, Trinity College Dublin</td>
</tr>
<tr>
<td><strong>Diarmuid O Donoghue</strong></td>
<td>Consultant Gastroenterologist, St Vincent’s Hospital and University College Dublin</td>
</tr>
<tr>
<td><strong>Pascal McKeown</strong></td>
<td>Public Health Medicine and Primary Care, Queens University Belfast</td>
</tr>
<tr>
<td><strong>Laurence Egan</strong></td>
<td>Department of Pharmacology &amp; Therapeutics, National University Ireland Galway</td>
</tr>
<tr>
<td><strong>Frank Kee</strong></td>
<td>Professor of Public Health Medicine, Dept of Epidemiology and Public Health, Queens University Belfast</td>
</tr>
<tr>
<td><strong>Alison Gallagher,</strong></td>
<td>School of Biomedical Sciences, University of Ulster</td>
</tr>
<tr>
<td><strong>Sean Ennis</strong></td>
<td>School of Medicine and Medical Science, University College Dublin and National Centre for Medical Genetics</td>
</tr>
<tr>
<td><strong>Ruth Barrington</strong></td>
<td>CEO, Molecular Medicine Ireland</td>
</tr>
<tr>
<td><strong>Peter Doran</strong></td>
<td>Director, University College Dublin Clinical Research Centre</td>
</tr>
</tbody>
</table>
## GeneLibrary Ireland Working Group 6 Funding and Finance

<table>
<thead>
<tr>
<th>Name</th>
<th>Organisation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chair</strong></td>
<td></td>
</tr>
<tr>
<td>Vincent McCabe,</td>
<td>Finance Controller, Irish Heart Foundation</td>
</tr>
<tr>
<td><strong>Rapporteur:</strong></td>
<td></td>
</tr>
<tr>
<td>Jan Guerin</td>
<td>Programme Manager for Research, Molecular Medicine Ireland</td>
</tr>
<tr>
<td>Mel Clifford</td>
<td>Director, Clifford Robbins Ltd</td>
</tr>
<tr>
<td>Paul Barry,</td>
<td>Finance and Operations Manager, Molecular Medicine Ireland</td>
</tr>
<tr>
<td>Peter Doran,</td>
<td>Director, UCD Clinical Research Centre</td>
</tr>
<tr>
<td>John McCormack,</td>
<td>CEO, Irish Cancer Society</td>
</tr>
<tr>
<td>Caroline Piggott</td>
<td>Finance Manager Mater Hospital Dublin</td>
</tr>
<tr>
<td>Peter Mangan</td>
<td>Finance Manager Research Office University College Dublin</td>
</tr>
<tr>
<td>Maurice O Kane</td>
<td>Director of Research and Development, Western Trust Research and</td>
</tr>
<tr>
<td></td>
<td>Development Office, C-TRIC, Altnagelvin Hospital, Londonderry</td>
</tr>
</tbody>
</table>
GeneLibrary Ireland – Draft Participant Information Leaflet

You are being asked to participate in GeneLibrary Ireland. The purpose of this biobank is to provide a long-term resource for researchers in Ireland to study the genetics of diseases that most commonly affect the population of Ireland and Northern Ireland today and into the future which in turn will allow us to understand more about how these diseases occur and determine more effective therapies and tests for these diseases.

We would like you to read this information sheet in order to decide if you would like to participate. Before you decide, it is important for you to be aware of why GeneLibrary Ireland has been set up, its aims and purposes, what research is likely to be done, and what your participation will involve. Please take your time to read the following information carefully. Talk to others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

1 What is GeneLibrary Ireland, and what are its aims?

GeneLibrary Ireland is a resource that contains biological materials, including blood and DNA samples, and personal information (data) on a large number of people. It has been set up so that it can be used as a resource for researchers undertaking a wide range of medical research over time.

This resource/biobank has two main aims. The first aim is to gain a better understanding of the interactions between genes, environment and the way we live that influence health or cause diseases. The second aim is to use this understanding to develop new drugs, genetic tests and treatments and to plan public health strategies that will benefit everyone.

Taking part in GeneLibrary Ireland involves you giving a broad consent for use of your samples and data in genetic studies of diseases that affect people living in Ireland and Northern Ireland.

Your samples and medical information will be used in a coded fashion so your identity will be protected at all times.

GeneLibrary Ireland involves the participation of over 10000 people between 30 and 60 years of age from all over Ireland. GeneLibrary Ireland is a long-term study, which will run indefinitely. If GeneLibrary Ireland has to close, all of the research results and information will be put into an archive.

2 How were you selected?

You have been selected at random by an independent directory of household names and addresses (for example the GEO directory, the Land and Property Service Agency Database and/or GP registry) in Ireland and Northern Ireland as someone who is in the correct age group from 30 to 60 years to take part in Genelibrary Ireland. You can also self-select to participate if you are aged between 30 and 60 years.

3 Who operates and manages GeneLibrary Ireland?

GeneLibrary Ireland is a joint research effort between Molecular Medicine Ireland, which incorporates Trinity College Dublin, University College Dublin, the Royal College of Surgeons in Ireland, University College Cork and National University of Ireland Galway along Queens University College, and University of Ulster. It is coordinated by Molecular Medicine Ireland. This GeneLibrary Ireland Management Team is responsible for the practical aspects, such as sample and data collection, and the oversight of the secure storage of your samples and data, which will be stored in two locations for back-up purposes. The GeneLibrary Ireland Management Team will be the point of contact for you, and for the researchers who use GeneLibrary Ireland. The person who has overall responsibility for the management of GeneLibrary Ireland is the Director [name Director]. If you need to contact the GeneLibrary Ireland for any reason please telephone [number], email, address] or write to [].
GeneLibrary Ireland is supported by Molecular Medicine Ireland and funded by [to include]. GeneLibrary Ireland has received approval from [Research ethics committee – insert relevant details when agreed].

4 What does participation involve?
If you would like to volunteer to take part, you will be asked to agree to the following:
(1) Complete a questionnaire about your health and lifestyle, family and medical history
(2) Have a physical examination (as described in the next section);
(3) Allow your samples and health-related information to be stored and used in coded form by researchers for many years.

In addition we will ask your permission separately to allow us to re-contact you to invite you to update the questionnaire or to provide other samples. Whether you want to be re-contacted for updating is entirely optional. You can still participate without agreeing to be re-contacted.

4.1 Physical examination
If you would like to take part, you will be asked:

- to attend an appointment at a time that is convenience for you at a Clinical Research Centre in your locality which will last approximately 2 hours
- to provide blood and samples (about 5 tablespoons) which GeneLibrary Ireland will store for use for future studies.
- to answer a questionnaire that will take approximately 30 minutes about your health and lifestyle, family and medical history.
- to allow staff to perform basic clinical measurements, including measuring your weight, height, waist/hip and blood pressure.

The physical examination will be conducted by a GeneLibrary Ireland trained research nurse. It will take approximately 30 minutes.

5 Are there any risks for you?
The physical examination involves little risk. The taking of a blood sample by venupuncture for DNA analysis may cause some bleeding, bruising, dizziness and/or discomfort. You should be aware that certain physical measurements that will be taken and/or some of the questions you will be asked in the questionnaire may be quite personal in nature.
Storage of your samples and the extraction of DNA involve minimal risk, as rigorous security measures are in place (as described below). All samples will be kept in a high security storage area.
Storage of your personal data in GeneLibrary Ireland involves some risk, as it puts together information about you from a number of sources. Unless required by law or a court order, access to this information will not be offered to third parties such as employers, insurance companies or other family members. Only authorized staff members will have access to the information. For requests for access by researchers, they will not be given any information that would enable them to identify you. The utmost care will be taken to ensure the confidentiality of all data as well as oversight by a number of independent bodies (see below: Sections 7-9).

6 What are the benefits?
6.1 Physical examination results
You can choose to receive your physical examination results, such as blood pressure and cholesterol. These results will be provided with the appropriate explanations, e.g. your measurements alongside ‘standard measures’. You can decide whether you want these results sent to you or you can ask that they also be sent to your GP. If, during the appointment for your physical examination, we find something that we feel should be explored further, we will advise you to see your personal doctor. Alternatively, you can choose not to receive your physical examination results if you prefer. GeneLibrary Ireland will not be in a position to cover any
expenses incurred with regard to a follow-up appointment you may make with your GP or any additional tests that you decide to undertake.

6.2 Long-term benefits
The most important health benefits from GeneLibrary Ireland will be realized many years from now, and will largely help future generations. GeneLibrary Ireland is intended to benefit the population as a whole in Ireland and Northern Ireland in the years to come. It will improve our understanding of the genetic and non-genetic factors that affect a person’s risk to developing certain diseases that are common in Ireland and Northern Ireland. It will also provide an invaluable resource for future research studies that will contribute to public health through development of new therapies and new tests for diagnosing disease.

6.3 General research results
Participation in GeneLibrary Ireland is not expected to provide you with any direct individual benefits or personal results beyond those offered at your initial visit. The results of research studies that use the GeneLibrary Ireland may be used for teaching, further research, publications or presentations at scientific meetings. Your identity will be kept confidential in any such presentations, reports or publications. All data will be presented as group data, rather than individual data. General results will also be made available to all participants and any other people who might be interested through the GeneLibrary Ireland website and newsletters.

7 What oversight bodies will ensure your privacy?
To ensure the highest standards for protecting your privacy and the confidentiality of samples and data, a number of bodies are responsible for overseeing GeneLibrary Ireland itself, as well as the research projects that are carried out using it. This governance structure is designed to ensure the highest levels of accountability, transparency, protection, security and control and to minimise the possibility of the data being used for unauthorised purposes.

7.1 Oversight of GeneLibrary Ireland
Scientific oversight
Scientific oversight of all research studies will be undertaken by GeneLibrary Ireland Scientific Steering Committee through a competitive peer review process.

Ethical oversight
GeneLibrary Ireland will be overseen by an independent research committee established within GeneLibrary Ireland.

8 How will your samples and information be stored?

8.1 Data/sample information storage
When data and samples are collected from you, or from other databases or sources, personal identifiers such as your name and address will be removed and replaced by a unique code. This unique code will enable us to link the information from different datasets to you, but, at the same time, will enable us to keep your identity confidential when we give your data to researchers to use. Researchers who use GeneLibrary Ireland will only be given access to coded information. They will not be able to access any information that would enable them to identify you or any other participants.

The information on data and samples will be stored in a password protected secure centralised database managed by GeneLibrary Ireland. In order to keep your information confidential, numerous safeguards are in place. In particular, we will:

- Remove personal identifiers such as your name or date of birth from your samples and records;
- Assign codes to your samples and records;
- Keep your personal details separate from your data and samples;
- Hold information in secure databases, which can only be accessed by the authorized staff and by approved researchers (who will only have access to coded information);
- Use stringent security measures to prevent unauthorized use, including: strict access controls, computer security and data encryption techniques, confidentiality agreements and staff training;
- Have a decoding step that will allow us to re-link your personal details with your samples and information, should you want to withdraw from the study or in order to make sure the database records are correct.

8.2 Sample storage
The samples will be stored at two locations for back-up purposes. These will be secure facilities, meeting international security and safety standards for laboratories. The same coding and security measures that are in place for your data will also apply to your samples.

9 Who can access your data and samples?

9.1 Access to your own samples and data
You cannot access your research results based on individual data and samples as GeneLibrary Ireland uses only aggregated data to create general results applicable to the population.

9.2 Access by researchers
GeneLibrary Ireland gives approved researchers access to data and samples (which may include researchers from academia, charitable organisations and private companies such as drug companies). All researchers will only have access to coded data or samples, in order to protect your privacy. They also have to obtain prior scientific and ethical approval, as described above, and their research must fit the purpose of GeneLibrary Ireland. Researchers have to sign appropriate agreements that control their permitted use of data and samples, and they are not permitted to disclose or transfer data or samples to anyone else or to use them for purposes other than those agreed with GeneLibrary Ireland when the samples were made available to them. Researchers must also agree that they will not attempt to re-identify you from your data and samples. The GeneLibrary Ireland will charge for researchers for access, but only a sufficient amount to be able to continue its work.

You should be aware that GeneLibrary Ireland may make the general results of the research studies conducted with GeneLibrary Ireland samples and data available on a website. This is done to make data more readily available to researchers and encourage medical advances by understanding more about genes and how they influence disease.

Such data will not have any identifiers that will enable anyone to link the data to you.

When any transferred samples are no longer needed for the purpose for which they were given to researchers, researchers must return them to GeneLibrary Ireland or destroy them. Researchers using GeneLibrary Ireland must also return their research results, so that those results are available for other researchers to use and to build upon in the future. This obligation helps to facilitate future research and improve the database.

9.3 International access
GeneLibrary Ireland expects to receive requests and, if approved, provide access to data and samples to overseas researchers and international collaborators. These researchers must follow the same procedures as all other researchers. All access is subject to the strictest scientific and ethical scrutiny, as described above.

10 What if you have concerns?
GeneLibrary Ireland aims to achieve the highest possible standards at all times. However, it is possible that you may have concerns. If you have any concerns or wish to make a complaint about any aspect of GeneLibrary Ireland at any time, you can telephone us free of charge on [ ] and ask to speak to [GeneLibrary Ireland contact]. Alternatively, you can write a letter or an email to [ ]. Please send your letter or email to [ ]. We take all comments seriously, and we will deal with them as quickly as possible.
11 Will there be any commercialisation?

GeneLibrary Ireland has been set up as guardian of the database and sample collection. The use of your data and samples might someday lead to the commercialization of a medical or genetic test or product. This may be done by a university or hospital, a commercial company or both working in partnership. This means that researchers, including, potentially, commercial companies, may benefit financially. You will not derive any personal financial advantage from this commercialization.

12 Will you receive any compensation for being involved?

Your participation is on a voluntary basis. You will not be paid.

13 How can you withdraw?

You are free to withdraw at any time from your participation without giving any reason. You can withdraw by telephoning us at GeneLibrary Ireland contact number or by writing to GeneLibrary Ireland [insert address]. You will receive a letter to confirm your withdrawal. If you withdraw, your samples and the data derived from your sample and other personal information will be no longer used. If the data is already part of a dataset it cannot be destroyed. The code that enables us to re-link your samples and personal information will be deleted so that no further information about you will be collected.
Appendix 3 Draft Consent form
GeneLibrary Ireland - Draft Consent form

Consent for use of blood samples and medical information

- **Confirmation of understanding of the information provided**

<table>
<thead>
<tr>
<th>Yes</th>
<th>Initials</th>
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1. I confirm that I have read and understood the information leaflet. I have had the opportunity to consider the information it contains. The risks and benefits of my participation have been discussed with me. I have had the chance to ask questions. These questions have been answered to my satisfaction.

2. I understand that

   My taking part is voluntary

   I am free to withdraw at any time, without giving any reason and without affecting my present or future medical treatment or legal rights. This can be done by telephoning GeneLibrary Ireland at xxxxxxx, by email to xxxxxxxxxxx or by writing to xxxxxxxxxxxxx

2. By agreeing to take part in GeneLibrary Ireland I agree to the following

<table>
<thead>
<tr>
<th>Yes</th>
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A. I agree that

1. GeneLibrary Ireland (or someone acting for them) may carry out a physical examination, including:
   - taking a blood sample of about 50mls (5 tablespoons)
   - a questionnaire about my health and lifestyle, family and medical history
   - basic clinical measurements, including measuring my weight, height and blood pressure etc.

2. The data and samples from this examination will be kept indefinitely. All samples will be kept in a secure facility overseen by GeneLibrary Ireland. If the resource/biobank has to close they will be archived

3. My personal and health information and my blood samples and DNA may be used at any time for future research studies which will be approved by an independent research ethics committee

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<th>Yes</th>
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</table>
### 3. Additional consent for follow-up contact

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>Initials</th>
</tr>
</thead>
<tbody>
<tr>
<td>I agree that GeneLibrary Ireland may contact me in the future for the following reasons.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. to provide additional samples to replenish the GeneLibrary Ireland sample stocks, (GeneLibrary Ireland will contact you no more than 3 times)</td>
<td></td>
<td></td>
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<tr>
<td>B. to invite me to participate in follow-up research studies which have been approved by an independent research ethics committee.</td>
<td></td>
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</table>

### 4. Results

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
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<tbody>
<tr>
<td>My participation will not provide me with any direct personal benefits, but I understand that general research results will be available at GeneLibrary Ireland website</td>
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</tbody>
</table>

1. I understand that the measurement and other results taken during the clinical assessment will be sent to me at the address given.

2. I also wish to have the measurements or other results taken during the clinical assessment sent to my GP

I understand that I can stay in the biobank even if I do not wish to be re-contacted.

### Confidentiality / security of data

I understand that the confidentiality of the sample(s) I donate and information derived there from will be protected. I have been told that all medical information/data pertaining to me and derived from the sample(s) will be protected by the principles of confidentiality and both national and EU data protection legislation. I have further been told and shown assurances that this also applies to all medical information/data pertaining to me and derived from the sample(s) that are utilised in any non-EU state.

### Access

I understand that unless access is required by law or court order, only approved researchers will have access to the information and samples of GeneLibrary Ireland. Access to my samples and data is subject to ethics approval and oversight. My samples and data will be provided in a coded format and my identity will be protected at all times.
Commercialisation

I understand that with proper oversight, results and samples may be exchanged with researchers in Ireland, Northern Ireland and other countries, along with those from commercial companies, for use in specific biomedical and genetic research studies. I will not receive any personal financial benefit from the commercialisation of any test or product that may result from this research.

Agreement to participate

[Name of person] has explained the procedures and implications of taking part to my satisfaction. I agree to participate and will receive a copy of this consent form after I sign it.

Participant Information

Name: _________________________________________

Signed _________________________________________ Date ___________

GeneLibrary Ireland Investigator or his/her designee confirmation

I described GeneLibrary Ireland, including the conditions of participation, to the participant. Any questions were answered. I explained that participation was voluntary.

Investigator/Desigee name ____________________ Signed ____________________ Date ________
Appendix 4 Frequently Asked Questions
GeneLibrary Ireland Frequently Asked Questions

What is the purpose of GeneLibrary Ireland

When researchers are trying to understand why some people develop diseases, they often study their DNA to see if there are certain changes that may cause disease. These samples can then be compared with DNA from people without the disease. GeneLibrary Ireland will provide the control DNA through the donations of 10,000 adults between 30 and 60 years old living on the island of Ireland.

Who are the Organisers?

GeneLibrary Ireland is an all-island initiative involving partnership between all the Universities with Medical schools in the Republic of Ireland (under the auspices of Molecular Medicine Ireland), Queen’s university in Belfast and the University of Ulster. In addition the Health Research Board of Ireland and the Northern Ireland Research and Development Office.

Who can take part?

Anyone between the ages of 30-60 may take part.

Can people from ethnic minorities take part?

Yes. GeneLibrary Ireland will be composed of DNA samples representative of all the people living on the Island of Ireland.

Will participants be paid for their contribution?

No. Participation in GeneLibrary Ireland is entirely voluntary.

What will taking part involve?

Participation in GeneLibrary Ireland involves a number of steps

2. when you agree to take part our team will contact you to arrange an appointment for you to come and visit one of our centres (these centres are based at major hospital sites)

3. we will send you some questionnaires to complete before you come for your visit

4. on the day of your visit, one of our highly experienced research team will meet with you to discuss the study and answer your queries

5. If after talking to our staff, you still want to participate, you will be asked to sign a consent form

6. You will then undergo a medical examination, to measure your health status.

7. Blood samples will also be taken for testing

8. A final blood sample will be taken from which your DNA will be extracted for use in research studies.

How much of my time will be required?

The visit with the research team will take approximately 2 hours
What are the benefits to me personally?

As part of your participation in GeneLibrary Ireland, you will have a comprehensive medical check up. The results of this check up will be given to you and to your GP if you would like.

How do you keep my information anonymous?

When you enrol in GeneLibrary Ireland, a unique participant identification number will be assigned to your sample. Only the research team at the site that you visit will know your name. Anyone else involved in the study will only see your identification number. This will be kept confidential and secure in a GeneLibrary Ireland database.

How long will samples be utilised?

Your samples will be utilised well into the future. Indeed you may be re-contacted in the future where we will ask if you would like to contribute another sample to the study. Any request to use your sample will always be subject to prior approval by the GeneLibrary Ireland ethics committee.

Will participants receive information on their genes?

No information regarding the results of genetic testing will be given to individual participants as these are research studies. However, the results from the larger GeneLibrary population will be published in the medical and scientific literature and updated on the GeneLibrary Ireland website.

Can you tell if genetic diseases run in my family?

No. This study will not be able to look at patterns of hereditary.

Who will have access to the information?

Access to the information and samples within GeneLibrary Ireland will be under the control of both a scientific and an ethical review board. Before anyone can access information they will apply to these boards for permission. Following scientific and ethics approval your sample and/or data will be provided to researchers but you will not be identifiable from this information.

Can insurance companies access this information?

No. The information collected in GeneLibrary Ireland is collected for Molecular Research Purposes only.

Will police have access to the information?

No. However, in the unlikely events that the courts would order information to be released, GeneLibrary Ireland would have to comply with this request.

Will pharmaceutical companies have access to the information?

Pharmaceutical companies may access the information and samples for use in research studies only. As above, all applications to utilise the resource will be subject to prior review and approval.
Can I change my mind and leave the study?

Yes. Should you so choose you can contact the research team and we will remove you from the study. It is not possible to withdraw data that has already been used on you but no new data will be generated and your samples will no longer be used within GeneLibrary Ireland.
Appendix 5 Questionnaires
Gene Library Ireland
Clinic Visit Questionnaire
Touch Screen Delivery
Draft 2

This questionnaire contains questions on the following elements for you to complete:

A. Personal Details
B. Personal and Family Health
C. Family History
D. Smoking History
E. Exposure to Tobacco Smoke
F. Alcohol
G. Personality and Mental Health trait measures – Community Assessment of Psychic Experience

Unique Participant ID

Signature

Date

Please tick boxes where prompted, enter text or dates as dd/mm/yy. In some questions, more than one box may be ticked.

Consent

Has informed consent been obtained?   |_Yes   |_No

Please specify date signed

Research Nurse Name

Research Nurse Code

d d / m m / y y y y
A. Personal Details

1. What is your age? |___|___| years

2. What is your sex? (Please tick one answer only)
   |_| Male
   |_| Female
   |_| Intersex
   |_| Not specified / Intermediate

3a. Where were you born?

Country |___|___|___|___|___|___|___|___|___|___|___|___|___|___|___|___|___|

3b. If Ireland and Northern Ireland, what county and town(land) (if known)?

County |___|___|___|___|___|___|___|___|___|___|___|___|___|___|___|___|___|
Town(land) |___|___|___|___|___|___|___|___|___|___|___|___|___|___|___|___|___|

3c. If you were born outside Ireland, what year did you come to live here? |___|___|___|___|

4. What is your cultural background? (Please tick one answer only)
   |_| White - Irish
   |_| White - British
   |_| White - any other white background (please specify below)
   |_| Mixed - any mixed background (please specify below)
   |_| Asian - Indian
   |_| Asian - Pakistani
   |_| Asian - Bangladeshi
   |_| Asian - Chinese
   |_| Asian - Any other Asian background (please specify below)
   |_| Black - Caribbean
   |_| Black - African
   |_| Black - any other Black background (please specify below)
   |_| Any other ethnic background (please specify below)
   |_| Not Known
   |_| Not Disclosed

Please Specify: ___________________________________________________________________________________
____________________________________________________________________________________________________
## B. Personal and Family Health

1. Have you ever been diagnosed with any of the following medical conditions?

Any treatment required (please specify)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Please Tick</th>
<th>Age at first diagnosis</th>
<th>None</th>
<th>Drug Treatment</th>
<th>Other Treatment</th>
<th>Operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Disease</td>
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<tr>
<td>Stroke</td>
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<tr>
<td>High Blood Pressure</td>
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<tr>
<td>High Cholesterol</td>
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<tr>
<td>Diabetes</td>
<td>[_]</td>
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<td>Alzheimer's disease</td>
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<td>Parkinson's disease</td>
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<td>Severe depression</td>
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</table>
**1b. Have you ever been diagnosed with any other serious illness, please tick the relevant box?**

<table>
<thead>
<tr>
<th></th>
<th>Certain infectious and parasitic diseases (eg hepatitis, diphtheria)</th>
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<tr>
<td></td>
<td>Diseases of the musculoskeletal system and connective tissue (eg osteoporosis, arthritis)</td>
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<td></td>
<td>Cancer (other than those itemised above)</td>
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<td></td>
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<td></td>
<td>Diseases of the blood and blood-forming organs (eg anaemia)</td>
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<td></td>
<td>Disease of Pregnancy and/or childbirth (eg rubella, neural tube defects)</td>
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<td></td>
<td>Endocrine, nutritional and metabolic Diseases (eg thyroid disease)</td>
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<td></td>
<td>Certain conditions originating in the perinatal period (eg varicose veins, placenta praevia)</td>
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<td></td>
<td>Mental and behavioural disorders (eg clinical depression, schizophrenia)</td>
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<td></td>
<td>Congenital malformations, deformations and chromosomal abnormalities (eg cleft palette)</td>
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<td></td>
<td>Diseases of the nervous system (eg Parkinson’s, MS, epilepsy, cerebral palsy)</td>
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<td></td>
<td>Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (eg, heart murmur, stutter)</td>
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<td></td>
<td>Diseases of the eye (eg cataracts, glaucoma)</td>
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<td>Diseases of the ear (eg otosclerosis)</td>
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<td></td>
<td>Diseases of the circulatory system (eg rheumatic fever, hypertension)</td>
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<td>Injury, poisoning and certain other consequences of external causes</td>
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<td></td>
<td>Diseases of the respiratory system (eg pneumonia)</td>
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<td></td>
<td>External causes of morbidity and mortality (eg accident, assault, alcoholism)</td>
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<td></td>
<td>Diseases of the digestive system (eg crohn’s, diverticulosis)</td>
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<td></td>
<td>Diseases of the skin and subcutaneous tissue (eg eczema, cellulitis, dermatitis)</td>
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<td>Other (please specify below)</td>
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________________________________________________________________________________________
2. Please tick the box if your father, mother or any brother, sister or grandparent has been affected by any of these conditions

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<tr>
<th></th>
<th>father</th>
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<th>brother</th>
<th>sister</th>
<th>grandparent</th>
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<td>Heart Disease</td>
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<td>Stroke</td>
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</table>

2b. Any other serious illness that runs in your family?

| | Certain infectious and parasitic diseases (eg hepatitis, diphtheria) | Diseases of the musculoskeletal system and connective tissue (eg osteoporosis, arthritis) |
| | Cancer (other than those itemised above) | Diseases of the genitourinary system (eg renal failure, venereal disease, nephritis) |
| | Diseases of the blood and blood-forming organs (eg anaemia) | Disease of Pregnancy and/or childbirth (eg rubella, neural tube defects) |
| | Endocrine, nutritional and metabolic Diseases (eg thyroid disease) | Certain conditions originating in the perinatal period (eg varicose veins, placenta praevia) |
| | Mental and behavioural disorders (eg clinical depression, schizophrenia) | Congenital malformations, deformations and chromosomal abnormalities (eg cleft palate) |
| | Diseases of the nervous system (eg Parkinson’s, MS, epilepsy, cerebral palsy) | Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (eg, heart murmur, stutter) |
| | Diseases of the eye | Diseases of the ear (eg otosclerosis) |
(eg cataracts, glaucoma)

|___| Diseases of the circulatory system  
|___| (eg rheumatic fever, hypertension)  

|___| Diseases of the respiratory system  
|___| (eg pneumonia)  

|___| Diseases of the digestive system  
|___| (eg crohn’s, diverticulosis)  

|___| Other (please specify below)  

Please Specify:
C. Family History

It is known that some health problems run in families. We have a family history section to help us to find out more about this. If you are adopted or if your parents remarried it would be better to know about your biological family (i.e. blood relations) for both your parents and your brothers and sisters.

1. When was your father's date of birth?  
   - [ ] Only Year Known  
   - [ ] Full Date Known  
   - [ ] Not Known

2. Where was your father born?

   Country

   ___________________________________________________________________________________________
   If Ireland and/or Northern Ireland, what county and town(land) (if known)?

   Country

   ___________________________________________________________________________________________
   Town(land)

3. Is your father still alive?  
   - [ ] Yes  
   - [ ] No  
   - [ ] Don’t Know

3a. If he has died, what was the date of his death?  
   - [ ] Only Year Known  
   - [ ] Full Date Known  
   - [ ] Not Known

3b. If he has died, what was the cause of his death? (tick one answer only)

   - [ ] Accident  
   - [ ] Influenza and pneumonia  
   - [ ] Alzheimer's Disease  
   - [ ] Kidney Disease  
   - [ ] Assault  
   - [ ] Liver Disease  
   - [ ] Blood Poisoning  
   - [ ] Stroke  
   - [ ] Cancer  
   - [ ] Suicide  
   - [ ] Diabetes  
   - [ ] Other Cause  
   - [ ] Heart Disease  
   - [ ] Not Disclosed  
   - [ ] HIV  
   - [ ] Not Known

4. Where was your father’s father born?

   Country

   ___________________________________________________________________________________________
   If Ireland and/or Northern Ireland, what county and town(land) (if known)?

   Country

   ___________________________________________________________________________________________
   Town(land)
5. Where was your father's mother born?

Country

_________________________________________________________________________________________

If Ireland and/or Northern Ireland, what county and town(land) (if known)?

County

_________________________________________________________________________________________

Town(land)

_________________________________________________________________________________________

6. When was your mother's year or date of birth?  
   |_| Only Year Known  |___|___|___|___|
   |_| Full Date Known  |___|___| |___|___| |___|___|
   |_| Not Known

7. Where was your mother born?

Country

_________________________________________________________________________________________

If Ireland and/or Northern Ireland, what county and town(land) (if known)?

County

_________________________________________________________________________________________

Town(land)

_________________________________________________________________________________________

8. Is your mother still alive?  
   |_| Yes      |_| No      |_| Don't Know

8a. If she has died, what was the date of her death?  
   |_| Only Year Known  |___|___|___|___|
   |_| Full Date Known  |___|___| |___|___| |___|___|
   |_| Not Known

8b. If she has died, what was the cause of her death? (Please tick one answer only)

   |_| Accident
   |_| Influenza and pneumonia
   |_| Alzheimer's Disease
   |_| Kidney Disease
   |_| Assault
   |_| Liver Disease
   |_| Blood Poisoning
   |_| Stroke
   |_| Cancer
   |_| Suicide
   |_| Diabetes
   |_| Other Cause
   |_| Heart Disease
   |_| Not Disclosed
   |_| HIV
   |_| Not Known
9. Where was your mother's father born?

Country

If Ireland and/or Northern Ireland, what county and town(land) (if known)?

County

Town(land)

10. Where was your mother's mother born?

Country

If Ireland and/or Northern Ireland, what county and town(land) (if known)?

County

Town(land)
D. Smoking History

1. Have you ever smoked tobacco?
   - [ ] Yes, currently smoke (GO TO QUESTIONS 2-3)
   - [ ] Yes but stopped within past 12 months (GO TO QUESTIONS 2-5)
   - [ ] Yes but stopped more than 12 months ago (GO TO QUESTIONS 2-5)
   - [ ] No, never smoked (GO TO SECTION E)

2. What age were you when you started smoking? [___] years old

3. What is the maximum number you have smoked per day for as long as a year?
   - [___] cigarettes per week
   - [___] packets of tobacco per week
   - [___] cigars per week

IF YOU HAVE STOPPED SMOKING, GO TO Q4, IF YOU CURRENTLY SMOKE, GO TO SECTION E

4. How long since you gave up smoking? [___] years [___] months [___] days

5. Why did you give up smoking? (please tick one answer only)
   - [ ] On doctor's advice
   - [ ] Family influence
   - [ ] Financial reason
   - [ ] Other reason (Please specify)

E. Exposure to Tobacco Smoke

1. Are you regularly exposed to other peoples tobacco smoke?

<table>
<thead>
<tr>
<th></th>
<th>Yes, a lot</th>
<th>Yes, some</th>
<th>Yes, a little</th>
<th>No, none at all</th>
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<tbody>
<tr>
<td>at work</td>
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<td>in your home</td>
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<tr>
<td>in other places (e.g. socially)</td>
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</table>

2. On average, for how many hours per week are you exposed to other people's tobacco smoke?
   [___] [___] hours per week

3. Do you live with anyone who smokes?
   - [ ] Yes
   - [ ] No
   - [ ] Don't Know
F. Alcohol

1. Have you ever had an alcoholic drink?
   (mark X in the box to indicate your response)
   |_| Yes, currently drink
   |_| Yes, but stopped within past 12 months
   |_| Yes, but stopped more than 12 months ago
   |_| No, never drank

2. During the past week, please record how many units of alcohol you have had:
   (If you have had no units, please enter 0)
   Number of units |___|___|

To help you calculate the number of units of alcohol you have had, the following is given as a
   guideline.

   Approximate Units

   1 pint of ordinary beer, cider or lager  2
   1 bottle/can of ordinary strength beer/lager  2
   1 bottle/can of extra strength beer /lager  4
   1 can of cider  2
   1 litre of cider  9
   1 small glass of wine (125ml)  1
   1 bottle of wine (75cl)  6
   1 small glass of sherry  1
   1 bottle of sherry  12
   1 pub measure of spirits (25ml)  1
   1 bottle of spirits (75cl)  30
   1 bottle of alcopops  2

3. How does this compare to what you usually drink in a week?
   More |___|   Same |___|   Less |___|

IF YOU HAVE STOPPED DRINKING ALCOHOL GO TO QUESTION 4, IF NOT GO TO SECTION G.

4. How long is it since you gave up drinking?
   |___|___| years   |___|___| months   |___|___| days

5. Why did you give up drinking? (please tick one answer only)
   |___| On doctor's advice
   |___| Family influence
   |___| Financial reason
   |___| Other reason (Please specify)

______________________________________________________________________________
Personality and Mental Health Traits

This questionnaire is a measure of personality and mental health traits and is entitled the Community Assessment of Psychic Experience (CAPE) (75)

1. Do you ever feel sad? (please tick)

Never  |  Sometimes  |  Often  |  Nearly always  

If you ticked "never", please go to question 2

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  |  A bit distressed  |  Quite distressed  |  Very distressed  

2. Do you ever feel as if people seem to drop hints about you or say things with a double meaning? (please tick)

Never  |  Sometimes  |  Often  |  Nearly always  

If you ticked "never", please go to question 3

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  |  A bit distressed  |  Quite distressed  |  Very distressed  

3. Do you ever feel that you are not a very animated person? (please tick)

Never  |  Sometimes  |  Often  |  Nearly always  

If you ticked "never", please go to question 4

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  |  A bit distressed  |  Quite distressed  |  Very distressed  

4. Do you ever feel that you are not much of a talker when you are conversing with other people? (please tick)

Never  |  Sometimes  |  Often  |  Nearly always  

If you ticked "never", please go to question 5

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  |  A bit distressed  |  Quite distressed  |  Very distressed  

5. Do you ever feel as if things in magazines or on TV were written especially for you? (please tick)

Never  |  Sometimes  |  Often  |  Nearly always  

If you ticked "never", please go to question 6
If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  []  A bit distressed  []  Quite distressed  []  Very distressed  []

6. Do you ever feel as if some people are not what they seem to be? (please tick)

Never  []  Sometimes  []  Often  []  Nearly always  []

If you ticked "never", please go to question 7

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  []  A bit distressed  []  Quite distressed  []  Very distressed  []

7. Do you ever feel as if you are being persecuted in some way? (please tick)

Never  []  Sometimes  []  Often  []  Nearly always  []

If you ticked "never", please go to question 8

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  []  A bit distressed  []  Quite distressed  []  Very distressed  []

8. Do you ever feel that you experience few or no emotions at important events? (please tick)

Never  []  Sometimes  []  Often  []  Nearly always  []

If you ticked "never", please go to question 9

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  []  A bit distressed  []  Quite distressed  []  Very distressed  []

9. Do you ever feel pessimistic about everything? (please tick)

Never  []  Sometimes  []  Often  []  Nearly always  []

If you ticked "never", please go to question 10

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  []  A bit distressed  []  Quite distressed  []  Very distressed  []

10. Do you ever feel as if there is a conspiracy against you? (please tick)

Never  []  Sometimes  []  Often  []  Nearly always  []

If you ticked "never", please go to question 11

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)
11. Do you ever feel as if you are destined to be someone very important? (please tick)

Never [] Sometimes [] Often [] Nearly always []

If you ticked "never", please go to question 12

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [] A bit distressed [] Quite distressed [] Very distressed []

12. Do you ever feel as if there is no future for you? (please tick)

Never [] Sometimes [] Often [] Nearly always []

If you ticked "never", please go to question 13

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [] A bit distressed [] Quite distressed [] Very distressed []

13. Do you ever feel that you are a very special or unusual person? (please tick)

Never [] Sometimes [] Often [] Nearly always []

If you ticked "never", please go to question 14

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [] A bit distressed [] Quite distressed [] Very distressed []

14. Do you ever feel as if you do not want to live anymore? (please tick)

Never [] Sometimes [] Often [] Nearly always []

If you ticked "never", please go to question 15

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [] A bit distressed [] Quite distressed [] Very distressed []

15. Do you ever think that people can communicate telepathically? (please tick)

Never [] Sometimes [] Often [] Nearly always []

If you ticked "never", please go to question 16

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [] A bit distressed [] Quite distressed [] Very distressed []

16. Do you ever feel that you have no interest to be with other people? (please tick)
Never  |  Sometimes  |  Often  |  Nearly always  |

If you ticked "never", please go to question 17

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  |  A bit distressed  |  Quite distressed  |  Very distressed |

17. Do you ever feel as if electrical devices such as computers can influence the way you think? (please tick)

Never  |  Sometimes  |  Often  |  Nearly always  |

If you ticked "never", please go to question 18

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  |  A bit distressed  |  Quite distressed  |  Very distressed |

18. Do you ever feel that you are lacking in motivation to do things? (please tick)

Never  |  Sometimes  |  Often  |  Nearly always  |

If you ticked "never", please go to question 19

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  |  A bit distressed  |  Quite distressed  |  Very distressed |

19. Do you ever cry about nothing? (please tick)

Never  |  Sometimes  |  Often  |  Nearly always  |

If you ticked "never", please go to question 20

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  |  A bit distressed  |  Quite distressed  |  Very distressed |

20. Do you believe in the power of witchcraft, voodoo or the occult? (please tick)

Never  |  Sometimes  |  Often  |  Nearly always  |

If you ticked "never", please go to question 21

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  |  A bit distressed  |  Quite distressed  |  Very distressed |

21. Do you ever feel that you are lacking in energy? (please tick)

Never  |  Sometimes  |  Often  |  Nearly always  |
If you ticked "never", please go to question 22

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience:(please tick)

Not distressed  |  A bit distressed  |  Quite distressed  |  Very distressed  |

22. Do you ever feel that people look at you oddly because of your appearance?(please tick)

Never  |  Sometimes  |  Often  |  Nearly always  |

If you ticked "never", please go to question 23

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience:(please tick)

Not distressed  |  A bit distressed  |  Quite distressed  |  Very distressed  |

23. Do you ever feel that your mind is empty?(please tick)

Never  |  Sometimes  |  Often  |  Nearly always  |

If you ticked "never", please go to question 24

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience:(please tick)

Not distressed  |  A bit distressed  |  Quite distressed  |  Very distressed  |

24. Do you ever feel as if the thoughts in your head are being taken away from you?(please tick)

Never  |  Sometimes  |  Often  |  Nearly always  |

If you ticked "never", please go to question 25

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience:(please tick)

Not distressed  |  A bit distressed  |  Quite distressed  |  Very distressed  |

25. Do you ever feel that you are spending all your days doing nothing?(please tick)

Never  |  Sometimes  |  Often  |  Nearly always  |

If you ticked "never", please go to question 26

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience:(please tick)

Not distressed  |  A bit distressed  |  Quite distressed  |  Very distressed  |

26. Do you ever feel as if the thoughts in your head are not your own?(please tick)

Never  |  Sometimes  |  Often  |  Nearly always  |

If you ticked "never", please go to question 27
27. Do you ever feel that your feelings are lacking in intensity? (please tick)

Never [ ] Sometimes [ ] Often [ ] Nearly always [ ]

If you ticked "never", please go to question 28

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [ ] A bit distressed [ ] Quite distressed [ ] Very distressed [ ]

28. Have your thoughts ever been so vivid that you were worried other people would hear them? (please tick)

Never [ ] Sometimes [ ] Often [ ] Nearly always [ ]

If you ticked "never", please go to question 29

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [ ] A bit distressed [ ] Quite distressed [ ] Very distressed [ ]

29. Do you ever feel that you are lacking in spontaneity? (please tick)

Never [ ] Sometimes [ ] Often [ ] Nearly always [ ]

If you ticked "never", please go to question 30

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [ ] A bit distressed [ ] Quite distressed [ ] Very distressed [ ]

30. Do you ever hear your own thoughts being echoed back to you? (please tick)

Never [ ] Sometimes [ ] Often [ ] Nearly always [ ]

If you ticked "never", please go to question 31

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [ ] A bit distressed [ ] Quite distressed [ ] Very distressed [ ]

31. Do you ever feel as if you are under the control of some force or power other than yourself? (please tick)

Never [ ] Sometimes [ ] Often [ ] Nearly always [ ]

If you ticked "never", please go to question 32

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)
Not distressed  []  A bit distressed  []  Quite distressed  []  Very distressed  []

32. Do you ever feel that your emotions are blunted? (please tick)

Never  []  Sometimes  []  Often  []  Nearly always  []

If you ticked "never", please go to question 33

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  []  A bit distressed  []  Quite distressed  []  Very distressed  []

33. Do you ever hear voices when you are alone? (please tick)

Never  []  Sometimes  []  Often  []  Nearly always  []

If you ticked "never", please go to question 34

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  []  A bit distressed  []  Quite distressed  []  Very distressed  []

34. Do you ever hear voices talking to each other when you are alone? (please tick)

Never  []  Sometimes  []  Often  []  Nearly always  []

If you ticked "never", please go to question 35

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  []  A bit distressed  []  Quite distressed  []  Very distressed  []

35. Do you ever feel that you are neglecting your appearance or personal hygiene? (please tick)

Never  []  Sometimes  []  Often  []  Nearly always  []

If you ticked "never", please go to question 36

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  []  A bit distressed  []  Quite distressed  []  Very distressed  []

36. Do you ever feel that you can never get things done? (please tick)

Never  []  Sometimes  []  Often  []  Nearly always  []

If you ticked "never", please go to question 37

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  []  A bit distressed  []  Quite distressed  []  Very distressed  []

37. Do you ever feel that you have only few hobbies or interests? (please tick)
If you ticked "never", please go to question 38

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [ ] A bit distressed [ ] Quite distressed [ ] Very distressed [ ]

38. Do you ever feel guilty? (please tick)

If you ticked "never", please go to question 39

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [ ] A bit distressed [ ] Quite distressed [ ] Very distressed [ ]

39. Do you ever feel like a failure? (please tick)

If you ticked "never", please go to question 40

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [ ] A bit distressed [ ] Quite distressed [ ] Very distressed [ ]

40. Do you ever feel tense? (please tick)

If you ticked "never", please go to question 41

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [ ] A bit distressed [ ] Quite distressed [ ] Very distressed [ ]

41. Do you ever feel as if a double has taken the place of a family member, friend or acquaintance? (please tick)

If you ticked "never", please go to question 42

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [ ] A bit distressed [ ] Quite distressed [ ] Very distressed [ ]

42. Do you ever see objects, people or animals that other people cannot see? (please tick)

If you ticked "never", please go to question 43

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [ ] A bit distressed [ ] Quite distressed [ ] Very distressed [ ]

43. Do you ever have the feeling that you are not real? (please tick)

If you ticked "never", please go to question 44

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [ ] A bit distressed [ ] Quite distressed [ ] Very distressed [ ]

44. Do you ever feel that you can influence things that happen without trying? (please tick)

If you ticked "never", please go to question 45

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [ ] A bit distressed [ ] Quite distressed [ ] Very distressed [ ]

45. Do you ever feel you are seeing things that are not there? (please tick)

If you ticked "never", please go to question 46

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [ ] A bit distressed [ ] Quite distressed [ ] Very distressed [ ]

46. Do you ever feel as if you are going to die? (please tick)

If you ticked "never", please go to question 47

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [ ] A bit distressed [ ] Quite distressed [ ] Very distressed [ ]

47. Do you ever feel that you need to protect yourself? (please tick)

If you ticked "never", please go to question 48

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [ ] A bit distressed [ ] Quite distressed [ ] Very distressed [ ]

48. Do you ever think you are going mad? (please tick)

If you ticked "never", please go to question 49

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [ ] A bit distressed [ ] Quite distressed [ ] Very distressed [ ]

49. Do you ever feel that other people are not real? (please tick)

If you ticked "never", please go to question 50

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed [ ] A bit distressed [ ] Quite distressed [ ] Very distressed [ ]

50. Do you ever feel that you are in a dream? (please tick)
If you ticked "never", you are now completed the questionnaire section

If you ticked "sometimes", "often" or "nearly always" please indicate how distressed you are by this experience: (please tick)

Not distressed  |   A bit distressed  |   Quite distressed  |   Very distressed  |
The GeneLibrary Ireland Research Nurse will have given you this questionnaire as part of your clinic visit to complete at home after the visit and in your own time. As part of your visit you will also have arranged a date and time with the Research Nurse when he/she will call you to check that you have completed this questionnaire and to help you with any difficult questions.

Please do not forget to put your completed form in the GeneLibrary Ireland pre-paid envelope and this will complete your enrollment in GeneLibrary Ireland.

Unique Participant ID |___|___|___|___|___|___|___|___|___|___|___|
Research Nurse Name ____________________________________
Date : d d / m m / y y y y |___|___| |___|___| |___|___|___|___|
Date/time of Research Nurse Telephone Call: Date|___|___| |___|___| Time|___|___|___|___|

Instructions to help with completion of questionnaire

- Complete using a black ballpoint pen if possible.
- Please complete as much of the form as possible.
- Enter numbers clearly inside the boxes.
- Enter a cross (X) inside appropriate boxes.
- Write all entries clearly using block capital letters when writing text.
- If you make a mistake and want to change an entry, please cross through the original and write the correct entry above or to the side.
- Please write only in designated areas.

Contents of this questionnaire

H. Medication
I. Educational and Occupational History
J. Siblings
K. Household
L. Income
M(1-4). Personality and Mental Health trait measures;
N. Neuropsychiatric Disorder Screening tools
H. Medications

Please fill out any medications or supplements that you REGULARLY take. These include:
- prescribed medicines from your GP or hospital,
- over the counter medicines bought from a chemist or shop
- supplements, vitamins, complementary or alternative medicines (eg evening primrose oil)

Don't forget to include contraceptive pill or injections; hormone replacement therapy; and inhalers (eg Ventolin)

I. Name of Prescribed or Bought Pills or other Oral Medication

(tablets or capsules) OR Write none here if you don’t take any

1.
2.
3.
4.
5.
6.
7.
8.
9.
10.

II. Name of Prescribed or Bought Cream/Ointment or Other Topical Preparation (such as patches)

OR Write none here if you don’t take any

1.
2.
3.
4.
5.

III. Name of Prescribed or Bought Inhaler or Nasal Spray

OR Write none here if you don’t take any

1.
2.
3.
4.
5.

IV. Name of Prescribed or Bought Injection or Suppository

OR Write none here if you don’t take any

1.
2.
3.
4.
5.
I. Educational and Occupational History

1. How many years altogether did you attend school or study full-time? years
   University degree

2. What is the highest educational qualification you have obtained?
   - None
   - Junior Certificate / Intermediate Certificate / 'O' Levels or equivalent
   - Leaving Certificate / A Levels or equivalent
   - University Degree
   - Other professional or technical qualification or diploma after leaving school

3. What is your employment?
   Please include here: |___|___|___|___|___|___|___|___|___|___|___|___|___|___|
   (if currently unemployed, what was your last job)
   Please include here: |___|___|___|___|___|___|___|___|___|___|___|___|___|___|
   If you are unemployed, please state for how long
   Months |___|___|___|___| Years|___|___|

4. If you are employed, what best describes the type of work your job mainly involves?
   - Self-employed employing others
   - Self-employed not employing others
   - Paid employee supervising others
   - Paid employee not supervising
   - In unpaid employment
   - Homemaker
   - Retired
   - Full-time student
   - Unemployed, sick or disabled
   - Unemployed, seeking work
J. Siblings

1. **How many biological brothers and sisters do you have?** (include those who have died, full, half brothers and twin brothers and sisters. Do not include stepbrothers or stepsisters, or adopted brothers or sisters):
   Number

2. **What is your birth rank?** (consider ONLY siblings from the same mother, including those who have died. Do not include stepbrothers or adopted brothers)
   (instructions: birth order from the oldest to the youngest, eg first born = 1, second born = 2 etc)
   Include Here:

3. **Are you a twin, triple or other multiple birth?**
   (instructions: twin = 1, triplet = 2, other multiple = 3)
   If yes, include here

K. Household Status

1. **Do you live with a spouse or a partner in a common household?** (Include those who usually live in the house such as partners in the armed forces or professions such as sailors or pilots)
   Yes  No

2. **Including yourself, how many people live in your household?** (include those who usually live in the house such a students living away from home during term, partners in the armed forces or in professions such as pilots.)
   Number

L. Income

**What is the average total income before tax received by your entire household** (including salaries, benefits, pensions, allowances)?

- €20,000 or less
- €20,000 - €40,000
- €50,000 - €80,000
- €80,000 - €150,000
- Greater than €150,000
### Personality and Mental Health Trait Measures

The following series questionnaires are related to your personality and mental health traits.

**M1 The Eyesneck Personality Questionnaire revised (EPQ-R) looks at personality traits (73)**

INSTRUCTIONS: Please answer each question by putting a circle around the 'YES' or 'NO' following the question. There are no right or wrong answers, and no trick questions. Work quickly and do not think too long about the exact meaning of the questions.

<table>
<thead>
<tr>
<th></th>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Does your mood often go up and down?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Do you take much notice of what people think?</td>
<td></td>
<td></td>
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<tr>
<td>3</td>
<td>Are you a talkative person?</td>
<td></td>
<td></td>
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<tr>
<td>4</td>
<td>If you say you will do something, do you always keep your promise no matter how inconvenient it might be?</td>
<td></td>
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<tr>
<td>5</td>
<td>Do you ever feel 'just miserable' for no reason?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Would being in debt worry you?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Are you rather lively?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Were you ever greedy by helping yourself to more than your fair share of anything?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Are you an irritable person?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Would you take drugs which may have strange or dangerous effects?</td>
<td></td>
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</tr>
<tr>
<td>11</td>
<td>Do you enjoy meeting new people?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Have you ever blamed someone for doing something you knew was really your fault?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Are your feelings easily hurt?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Do you prefer to go your own way rather than act by the rules?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Can you usually let yourself go and enjoy yourself at a lively party?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Are all your habits good and desirable ones?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Do you often feel 'fed-up'?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Do good manners and cleanliness matter much to you?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>Do you usually take the initiative in making new friends?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Have you ever taken anything (even a pin or button) that belonged to someone else?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Would you call yourself a nervous person?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Do you think marriage is old-fashioned and should be done away with?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>Can you easily get some life into a rather dull party?</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Question</td>
<td></td>
<td></td>
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<td>---</td>
<td>--------------------------------------------------------------------------</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>24</td>
<td>Have you ever broken or lost something belonging to someone else?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>25</td>
<td>Are you a worrier?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>26</td>
<td>Do you enjoy cooperating with others?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>27</td>
<td>Do you tend to keep in the background on social occasions?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>28</td>
<td>Do you worry if you know there are mistakes in your work?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>29</td>
<td>Have you ever said anything bad or nasty about anyone?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>30</td>
<td>Would you call yourself tense or ‘highly-strung’?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>31</td>
<td>Do you think people spend too much time safeguarding their future with</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td></td>
<td>savings and insurance?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>32</td>
<td>Do you like mixing with people?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>33</td>
<td>As a child were you ever cheeky with your parents?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>34</td>
<td>Do you worry too long after an embarrassing experience?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>35</td>
<td>Do you try not to be rude with people?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>36</td>
<td>Do you like plenty of bustle and excitement around you?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>37</td>
<td>Have you ever cheated at a game?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>38</td>
<td>Do you suffer from ‘nerves’?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>39</td>
<td>Would you like other people to be afraid of you?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>40</td>
<td>Have you ever taken advantage of someone?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>41</td>
<td>Are you mostly quiet when you are with other people?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>42</td>
<td>Do you often feel lonely?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>43</td>
<td>Is it better to follow society’s rules than go your own way?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>44</td>
<td>Do other people think of you as being very lively?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>45</td>
<td>Do you always practice what you preach?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>46</td>
<td>Are you often troubled about feelings of guilt?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>47</td>
<td>Do you sometimes put off until tomorrow what you ought to do today?</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>48</td>
<td>Can you get a party going?</td>
<td>yes</td>
<td>no</td>
</tr>
</tbody>
</table>

This questionnaire is copyright to H J Eysenck and S.B.G. Eyseneck 1991.
M  Personality and Mental Health Traits

M4  This questionnaire is called the SCID screening questionnaire and is a measure of any history of major mood disorder (80)

SECTION A
1. Have you ever had a period when you felt depressed or down most of the day nearly every day?
   yes, | no | don’t know | don’t want to answer.

   IF NO:
   2. What about a time when you lost interest or pleasure in things you usually enjoyed?
      yes, | no | don’t know | don’t want to answer.

   IF NO to 1 and 2 MOVE TO NEXT SECTION (section complete)

   IF YES to 1 and/or 2:
   Did this last for more than two weeks?
      yes, | no | don’t know | don’t want to answer.

   IF NO, MOVE TO NEXT SECTION N (this section is now complete)

   IF YES : At this time:
   3. How was your appetite? Did you lose or gain more than 5% of your body weight in a month?
      yes, | no | don’t know | don’t want to answer.

   4. How did you sleep? Did you sleep more or less than usual?
      yes, | no | don’t know | don’t want to answer.

   5. Were you fidgety or restless to the point that you couldn’t sit still?
      yes, | no | don’t know | don’t want to answer.

   IF NO: were you talking or moving more slowly than is normal for you?
      yes, | no | don’t know | don’t want to answer.

   6. Were you tired all the time?
      yes, | no | don’t know | don’t want to answer.

   7. Did you feel worthless or excessively guilty?
      yes, | no | don’t know | don’t want to answer.

   8. Did you have trouble thinking or concentrating?
      yes, | no | don’t know | don’t want to answer.

   IF NO: was it hard to make decisions about everyday things?
      yes, | no | don’t know | don’t want to answer.

   9. Were things so bad that you were thinking a lot about death or that you would be better off death?
      yes, | no | don’t know | don’t want to answer.

      Have you had more than one episode like this?
      yes, | no | don’t know | don’t want to answer.

      Have you received treatment by a GP or psychiatrist for these symptoms?
      yes, | no | don’t know | don’t want to answer.
This questionnaire is called the General Health Questionnaire and is a measure of mental well being which has been developed by David Goldberg (79).

We should like to know if you have had any medical complaints and how your health has been in general, over the past few weeks. Please answer ALL the questions on the following pages simply by underlining the answer which you think most nearly applies to you. Remember that we want to know about present and recent complaints, not those that you had in the past.

It is important that you try to answer ALL the questions.

<table>
<thead>
<tr>
<th>Question</th>
<th>Better</th>
<th>Same</th>
<th>Worse</th>
<th>Much worse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have you recently</td>
<td></td>
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<tr>
<td>A1 been feeling perfectly well and in good health?</td>
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<tr>
<td>A2 been feeling in need of a good tonic?</td>
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<td>A3 been feeling run down and out of sorts?</td>
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<tr>
<td>A4 felt that you are ill?</td>
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<tr>
<td>A5 been getting any pains in your head?</td>
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<tr>
<td>A6 been getting a feeling of tightness or pressure in your head?</td>
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<tr>
<td>A7 been having hot or cold spells?</td>
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<tr>
<td>B1 lost much sleep over worry?</td>
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<tr>
<td>B2 had difficulty in staying asleep once you are off?</td>
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<tr>
<td>B3 felt constantly under strain?</td>
<td></td>
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<tr>
<td>B4 been getting edgy and bad-tempered?</td>
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<tr>
<td>B5 been getting scared or panicky for no good reason?</td>
<td></td>
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<tr>
<td>B6 found everything getting on top of you?</td>
<td></td>
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<tr>
<td>B7 been feeling nervous and strung-up all the time?</td>
<td></td>
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<tr>
<td>Have you recently</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>C1 been managing to keep yourself busy and occupied?</td>
<td></td>
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<tr>
<td>C2 been taking longer over the things you do?</td>
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<tr>
<td>C3 felt on the whole you were doing</td>
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</tr>
<tr>
<td>Question</td>
<td>Options</td>
<td></td>
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<tr>
<td>------------------------------------------------------------------------</td>
<td>----------------------------------------</td>
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<tr>
<td>things well?</td>
<td>than usual</td>
<td>the same</td>
<td>than usual</td>
<td>less well</td>
</tr>
<tr>
<td>C4 been satisfied with the way you've carried out your task?</td>
<td>More</td>
<td>About same</td>
<td>Less satisfied</td>
<td>Much less</td>
</tr>
<tr>
<td>C5 felt that you are playing a useful part in things?</td>
<td>More so</td>
<td>Same</td>
<td>Less useful</td>
<td>Much less</td>
</tr>
<tr>
<td>C6 felt capable of making decisions about things?</td>
<td>More so</td>
<td>Same</td>
<td>Less so</td>
<td>Much less</td>
</tr>
<tr>
<td>C7 been able to enjoy your normal day-to-day activities?</td>
<td>More so</td>
<td>Same</td>
<td>Less so</td>
<td>Much less</td>
</tr>
<tr>
<td>D1 been thinking of yourself as a worthless person?</td>
<td>Not at all</td>
<td>No more</td>
<td>Rather more</td>
<td>Much more</td>
</tr>
<tr>
<td>D2 felt that life is entirely hopeless?</td>
<td>Not at all</td>
<td>No more</td>
<td>Rather more</td>
<td>Much more</td>
</tr>
<tr>
<td>D3 felt that life isn't worth living?</td>
<td>Not at all</td>
<td>No more</td>
<td>Rather more</td>
<td>Much more</td>
</tr>
<tr>
<td>D4 thought of the possibility that you might make away with yourself?</td>
<td>Definitely</td>
<td>I don't think so</td>
<td>Has crossed</td>
<td>Definitely</td>
</tr>
<tr>
<td>D5 found at times you couldn't do anything because your nerves were too bad?</td>
<td>Not at all</td>
<td>No more</td>
<td>Rather more</td>
<td>Much more</td>
</tr>
<tr>
<td>D6 found yourself wishing you were dead and away from it all?</td>
<td>Not at all</td>
<td>No more</td>
<td>Rather more</td>
<td>Much more</td>
</tr>
<tr>
<td>D7 found that the idea of taking your own life kept coming into your mind?</td>
<td>Definitely</td>
<td>I don’t think so</td>
<td>Has crossed</td>
<td>Definitely</td>
</tr>
</tbody>
</table>
THANK YOU MOST SINCERELY FOR TAKING THE TIME TO COMPLETE THIS QUESTIONNAIRE YOUR INPUT IS INVALUABLE TO GENELIBRARY IRELAND YOUR ENROLLMENT WILL BE COMPLETED ONCE YOU HAVE RETURNED THIS QUESTIONNAIRE TO GENELIBRARY IRELAND IN THE PRE-PAID ENVELOPE.

The contents of this questionnaire and all information you have provided to GeneLibrary Ireland will be considered as medically confidential and will be covered by the Data Protection Act 1998 and 2003.

GeneLibrary Ireland Contact details

If you would like to find out more information about the study please find details below:

Web address:

GeneLibrary Ireland Contact Person