



Recommendations for the Establishment of a National Cancer Biobank

Report of the Expert Group on a National Cancer Biobank

The **purpose** of the proposed National Cancer Biobank is to be a standardised, or at least defined, collection of biological samples for patient-oriented research, to include hypothesis-driven collections, as well as collections for questions arising, for the ultimate improvement of diagnosis, prognosis, and treatment of patients.

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Table of contents

Acknowledgements	3
Abbreviations	8
Foreword	11
Executive summary	13
Summary of recommendations	15
1.0 Introduction	23
1.1 Background	23
1.2 Membership of the Expert Group	24
1.3 Aims and terms of reference of the Expert Group	25
1.4 Meetings and action plan of Group	27
2.0 Scientific rationale	28
2.1 Rationale and motivation	28
2.1.1 Research landscape	29
2.1.2 Biobanking in Ireland	30
2.2 Research benefits	31
2.3 Healthcare benefits	31
2.4 Economic benefits	32
2.5 The purpose of the National Cancer Biobank	33
2.6 Recommendations	34
3.0 Models of delivery	35
3.1 Biobank models	35
3.1.1 Decentralised sample collection, centralised storage and centralised informatics	35
3.1.2 Decentralised sample collection, decentralised storage and centralised informatics	36
3.2 The Irish context	39
3.2.1 Irish biobanks	39
3.2.2 Recommended model for the National Cancer Biobank	39
3.2.3 Other considerations	41
3.3 Recommendations	42
4.0 Governance, structure and organisation	43
4.1 Principles for biobank governance	43
4.2 Governance principles for the National Cancer Biobank	44
4.3 Governance models	45
4.3.1 The Spanish National Tumour Bank Network	46
4.3.2 Wales Cancer Bank	47
4.4 Proposed governance structure for the National Cancer Biobank	48
4.5 Recommendations	50

5.0	Operations and cost estimates	51
5.1	Introduction	51
5.2	Sample collection and processing	51
5.3	Biobank operations	53
5.3.1	HR requirements at sample collection sites	53
5.3.2	HR requirements for central office	56
5.4	Capital investment for space and equipment	57
5.5	Appropriate funding sources	59
5.5.1	Statutory funding	59
5.5.2	Cost-sharing	59
5.6	Recommendations	60
6.0	ICT requirements	62
6.1	Bioinformatics and data management	62
6.2	ICT strategy	62
6.3	Buy or build?	63
6.4	Best practices	64
6.5	Recommendations	64
7.0	Standards and quality assurance	66
7.1	Background	66
7.2	Data coding, classification, storage and protection	66
7.3	Sample collection, handling, and storage	68
7.4	Safety, security and appropriate back-up for physical samples	69
7.5	Quality assurance and quality control	70
7.6	Recommendations	71
8.0	Ethical issues	73
8.1	Introduction	73
8.2	Ownership	73
8.3	Consent	74
8.4	Privacy/anonymisation	75
8.5	Feedback, ethical oversight and benefit-sharing	76
8.6	Irish context	77
8.7	Recommendations	79
9.0	Relationships and links	80
9.1	North/South collaboration and the potential for an all-island biobank	80
9.2	Academia/industry partnerships	81
9.3	Incorporation of existing biobanks, and linkages with other Irish biobanks and clinical research facilities	82
9.4	Linkage with existing international cancer biobanks	84
9.5	Appropriate linkages with research programmes and potential for collaborative initiatives, including cancer clinical trials	86
9.6	Collaboration with the National Cancer Institute under the Consortium	87
9.7	Recommendations	88

10.0 Patient education and awareness	89
10.1 Introduction	89
10.2 Outreach and information	90
10.3 Requirements and approaches	91
10.4 Recommendations	93
11.0 Conclusion	94
References	95
Appendix A	98
Assigning responsibilities within governance structure	98
Appendix B	100
National Cancer Biobank Meeting, 10–11 December 2007	100
Appendix C Consultation process	102
Background	102
Scope	102
Response	102
Summary of feedback	103
Model	103
Governance	103
Standards/QA	105
ICT	105
Operations/cost	105
Ethical issues	107
Relationships and links	109
Patient education and awareness	111
Appendix D Implementation strategy	113
Introduction	113
Who should be involved at the implementation stage?	113
How to proceed?	114
Work packages and working groups	115
1. Model and governance	115
2. ICT strategy	116
3. Sample and data collection, standards and QA	116
4. Ethical, legal and societal issues (ELSI)	117
5. Relationships and links	117
6. Implementation: costing and financing	118

Abbreviations

BBMRI	Biobanking and Biomolecular Resources Research Infrastructure
BCC	Biorepository Coordinating Committee
BCCA-TTR	British Colombia Cancer Agency Tumour Tissue Repository
BP	Best Practice
caBIG	Cancer Biomedical Informatics Grid™
caNISC	Cancer Network Information System Cymru
CCB	Confederation of Cancer Biobanks
CDBI	Council of Europe Steering Committee on Bioethics
CDE	Common Data Element
CGP	Current Good Practice
CNIO	Centro Nacional de Investigaciones Oncológicas (Spanish National Cancer Research Centre)
CRF	Clinical Research Facility
DHSSPS	Department of Health, Social Services and Public Safety
DMMC	Dublin Molecular Medicine Centre
DNA	Deoxyribonucleic Acid
DoHC	Department of Health and Children
EPIC	European Prospective Investigation into Cancer
EU	European Union
HEA	Higher Education Authority
HIQA	Health Information and Quality Authority
HR	Human Resources
HRB	Health Research Board
HSE	Health Service Executive
HTA	Human Tissue Authority
IARC	International Agency for Research on Cancer
ICORG	All-Ireland Co-operative Oncology Research Group
ICRIN	Irish Clinical Research Infrastructure Network
ICS	Irish Cancer Society

ICT	Information and Communications Technology
IP	Intellectual Property
IPPOSI	Irish Platform for Patients' Organisations, Science and Industry
IRB	Institutional Review Board
ISBER	International Society for Biological and Environmental Repositories
ISO	International Standards Organisation
IT	Information Technology
QA/QC/QMS	Quality Assurance/Quality Control/Quality Management System
LIMS	Laboratory Information Management System
MMI	Molecular Medicine Ireland
NBN	National Biospecimen Network
NCCP	National Cancer Control Programme
NCI	National Cancer Institute
NCRI	National Cancer Research Institute
NHS	National Health Service
NUIG	National University of Ireland, Galway
OBBR	Office of Biorepositories and Biospecimen Research
OECD	Organisation for Economic Co-operation and Development
OHRP	Office for Human Research Protections
PRTL	Programme for Research in Third-Level Institutions
RCSI	Royal College of Surgeons in Ireland
RNA	Ribonucleic Acid
SFI	Science Foundation Ireland
SNTBN	Spanish National Tumour Bank Network
SOP	Standard Operating Procedure
TCD	Trinity College Dublin
UCC	University College Cork
UCD	University College Dublin
UPS	Uninterruptible Power Supply
WCB	Wales Cancer Bank
WTE	Whole-time Equivalent

Foreword

The availability of the complete sequence of the human genome, annotated with a comprehensive catalogue of genes and sites of sequence variation (polymorphisms), has opened up new possibilities for research into genetic effects on human health as well as possibilities for the development of new diagnostics and treatment modalities. In addition, exciting advances in biomolecular technology have increased the power and precision of the analytical tools used in such research. An essential element of biomolecular research and its translation into medical, scientific, economic and societal benefits is the availability of large collections of patient samples and corresponding clinical data. The term biobank or biospecimen resource is used to describe such collections. The reliability of data derived from these collections is dependent on the quality and consistency of the biospecimens being analysed.



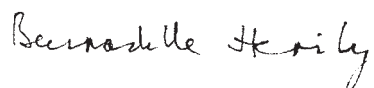
Professor Bernadette Herity

The National Cancer Forum in its document *A Strategy for Cancer Control in Ireland (2006)* recommended the establishment of a national cancer tissue bank to support research and service delivery for cancer. In June 2007, the Minister for Health and Children, Ms Mary Harney TD, established the Expert Group on a National Cancer Biobank, with comprehensive terms of reference to develop proposals for the establishment of a National Cancer Biobank.

It has been a rewarding experience for me to chair this Group. I am pleased to acknowledge the commitment and wide-ranging expertise which members of the Group and other stakeholders have brought to the deliberations and consultation process leading up to the production of this report. The administrative support provided by the Health Research Board, overseen by Dr Anne Cody, Head of Research Infrastructure and Special Initiatives and a member of the Group, has been invaluable. Dr Catriona Creely and, subsequently, Dr Catherine Gill acted as Secretary to the Group, and both brought their own special skills to the task. The response of the Group members to the pressure to deliver the draft report early in 2008, in order to facilitate a wide-ranging consultation process, was exemplary given the complexity of the undertaking. We are grateful to Dr Gill for her expert drafting and communications skills, which contributed greatly to the timely production of the report.

The Group considered a range of options in their recommendations, taking cognisance of advances in biobanking internationally. The report includes outline proposals for an implementation strategy which identifies where further development of the

recommendations in the report are required. It is important that the impetus created by Minister Harney's admirable initiative in establishing the Expert Group to produce recommendations on a National Cancer Biobank is maintained, and the implementation phase should follow without undue delay. The establishment of this biobank will give added momentum to the excellent cancer research ongoing in Ireland and will, undoubtedly, lead to further advances in diagnosis and treatment for cancer patients.

A handwritten signature in black ink, reading "Bernadette Herity". The script is cursive and fluid, with the first name and last name clearly distinguishable.

Professor Bernadette Herity MD FRCPI

Chair

November 2008

Executive summary

The development of more effective interventions against cancer requires a better understanding of its molecular basis and a more rapid translation of laboratory findings into improved patient care. Research studies aimed at advancing cancer prevention, diagnosis and treatment depend on a number of key resources, including a ready supply of high-quality annotated biospecimens which can be used to test new drugs, assess the validity of prognostic biomarkers, and develop tailor-made therapies. Therefore collections of patient samples and related information, or biobanks, are essential for the advancement of cancer research.

The evidence in support of biobanks is compelling. The need to develop a biobank in Ireland has been highlighted in a number of reports including the National Cancer Forum's Strategy for Cancer Control. As a result of the implementation of the National Cancer Control Programme and the establishment of designated cancer centres, the opportunity now exists to develop a National Cancer Biobank offering the highest standards of sample collection, processing and distribution aimed at serving the needs of researchers and, ultimately, the needs of patients.

While the primary goal of the National Cancer Biobank is to ensure the delivery of improvements in the prevention, diagnosis and treatment of cancer, the establishment of such a resource also represents a major investment in Ireland's knowledge economy as it will facilitate cutting-edge academia/industry research and development.

This report outlines recommendations for the establishment of a National Cancer Biobank. It sets out the Expert Group's vision of a working National Cancer Biobank. It is informed by the views of stakeholders, as recorded by a national stakeholder consultation process which took place from March to May 2008 (Appendix C). Included with this report is an implementation strategy which outlines the necessary steps which must be taken in order to develop a plan for the implementation of the National Cancer Biobank (Appendix D); this strategy also has been informed by the consultation process.

There was overwhelming support both within the Expert Group and nationally for a decentralised biobank model, based around the eight proposed cancer centres and the main paediatric hospital which provides cancer care for children. The proposed model of decentralised collection and storage with centralised informatics will be co-ordinated under a central structure, and be overseen by central management. In order to ensure that the Biobank becomes completely integrated with clinical practice, it is recommended that it is established as a separate entity within the National Cancer Control Programme and therefore the Health Service Executive (HSE). Outlined in this report are the principles to which the governance of the Biobank should adhere; also

outlined is a proposed structure, which is informed by international models and which accommodates the needs of local stakeholders.

If it is to succeed, the Biobank must be adequately resourced. It must address HR requirements at each collection centre and at the central management office, and the necessary infrastructure must be provided. Establishing resource requirements requires consultation during the implementation phase with relevant stakeholder groups including pathologists, surgeons, researchers and other clinical staff. Local buy-in will require adequate staffing including laboratory personnel and research nurses; it will also require provision for pathologists' time. In order to ensure that the Biobank is not under-funded, this report aims to demonstrate the significant staffing requirement involved in biobank operations. While a detailed costing cannot be provided at this stage, it is clear that a government commitment to funding will be required; this would see the Biobank publicly funded through the National Cancer Control Programme (NCCP). In the long term, the Biobank may be able to recoup some administrative costs from researchers, and through partnerships with industry and other private healthcare providers. However, it is unlikely that the Biobank will be financially independent in the foreseeable future. A biobank cannot be built in a stop-start fashion and continuity and reliability of funding is a cornerstone of success.

A key recommendation in this report is that an IT manager should be in place from the outset. This recommendation from those who have previous experience in setting up biobanks cannot be overemphasised. The establishment of an appropriate IT platform is fundamental to the success of the Biobank. In relation to standards for biobank operations, a number of documents have been produced internationally; these include the *National Cancer Institute Best Practices for Biospecimen Resources*, the *OECD Best Practice Guidelines for Biological Resource Centres* and *ISBER Best Practices for Repositories*. The Expert Group recommends that, rather than duplicating what is already in place, the National Cancer Biobank should follow established international best practices, modified to suit Irish needs as appropriate.

Protecting the privacy and confidentiality of patients is crucial. While there is currently a lack of legislation relating to biobanking in Ireland, the Expert Group recommends that in line with other European countries, practices such as the use of broad consent and linked anonymisation should be used. The Biobank should seek legislation to underpin its activities, and a generic, streamlined consent process must be put in place for samples that are being submitted to the Biobank. Other issues, such as the use of retrospective consent and consent by proxy, must be clarified prior to implementation.

As twenty-first century research is dependent on collaboration and co-operation, the Biobank should forge links both within and outside the island of Ireland. Consultation with counterparts in Northern Ireland will be necessary in order to ensure that

appropriate links are developed between the evolving biobank in Northern Ireland and the National Cancer Biobank. The Expert Group recognises the importance of academia/industry collaboration in bringing basic research findings through clinical trials and, in the long term, to the patient's bedside. The Group also recognises the potential that such collaboration could offer by way of providing a source of cost recovery for the Biobank and also by way of making a significant contribution to Ireland's knowledge economy. The importance of defining guidelines for the incorporation of, or collaboration with, existing biobanks is outlined. Forging links with international organisations is also recommended. The Biobank must also link into existing structures such as ICORG and the Ireland-Northern Ireland-NCI Cancer Consortium. The latter will be of particular importance if an all-Ireland approach to biobanking is to be achieved.

Finally, as the ultimate aim of the Biobank is to improve patient care, it is essential that patients as well as the public in general understand the purpose of the Biobank and the role that patients and the public alike can play in making it a success. Two-way communication will be essential. There are requirements for an appropriate website, public debate and regular assessments of public opinion. Most importantly, patients and families must be fully informed in a hospital setting in relation to issues such as consent and privacy.

It is imperative that people understand that each of us must play our part if we are to maximise the future benefits for all the people of Ireland that would be created as a result of the establishment of the Biobank.

Summary of recommendations

- The establishment of a National Cancer Biobank, the purpose of which should be standardised/defined collection of biological samples for patient-oriented research, to include hypothesis-driven collections, as well as collections for questions arising, for the ultimate improvement of patient diagnosis, prognosis and treatment.
- The National Cancer Biobank should align with the eight cancer centres established under the NCCP and the main paediatric hospital providing cancer care for children.

Model

- The optimum model in an Irish context is **decentralised collection, decentralised storage, centralised and compatible informatics**, with a central point of access for researchers who wish to use biobank samples and data.

- The primary sample collection sites for the National Cancer Biobank should be the eight cancer centres designated under the National Cancer Control Programme and a dedicated national centre for paediatric oncology.
- The number of decentralised storage facilities needs to be determined during the implementation phase.
- The option of including centralised storage for some types of samples should be considered during the implementation phase.
- Adequate infrastructures and dedicated specialist personnel must be located at each sample collection point.
- There must be excellent communication between everyone involved in biobank operations – medical and paramedical staff, hospital and central management, and researchers.
- SOPs must be followed at all sites, and an overarching quality management system will be vital.
- An efficient communications network will be essential for the collection of samples for prospective studies.
- A key objective must be to build trust and maximise buy-in from hospitals, clinicians, nurses, technical staff, researchers and other stakeholders, particularly patients, patient groups, and the public.
- Governance within the National Cancer Control Programme will help address many of these issues.

Governance

- The governance structure should follow the principles outlined in section 4.2 of this report.
- Governance must be inclusive of a director (informed by the Strategic Advisory Group), a central management structure, hospital administration and clinicians, and the principal investigators who wish to access material. A scientific review board including international experts will be required to assess the scientific merit of applications for the use of Biobank material.
- Feedback between the various levels of governance will be crucial. At all times communications between these levels will be of paramount importance in order to maximise the efficiency of the Biobank and ensure that best practice is followed.
- The Biobank must have the built-in flexibility to accommodate the evolution and changing needs of the Biobank over time.

- Assignment of responsibilities must be finalised/clarified during the implementation phase. A proposal detailing plans for implementation should be peer reviewed. Periodic reviews of the governance and operations of the Biobank should be carried out by an independent international panel.

Operations and cost estimates

- The Biobank must be an integral part of the culture of clinical practice.
- While frozen tissue is the gold standard, all sample types should be collected where possible. Multiple samples must also be collected.
- For each tumour type, a ranking order should be established. This would indicate which type of sample processing should be available for all cases, and which types of processing should be carried out if sufficient material were available.
- Pilot studies/feasibility studies should be carried out around specific disease areas/sample types in order to ensure that the appropriate and practical standards are applied.
- Sample processing should be performed by the relevant laboratory in order to ensure that only the material that has been requested by the researcher is actually released, thus avoiding the unnecessary waste of valuable material.
- Research nurses are essential to the entire process including the co-ordination of the consent, implementation of SOPs for sample collection, and the acquisition of follow-up data.
- The collection and storage of appropriate tissue samples should be overseen by a pathologist and it should be co-ordinated through the pathology laboratories in close consultation with and in collaboration with surgeons and other relevant clinical teams.
- The local histopathology department should be paid for a service post for laboratory staff. There should be dedicated biobanking sessions for pathologists. There should also be provision of resources to support the collection of samples in other departments such as haematology.
- An initial fund should be allocated for the training and education of surgical/medical and other clinical staff on the requirements of the National Cancer Biobank.
- From the outset, up to five senior posts will be required for the central management office function, with requirements for the IT (minimum one person), finance and communications functions to be finalised during the implementation phase.

- The Biobank should be established within the NCCP and therefore the HSE, using a financial structure that would enable the Biobank to receive HSE funding while retaining the ability to accept funding from other sources such as charities, industry, funding agencies and philanthropic bodies.
- Funding must be dedicated within the NCCP budget. Any Biobank posts must be protected, and not subject to recruitment embargos (derogation from WTE ceilings).
- Once the Biobank is up and running, cost-recovery measures should come into play; these could include administrative charges to industry and academia as well as revenues generated by the provision of value-added services.
- As is the case in other countries, a government commitment to long-term funding is required.

Information and Communications Technology (ICT) requirements

- An ICT manager with a strong background in the delivery of ICT solutions should be appointed from the outset to ensure that the ICT system fits within the overall strategy.
- There must be strong user input into the design of the ICT system, taking into account both the relevant issues outlined in Chapter 6 and best practice.
- The system must be compatible with hospital networks and should aim for automatic data capture from other hospital information systems.
- Data Protection Commissioner approval must be obtained before applying for ethical approval.
- It must be possible for all relevant raw data and analysed data to be entered and retrieved easily, and the system must be scalable.
- Strong security systems and a complete audit trail for all data entries and retrievals will be required.

Standards and quality

- Best practices for data coding, classification, storage and protection as outlined in *National Cancer Institute Best Practices for Biospecimen Resources* should be followed including:
 - All relevant data associated with samples collected where possible.
 - Use of uniform vocabulary and CDEs.
 - Data should be coded, and a secure link to the patient should be maintained.

- The data management system must be able to track all aspects of data/sample collection, processing, and distribution.
- Permissions and roles must be defined.
- Procedures regarding patient follow-up must be defined during the implementation phase.
- Data collection, including collection of follow-up data, should be co-ordinated between centres, and a minimum clinical dataset should be defined.
- Sample collection, handling and storage procedures should adhere to *ISBER 2008 Best Practices for Repositories*. These would include the following:
 - Pilot studies/feasibility studies should be carried out in order to identify any problems associated with the collection and processing of particular sample types.
 - A pathologist should supervise tissue procurement.
 - Appropriate inventory systems and SOPs for sample inventory and tracking are needed.
- Recommendations for safety, security and back-up as outlined in ISBER guidelines as follows:
 - Security systems should be in place and monitored 24 hours a day, seven days a week.
 - Access systems should prevent unauthorised entry. A hierarchal system of security should be in place.
 - A back-up power supply in the form of uninterruptible power supply (UPS) or generators will be required.
 - Back-up storage of sufficient capacity will be required.
 - An appropriate safety programme should be developed; a safety officer should be designated, and a training procedure should be implemented.
- Implementation of the QA standards and QC standards outlined in ISBER guidelines including:
 - An effective QMS should be developed which incorporates appropriate SOPs and quality checking.
 - A dedicated Quality manager should be in place.

- Detailed policies and procedures must be outlined in a SOP manual, and appropriate training should be provided and monitored.
- The Biobank should aim to attain quality standards where appropriate.
- Irish biobanks will have to meet certain requirements in order to participate in European biobanking initiatives such as BBMRI. As such it is important that the National Cancer Biobank ensures that it is compatible with the best practice guidelines, such as the OECD guidelines, used by the BBMRI.

Ethical issues

- Legislation to underpin biobanking is required. This might be discussed in the context of the proposed human tissue legislation and the Health Information Bill.
- An approach in line with other European countries towards issues such as consent and privacy is preferable.
- In terms of ownership, the 'conditional gift model' is the most appropriate.
- In relation to privacy/anonymisation, linked anonymisation should be used, as it is the most valuable.
- Consent should be given in the form of general consent or broad consent for 'unspecified future research use'.
- A generic, national consent process must be enacted.
- The Biobank should lobby for a single streamlined ethical review process for research.
- The issue of consent by proxy must be addressed during the implementation phase.
- Contingency for retrospective consent in special circumstances should be considered.
- Consent forms for surgery and tissue procurement should be separate.
- Seeking consent from patients should not take place immediately before surgery, as this is a time when patients may be vulnerable. Consent should be sought in the context of the discussion between the physician/research nurse and the patient regarding the procedure that the patient will be undergoing.

Relationships and links

- Collaborative links between the National Cancer Biobank and the evolving biobank in Northern Ireland should be developed, with further consideration being given to developing an all-island biobank.

- The National Cancer Biobank should provide access for industry using a clear governance and administrative charging structure. Industry is a key partner, and potential concerns from both sides should be explored during the implementation phase in order to develop a resource that will deliver maximum benefit to all stakeholders.
- If existing biobanks are to be incorporated, decisions should be taken on a case-by-case basis to determine whether they meet the quality requirements of the National Cancer Biobank and whether their owners should be invited to incorporate these biobanks into the National Cancer Biobank.
- The National Cancer Biobank must work harmoniously with the CRFs, and vice versa. Expertise in the CRFs around the management of infrastructures should be leveraged where possible.
- Collaboration with the ICORG cancer clinical trials initiative should be encouraged where appropriate.
- The option of linking with the National Cancer Registry should be explored.
- The National Cancer Biobank should develop close links with international organisations such as ISBER, BBMRI, P3G and the Marble Arch Group, and in particular the NCI through the Ireland-Northern Ireland-NCI Cancer Consortium. These links will be important during the implementation phase and when the National Cancer Biobank is fully operational. Much can be learned from these organisations, and collaboration with them should be the norm.

Education and awareness

- A website which provides comprehensive definitions and information tailored to all population groups is required.
- Comprehensive information must be provided to patients and families in a hospital setting.
- Patient organisations should be represented in the Biobank's governance.
- An annual report should be presented to the Dáil Health Committee.
- The Biobank requires a well-resourced communications function in order to create opportunities for public debate as well as media (TV and radio) discussions.
- Public information campaigns to highlight the important roles of the public, researchers, funders etc. are essential. Evaluation of the effectiveness of these campaigns and surveys to gauge public opinion should be carried out regularly.
- Communication of research to the public must be facilitated.

- The importance of the pharmaceutical industry's role in furthering the development of new drugs must be communicated.
- The preparation of guidelines for consent and the collection of tissue should involve patients/public.

1.0 Introduction

1.1 Background

One in three people in Ireland will develop cancer by the age of 75¹. Recent projections by the National Cancer Registry suggest that if current trends continue, the number of new cancer cases in Ireland will double between the years 2000 and 2020². While it is improving, the prognosis for Irish cancer patients is poorer than for those in other prosperous European countries. Reasons for this include late clinical presentation, delayed diagnosis and inequitable access^{3,4}.

One of the most precious resources for patient-directed cancer research is a collection of frozen and fixed tumour samples, normal tissue samples and blood or other biological fluids which are held in a biobank. When donated with informed consent which respects patient confidentiality and privacy, such samples enable examination of the molecular basis of disease. In order to achieve essential added value, sample data must be complemented by pathology data and detailed clinical data. Although specific patient benefits arising from such research may take many years, biobanked samples are the basis for the identification of biomarkers and drug targets, the testing of new drugs and the identification of patients who will benefit from specific treatments. Large co-ordinated sample collections are a prerequisite for translational cancer research throughout the world and will transform our capacity in Ireland to carry out collaborative cancer research, with the ultimate aim of improving patient care.

Within the last five years, national cancer biobanking initiatives have either commenced or have gained momentum in many countries including Spain, the United States, France, Italy, Canada, Singapore, and Korea. No two national cancer biobanks are exactly alike, and European biobanks are at different stages of maturity. The UK Biobank is a large facility for molecular epidemiology research. onCore UK, the UK's cancer biobank, has recently begun collecting samples, while the Wales Cancer Bank, established in 2003, is an excellent example of a well-co-ordinated, population-based collection of blood samples and tissue samples. In addition, a working group in Northern Ireland has established the need for a biobank in Northern Ireland with links to other national biobanks. These national developments are complemented by international efforts to (i) harmonise biobanking operations through the development of standards and guidelines by organisations such as ISBER, OECD and the NCI, and to (ii) provide tools to harmonise research and enhance collaborations such as the P3G Observatory. At European level, the Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) aims to network biobanks across borders. This will become increasingly relevant as the complexity of studies grows and sound statistical analysis requires ever-increasing numbers of samples.

In line with international developments, the need for a National Cancer Biobank in Ireland has been recognised in recent years^{3,5,6}. The 2006 *Towards Better Health* report from the Advisory Science Council⁶ recommended the prioritisation of funding for infrastructures including biobanking facilities in Ireland, while the National Cancer Forum report *A Strategy for Cancer Control in Ireland*³ specifically recommends that 'Ireland should establish a national tissue biobank that is based on international standards and collects appropriate data on stored samples. The initial aim of such a development will be to support patient-relevant research, but as technology develops it may have a more direct service delivery benefit'.

In June 2007, the Minister for Health and Children nominated members of an expert group to develop proposals for the establishment of a National Cancer Biobank. Professor Bernadette Herity, Emeritus Professor of Public Health Medicine and Epidemiology at University College Dublin (UCD) and a former Board Member of the Health Research Board (HRB), was invited to convene and chair a group of national and international experts who would produce recommendations for a National Cancer Biobank and report directly to the Department of Health and Children in 2008. The first meeting of the Group took place on 26 July 2007.

1.2 Membership of the Expert Group

Professor Bernadette Herity (Chair and Convenor),
Emeritus Professor of Public Health Medicine and Epidemiology at University College Dublin (UCD) (Ministerial nominee).

Dr Anne Cody, Head of Research Infrastructure and Special Initiatives Unit,
Health Research Board (HRB nominee).

Dr Carolyn Compton, Office of Biorepositories and Biospecimen Research (OBBR),
National Cancer Institute (NCI nominee).

Dr Davida de la Harpe, Assistant National Director,
Health Intelligence, Health Service Executive (HSE nominee).

Professor Eoin Gaffney, Consultant Histopathologist,
St James's Hospital, Dublin (Irish Cancer Society nominee).

Dr Pierre Hainaut, Head of the Molecular Carcinogenesis and Biomarkers Group,
International Agency for Research on Cancer (IARC nominee).

Dr Joe Harford, Director,
Office of International Affairs, National Cancer Institute (NCI nominee).

Dr Tony Holohan, Deputy CMO,
Department of Health and Children (Ministerial nominee).

Dr Jackie James, Senior Lecturer and Consultant Pathologist,
Centre for Cancer Research and Cell Biology, Queen's University Belfast and Royal
Victoria Hospital, Belfast (Department of Health, Social Services and Public Safety
(DHSSPS) nominee).

Professor Elaine Kay, Consultant Histopathologist,
Beaumont Hospital, Dublin (Irish Cancer Society nominee).

Professor Mark Lawler, Consultant Clinical Geneticist,
Cancer Molecular Diagnostics Laboratory, St James's Hospital, Dublin (Irish Cancer
Society nominee).

Mr John McCormack, CEO,
Irish Cancer Society (Irish Cancer Society nominee).

Dr Brian Moulton PhD, CEO,
All-Ireland Co-operative Oncology Research Group (ICORG) (ICORG nominee).

Dr Kate Williamson, Senior Lecturer,
Centre for Cancer Research and Cell Biology, Queen's University Belfast and Royal
Victoria Hospital, Belfast (DHSSPS nominee).

Secretary to the Expert Group

Dr Caitriona Creely (July to September 2007)

Dr Catherine Gill (October 2007 to completion of report)
Research Infrastructure and Special Initiatives Unit, HRB.

1.3 Aims and terms of reference of the Expert Group

Aim: To develop a proposal for a National Cancer Biobank, for submission to the
Minister for Health and Children, including a discussion of each of the following terms
of reference.

1. The research and healthcare benefits achievable in the immediate, short and
long term.
2. Assessment of workable, quality-assured and cost-effective models of delivery
(to include centralised or distributed models) and a recommendation on the
preferred model.

3. Governance, structure and organisation of the preferred model.
4. The operation and costings of a biobank to include:
 - Information governance, including security and confidentiality.
 - An IT platform and associated integrated infrastructure for the implementation and maintenance of the network.
 - ICT requirements including hardware and software integration with existing systems.
 - Protocols for access to information and specimens.
 - Human resource requirements.
 - Funding requirements, both capital and revenue.
 - Appropriate funding sources.
5. Standards and quality assurance arrangements in line with international best practice for:
 - Data coding, classification, storage and protection.
 - Specimen collection, handling and storage.
 - Security and appropriate back-up.
6. Ethical issues, including patient consent and confidentiality.
7. The appropriate relationships which could be developed:
 - Academia/industry partnerships.
 - Incorporation of existing Irish cancer biobanks.
 - Linkage with other Irish biobanks.
 - Linkage with existing international cancer biobanks.
8. Appropriate linkages with research programmes and potential for collaborative initiatives, including cancer clinical trials.
9. Patient education and awareness.
10. Recommendations on North/South collaboration and potential for an all-island biobank.
11. Recommendations on collaboration with the National Cancer Institute under the Consortium.

1.4 Meetings and action plan of Group

The first meeting of the Group was convened on 26 July 2007. There was consensus at this meeting that the establishment of a cancer biobank in Ireland was both feasible and desirable. It was agreed that the Group should develop a plan for a national biobank which would address the issues set out in the terms of reference. It was agreed that, in the short time available, the Group should compile a set of specific recommendations for the Department of Health and Children; these recommendations could be used to develop a national biobank if funding for the project were to be forthcoming.

The Group met a total of seven times at the offices of the HRB in Dublin. On a number of occasions experts from other institutions were invited to meetings focusing on their areas of expertise; their contributions were considered particularly valuable. These experts included Professor Grace Callagy, National University of Ireland Galway (NUIG); Dr Louise Burke, Cork University Hospital, and Dr Deirdre Madden, University College Cork (UCC). In addition, a symposium was held on 10 December, 2007, when national and international experts gave presentations on relevant biobanking topics. On 11 December 2007, workshops focusing on specific terms of reference took place; at these workshops a number of experts and stakeholders informed the Group (Appendix B).

Draft papers on various aspects of the Biobank were produced by Group members; other contributors to draft documents included Professor William Watson, Dr Geoff Bradley and Dr Deirdre Madden. Drafts were considered and discussed by the Group. Various members suggested amendments and the final report was compiled by **Professor Bernadette Herity, Dr Anne Cody and Dr Catherine Gill**. An initial draft of the report was opened to stakeholder consultation in March 2008 (Appendix C). Written submissions were invited, and in May regional consultation meetings took place in Cork, Dublin and Galway. Feedback from the consultation process informed the final draft of the report, which was completed in November 2008.

2.0 Scientific rationale

2.1 Rationale and motivation

Biobanks or biospecimen repositories are a critical bridge for enabling translational research. Maximising the promise of the epoch-defining Human Genome Project for advances in human health requires the ability to capture molecular information from state-of-the-art “omics” technology and the ability to integrate this data with clinical information in order to provide better diagnosis and treatment for the patient. Biobanking has been recognised as a critical resource for enabling twenty-first century research in an era when, increasingly, emphasis is being placed on predictive and preventive personalised medicine.

“Access to appropriately collected and annotated tissue is a critical need for fully capitalising on these new genomic and proteomic technologies to accelerate progress against cancer. Lack of access is one of the major barriers to realising the promise of developing targeted cancer diagnostics, preventatives and therapies”. National Dialogue on Cancer (NDC) Research Team Forum, March 2002⁷.

“Unless substantial action is taken with biobanking and biospecimens, we’ll delay personalised medicine by thirty to forty years”. Dr Anna Barker, Deputy Director NCI, Biobank Summit II, New York, November 2004⁸.

Biobank repositories have actively contributed to a number of advances in personalised medicine, providing the key resource for identifying cohorts of patients who would respond to the tyrosine kinase inhibitor Imatinib Mesylate (Glivec) in both Chronic Myeloid Leukaemia (CML) and Gastrointestinal Stromal Tumours (GIST), and the anti-her-2 monoclonal antibody Herceptin in erb-b2 positive breast cancer. Herceptin and Glivec are examples of new therapies where success has relied on the ability to interrogate biorepositories to (i) identify molecular abnormalities that may serve as targets for new therapies and (ii) identify cohorts of patients who will respond to these new therapies, thus demonstrating the potential for success for personalised medicine. These successful new cancer treatments have paved the way for the development of many more new forms of targeted therapy⁹.

The scientific case for cancer biobanks is compelling. While fundamental studies which contribute to the cellular and molecular understanding of cancer can be performed using cell lines and/or animal models, there is a clear requirement for observations generated through these approaches to be confirmed and greatly extended by *in vivo* studies of surplus patient material. The collection of both normal material and tumour material allows the specificity of a biomarker or cellular process to be determined,

while the access to linked clinical data maximises the potential of the resource and allows the clinical and biological significance of the scientific observation to be evaluated. In the Irish context, the ability to conduct high throughput translational research utilising accurately annotated clinical material will provide competitive advantage and scientific rigour in clinical research studies.

2.1.1 Research landscape

The research landscape has changed significantly in Ireland over the last number of years due to a series of initiatives which have helped to create a stronger research base, coupled with an appropriate infrastructure which enables high quality research to be carried out. The Programme for Research in Third Level Institutions (PRTLTI) has provided state-of-the-art research facilities and technology platforms that enable programmatic interdisciplinary research. The PRTLTI has helped to break down institutional barriers through partnerships such as Molecular Medicine Ireland (MMI) a research and educational programme between National University of Ireland Galway (NUIG), the Royal College of Surgeons in Ireland (RCSI), Trinity College Dublin (TCD), University College Cork (UCC) and University College Dublin (UCD)¹⁰. Science Foundation Ireland (SFI) has invested in, and given impetus to, basic research in the areas of Biotechnology (Bio) and Information and Communications Technology (ICT). The Irish Cancer Society (ICS) has significantly increased its funding of cancer research in Ireland, while the HRB has made a significant contribution to clinical research through project, programmatic and infrastructure grants.

The commitment of the HRB, in association with the Wellcome Trust and the Health Service Executive (HSE), to the establishment of three new clinical research facilities (CRFs) in Ireland will provide added impetus to biobanking initiatives. This brings the total number of CRFs in Ireland to six; all of these are located in the major centres for cancer diagnosis and treatment. This suggests the mutual benefits that could derive from a CRF being associated with a National Cancer Biobank collection site. A national co-ordination mechanism for the CRFs and for patient-oriented research in Ireland is provided by ICRIN, the Irish Clinical Research Infrastructure Network which is funded by the HRB and the HSE. ICRIN aims to harmonise and standardise procedures – e.g. data management, education and training – in clinical research in Ireland.

From a cancer perspective, one of the major developments of the last 10 years has been the establishment of the National Cancer Institute (NCI) – All-Ireland Memorandum of Understanding, which was signed in Stormont in 1999. This has led to significant developments in cancer clinical trials, cancer epidemiology, training fellowships and ICT through the roll-out of a national telesynergy network. It has also enabled more extensive collaborative links to be established between the NCI and Irish researchers.

2.1.2 Biobanking in Ireland

In order to maximise the advances from basic sciences to clinical care, the defining and populating of the translational research space is critical. Crucial to the development of a patient-oriented research strategy in cancer is the establishment of collections of biospecimens – all collected, stored and annotated appropriately in order to provide a rich resource for research projects and clinical trials. The ability to collect significant numbers of biospecimens prospectively and in a serial fashion, coupled with cumulative clinical information, would facilitate both all-Ireland and international research collaborations. While no uniform biobanking structure exists, there are a number of disease-specific collections in existence e.g. the biobank of the Prostate Cancer Research Consortium (supported by the Irish Cancer Society) which provides a valuable resource for research. The Prostate Cancer Research Consortium is an integrated MMI programme in prostate cancer research. It aims to harness the expertise of researchers in Dublin as well as international collaborators to identify new diagnostic, prognostic and therapeutic approaches in prostate cancer. Crucial to the development of the Consortium has been the establishment of a prostate cancer biobank with appropriate research nurse support. It provides access for researchers to tumour material and normal material and it helps to accelerate basic science discoveries through testing in clinically annotated material.

The National Cancer Control Programme (NCCP), launched in November 2006, formulated a vision: ‘Ireland will have a system of cancer control which will reduce our cancer incidence, morbidity and mortality rates relative to other EU-15 countries by 2015. Ireland will have a network of equitably accessible state-of-the-art cancer treatment facilities and we will become an internationally recognised location for education and research into all aspects of cancer’³.

The implementation of the strategy¹¹ involves the establishment of eight cancer centres, each serving a minimum population of 500,000 and networked together in four managed cancer control networks. Multidisciplinary care for cancer will be concentrated in these centres, and, as they will have the maximum cancer caseload, they are the logical locations for nationally-designated hospital biobanks. It is therefore recommended that the eight cancer centres should participate in the National Cancer Biobank with the main paediatric hospital providing cancer care for children. It will be important to encourage all potential stakeholders to be part of the establishment of a National Cancer Biobank, irrespective of whether or not they are providing sample material to the Biobank. It will also be critical to ensure that biobank initiatives are linked to cancer clinical trials groups, thus maximising the benefit for all stakeholders.

2.2 Research benefits

A number of immediate research benefits should follow the introduction of a national cancer biobank. The harmonisation of standard operating procedures (SOPs) and best practice should yield a more efficient and time-saving collection of samples which are quality assured. These quality samples will permit better research to be carried out, thus delivering better value for all stakeholders including academic researchers, industry researchers, future patients and the taxpayer. More samples will be acquired quickly for current and future use, while the development of infrastructure and the requisite central database will create access for many more users. It will also create an incentive to collaborate. In this way, resources will be maximised and expertise will be shared.

In the short term, the biobanking initiative will facilitate the identification of molecular mechanisms. This will allow researchers to correlate molecular, pathological and clinical data. The large numbers of samples available for collaborations will create much greater potential for translational research projects and will facilitate clinical trials. Also, in the short term, a national cancer biobank would be complementary to the National Cancer Strategy aspirations.

The long-term effects of investing in such an initiative would include stronger academia/industry partnerships. Results should begin to flow in relation to specific drug targets for cancer, and the efficacy and toxicity of drugs, while the availability of data on biomarkers will facilitate improved diagnostics. The Biobank would complement the Ireland-Northern Ireland-NCI Cancer Consortium activities, particularly in relation to clinical trials and informatics. National and international collaboration would be enhanced and the knowledge gained could be shared with developing countries where research infrastructure is poor.

2.3 Healthcare benefits

While the goal of personalised medicine for all is unrealistic in the short term, there will be some immediate benefits for patients as a result of biobanking and related activities. The availability of samples will provide more data for current and recurrent molecular diagnostics. In the short term, the initiative will add value to and increase the scope of clinical trials which may directly benefit all patients¹². As noted in the *Strategy for Cancer Control in Ireland*, the percentage of patients enrolled in clinical trials is a marker of quality of care³. As a result of clinical trial and research activities, prognosis and care will be more consistent, standardised and precise.

Through the communications function of the Biobank it is hoped that patients, patient groups and the general public will be better informed about biobanking, associated

research and clinical trial activities, and how they relate to their own healthcare. It is also hoped that GPs and other healthcare professionals will be better informed through the education and awareness aspect of the initiative. As a result, patients may be referred for diagnosis and treatment at an earlier point than is currently the case. Late presentation is one of the reasons for Ireland's poor survival rates for a number of cancers. Furthermore the communication of research outcomes will influence health strategies.

The long-term healthcare benefits are clearer and more defined. The availability of biobank samples will help reduce the time required for drug development, ensuring novel treatments reach the patient sooner. The availability of better drugs will be complemented by improved diagnostics through the availability of new and better biomarkers as a result of research on biobanked samples. Thorough validation and optimisation of new technologies using biobanked samples will ensure the appropriate diagnosis and classification of tumours, which will provide the basis for administering more effective personalised treatments as demonstrated by the development of novel drugs like Glivec and Herceptin. This shift towards more personalised medicine will allow the use of therapies that are best suited to the individual patient, thereby improving efficacy and reducing adverse effects.

2.4 Economic benefits

While the ultimate goal of the National Cancer Biobank is to deliver improvements in the prevention, diagnosis and treatment of cancer, the establishment of such a resource would also represent an important economic investment for Ireland. The knowledge economy requires that information be available to industry, and a biobank is an extremely rich source of relevant information. The knowledge economy also requires a lively academic research environment – one that feeds into the translation of research results into products. The National Cancer Biobank will stimulate cutting-edge research in both academia and industry. Research arising from studies using biobank material will lead to knowledge generation and the development of research skills, and will contribute to the building of research capacity. Such a valuable infrastructure should see an increase in industry research and development which would strengthen the economy and attract additional pharmaceutical companies and increased foreign investment to Ireland.

A recent HRB-RAND study¹³ outlined some important economic returns from health research including benefits from improved health such as a healthier workforce; more cost-effective new treatments and technologies, and savings to other parts of the healthcare system; and commercialisation of products/technologies, leading to increased employment, tax revenues and exports.

The BBMRI¹⁴ are currently carrying out a survey of health and economic benefits in relation to their proposed biobanking network. Among the key areas on which they will be focusing are the impact on public health; innovations, outcomes and outputs from biobanks; knowledge generation and transfer; investment in research and innovation; partnering/collaboration.

Impacts on all of these areas can be anticipated as a result of establishing a biobank in Ireland. As well as facilitating improved diagnosis and treatment, biobanking will also influence public health strategies. Research outcomes and innovations will lead to improved processes and products, and the creation of industry and intellectual property (IP). Extensive knowledge generation in terms of new products and technologies, together with the training of a more skilled workforce due to the interdisciplinary nature of biobank research, can be expected. Partnership with industry will be encouraged, thus ensuring competitiveness on both a European and a worldwide stage.

The Biobank will also lead to more efficient use of resources already targeted at research. Increased collaboration and access to research findings on biobank material will enable state-of-the-art research projects, will reduce duplication, and will therefore prevent resources being wasted. This can be facilitated by obliging all recipients of biobank materials to deposit both raw data and analysed data in an open-data repository.

Thus, the benefits of the Biobank and related research may range from the better use of resources and employment creation to more indirect economic benefits such as a healthier workforce. By enabling and supporting health research, the Biobank can contribute significantly to the economy. The relatively small investment required to establish the Biobank will continue to yield benefits for years to come – not only in terms of health benefits, but also in terms of making an important contribution to the growth of Ireland's knowledge economy.

2.5 The purpose of the National Cancer Biobank

The purpose of the proposed National Cancer Biobank may be summarised as:

A standardised, or at least defined, collection of biological samples for patient-oriented research, to include hypothesis-driven collections, as well as collections for questions arising, for the ultimate improvement of diagnosis, prognosis and treatment of patients.

2.6 Recommendations

- The establishment of a National Cancer Biobank, the purpose of which should be standardised/defined collection of biological samples for patient-oriented research, to include hypothesis-driven collections, as well as collections for questions arising, for the ultimate improvement of patient diagnosis, prognosis and treatment.
- The National Cancer Biobank should align with the eight cancer centres established under the NCCP and the main paediatric hospital providing cancer care for children.

3.0 Models of delivery

3.1 Biobank models

The Expert Group was asked to provide an assessment of workable, quality-assured and cost-effective models of delivery (to include centralised or distributed models) and to make a recommendation on the preferred model. Three models for biobanking have been identified in the literature¹⁵.

1. Centralised sample collection, storage and informatics.
2. Decentralised sample collection, centralised storage and centralised informatics.
3. Decentralised sample collection, decentralised storage and centralised informatics.

The first model is not applicable for the purposes of the National Cancer Biobank and would not result in a national facility. The difference between Models 2 and 3 is the sample storage location – whether it is located within the hospitals or located at a remote site. In order to assess the suitability of a particular model in an Irish context, the Group examined different models of operational biobanks.

3.1.1 Decentralised sample collection, centralised storage and centralised informatics

European Prospective Investigation into Cancer (EPIC) is a multi-centre prospective study aimed at investigating the relationships between diet, nutritional status, lifestyle and environmental factors, and the incidence of cancer and other chronic diseases¹⁶. It was initiated in 1992 with the collection of data and blood samples in 22 regional centres located in ten European countries; it is the largest study into diet and health ever undertaken.

The EPIC study is prospective – in other words healthy people were recruited with a view to following their health for at least ten years. Participants completed carefully designed and tested questionnaires, and provided blood and urine samples so that researchers could analyse their nutrient levels. All participants in EPIC are followed up by completing additional questionnaires every three to five years. Each EPIC centre or country is able to identify all cancer registrations, all deaths and causes of death relating to participants.

EPIC-Europe is co-ordinated by a team of scientists at the International Agency for Research on Cancer (IARC), Lyon, France, where the dietary, non-dietary and follow-up

data from each of the collaborating centres is held in secure Oracle databases. One half of the blood samples collected by each centre is also held at IARC in liquid nitrogen tanks. A total of 395,713 blood samples were collected and stored under liquid nitrogen vapour for future analyses on cancer cases and controls. In total, this represents over seven million aliquots of plasma, serum and blood cells.

In the EPIC study the *sample storage, processing, shipping and analysis was carried out at a central biobank*. One problem identified with this particular model was the high cost of central storage. In addition, the samples concerned are blood and serum; in terms of storage and shipping, these samples present less logistical problems than solid tissue samples.

onCore UK¹⁷ is a charity established to provide high-quality cancer tissue samples coupled with anonymous patient information for cancer research. It is funded by Cancer Research UK, the Department of Health, and the Medical Research Council, and it has partnered with selected NHS trusts to form 'biosample donation networks' within the NHS. It has linked up with other existing tissue banks (NCRI Confederation of Cancer Biobanks) to develop common standards for the collection and storage of samples, and also develop IT systems in order to make it easier for researchers to find and access the samples that they need.

onCore UK works with a number of NHS partners. Cancer patients at participating hospitals are asked if they would like to donate their tissues for research. It is *managed by a central office*, and donated samples are *stored centrally* at a separate facility. onCore UK aims to develop a powerful 'Biosample Information Management' system designed to deal with data acquisition, sample tracking, inventory management, quality assurance and quality control (QA/QC). The system will link the 'Biosample Donation Networks' to the central repository of samples and information. From there, the system will link to the IT systems of other members of the Confederation of Cancer Biobanks, thereby creating a large resource of samples and data for cancer researchers. onCore UK has begun collecting donated blood and paraffin-embedded tissue samples which researchers will be able to access in 2008.

3.1.2 Decentralised sample collection, decentralised storage and centralised informatics

The Spanish National Tumour Bank Network (SNTBN)¹⁸ of Centro Nacional de Investigaciones Oncológicas (Spanish National Cancer Research Centre; CNIO) aims to satisfy the demand for human cancer tissue and normal tissue for the development of large-scale studies of clinical significance. Their main goal is to promote high-quality tumour banks within Spanish hospitals, based on the standardised collection, processing

and storage of both cancer samples and normal tissue samples. These hospital tumour banks are autonomous and are interconnected by a computer-based network.

In 2002 there were a total of four hospitals in the network. This has now expanded to 45 participating hospitals and it is projected that there will be 51 participating hospitals by 2008. In the Spanish model, each biobank is a hospital facility. The hospital, through its pathology department, is the guardian and custodian of samples donated under (patients) informed consent. It is a 'hub and spoke' model whereby *decentralised sample collection* encourages individual hospital participation, and material is *stored locally* at each hospital site. In this way, each centre's tissue resides within the corresponding hospital, where it can then be used for the welfare, teaching and research activities of each individual hospital. Dedicated biobank staff are employed in each hospital; this includes medical laboratory scientists and protected sessions for a consultant histopathologist.

The central office is located at the CNIO in Madrid. This office, which is responsible for the management of the network, develops and reviews SOPs and ensures compliance in the different hospitals within the network. It has a major role to play in training, through individual workshops and meetings, and it also manages a *shared bioinformatics platform*. Restricted data from hospitals is updated daily via the internet for online researcher access, and a series of website bioinformatics tools are also available for data mining.

Any Spanish cancer research team can request tissue from the biobank network simply by submitting an application outlining the project description, the funding sources behind the project and the estimated costs of the project. An anonymous assessment mechanism is used to guarantee the scientific and technical viability of all projects. The SNTBN is effective – as a network, it participated in more than 150 research projects in the 2001–2005 period. This included 11 clinical trials and 47 multi-centre collaborative group studies, with 440 requests for tissue.

The Wales Cancer Bank (WCB) was established in 2003 and aims to collect samples of tumour tissue, normal tissue and blood from all patients in Wales who are undergoing an operation to remove tissue in cases where cancer is a possible diagnosis¹⁹. These samples will be banked in order to build up a research resource which will be used by cancer research groups with a view to developing optimum targeted treatment for individuals.

The WCB provides another example of *decentralised sample collection and storage*. Currently, it comprises seven hospital-based acquisition centres across Wales. A variety of tumour types are collected at each site following uniform SOPs. Paired samples of normal tissue and tumour tissue (both fresh frozen and paraffin blocks) are routinely

sampled from resection specimens after all diagnostic tests have been carried out. Bloods are also taken where possible, and spouses or partners are asked to donate a blood sample as a 'control' matched for environmental exposure. All data collected is stored on a database housed in the NHS in order to ensure security and confidentiality. An 'all-Wales clinical database' (CaNISC) which is specifically designed to enable good correlation of scientific findings with clinical follow-up, is currently under development.

As Wales has a similar population size to Ireland, the WCB serves as a useful model in terms of the scale of its operation and the resources available to it. For example, the WCB consists of seven acquisition centres, while in Ireland it is envisaged that the National Cancer Biobank will exist within the framework of the eight cancer centres as well as the main paediatric hospital providing cancer care for children.

The **National Biospecimen Network (NBN)** in the US outlines the principles of a proposed biobanking infrastructure to harness the potential of new technologies for cancer research, while ensuring that the privacy of sample donors is preserved²⁰. It creates a comprehensive framework for sharing and comparing research results through a robust, flexible, scalable and secure bioinformatics system which supports all aspects of biobanking from collection through to distribution of samples and data and uses SOPs based on best practices, harmonised consent and use of common material transfer agreements. Although it has not yet been implemented, the NBN was developed to address the problems of heterogeneity of practices and limited access to samples within NCI-supported banks.

This heterogeneity among existing repositories, as a result of samples being collected and stored under varying conditions, creates obstacles for researchers. The NBN model is designed to standardise resources so that obstacles can be overcome. Its recommendations provide a framework for developing a nationwide, standardised biospecimen resource to facilitate genomic and proteomic research in the US.

Thus, the NBN may be viewed as an example of *decentralised collection and storage with centralised co-ordination and management* by offices including the NCI Office of Biorepositories and Biospecimen Research (OBBR) and the Biorepository Coordinating Committee (BCC). In addition, the NCI has pioneered a *centralised informatics* system in the form of the cancer Biomedical Informatics Grid™ (caBIG™) which aims to help biospecimen resources implement NCI best practices in the areas of bioinformatics. This IT initiative has established both the infrastructure and the tools required to share sample-related data across a network of cancer researchers.

Importantly, it is not necessary for a biobank to operate on an exclusively decentralised or centralised storage basis. A **hybrid** model, which can facilitate both centralised and decentralised storage, might be considered. The EPIC study stored only half of its

samples at the central storage facility at IARC; the remainder were stored at regional centres – a move that was made possible due to the sample types being stored (e.g. blood and serum). onCore UK is a centralised biobank with links to decentralised facilities in large academic centres in the UK via the NCRI Confederation of Cancer Biobanks. Similarly, in the US, discussions are underway regarding the possibility of incorporating central storage as part of the biobank network in an effort to facilitate standardisation.

3.2 The Irish context

3.2.1 Irish biobanks

There are a number of biobanks operating on a smaller scale in Ireland. The best example of a cross-institutional biobank is that of the **Prostate Cancer Research Consortium (PCRC)**²¹. The PCRC, established in October 2003 under the auspices of the Dublin Molecular Medicine Centre (DMMC; now MMI) and funded by the Irish Cancer Society (ICS), has set up a prostate cancer bio-resource in a number of Dublin hospitals using the *decentralised collection, decentralised storage and centralised and compatible informatics* model of operation. Across the different sites, dedicated research nurses implement agreed SOPs for the securing of informed patient consent and for practices such as sample collection and processing. By adopting a common approach, the uniformity of the resource is maintained. Samples are stored, using monitored storage facilities, at the collection centres. SOPs are monitored by the 'bio-resource management and implementation committee'. This federated bio-resource has been made possible as a result of the establishment at each collection site of clinical research facilities under Molecular Medicine Ireland.

The Bio-resource currently has over 450 tissue samples with matched serum/plasma and DNA samples, and 190 urine samples with comprehensive clinical information and follow-up. Central to the federated bio-collection is the Bioresource Information and Management System (BIMS)²¹ architecture which accommodates the collection and tracking of samples and the integration of clinical information. This system, which has been approved by the Data Protection Commissioner, allows investigators to identify what samples are available and where they are located. It also provides links to the relevant clinical data while maintaining patient confidentiality at all times. Priority and external access policies have been put in place to enable members of the consortium to apply for access to this material for specific research projects if the study has been approved by the relevant ethics committee.

3.2.2 Recommended model for the National Cancer Biobank

It is envisaged that the National Cancer Biobank will exist within the framework of the eight cancer centres (as set out in the National Cancer Control Strategy 2007) and the

main paediatric hospital providing cancer care for children. A designated cancer centre has to fulfil a number of criteria in terms of patient numbers and services offered, but international best practice suggests that clinical trials and a biobanking resource are also required. This has been acknowledged in the criteria for the designation of cancer centres, where appropriate research infrastructure and full participation in research including clinical trials was specifically identified³.

Tissue samples will be collected in the centres where cancer surgery takes place i.e. a system of decentralised collection will be used. The informatics system should be centralised; it should conform to all ICT requirements such as coding, data security and privacy (as outlined in Chapter 6), and it should be compatible with other systems such as the system to be used in the proposed biobank in Northern Ireland and caBIG which has been developed at the NCI. A single central point of access for researchers who wish to use biobank material will be essential for the provision of a single biobanking network. The main issue to be decided in relation to this model is whether samples are stored in the hospitals where they are collected i.e. decentralised storage, or whether they are moved to a single central storage location.

There are arguments for and against both models. Following extensive discussions, the Expert Group agreed that a decentralised storage model would be the most appropriate for Ireland. Arguments in favour of the decentralised storage model include:

- The value of the National Cancer Biobank is crucially dependent on the quality of the physical samples and the accompanying information. This is best safeguarded if a wide cross-section of hospital staff feel that they have some ownership of the Biobank.
- Samples should be readily accessible to hospital staff in case further diagnostic tests are necessary for the welfare of the patient.
- Even if a centralised storage model were to be chosen, there would still be a requirement for smaller-scale, temporary decentralised storage at all collection sites, in order to cover the period between processing the sample and transporting it to the central storage facility.
- The existence of a number of storage sites would provide some back-up storage in case of a catastrophe such as a fire destroying one of the storage sites.
- Every transport of a sample carries a risk of damage, and a central storage model introduces an additional transport step.

Arguments against decentralised storage/in favour of centralised storage include:

- The difficulty of imposing standards in multiple centres.

- The potential cost implications of a roll-out to multiple centres, in particular the provision of space and equipment.
- Greater efficiency in the dispatch of samples to researchers from a central store.

While each model has its advantages and its disadvantages, the Expert Group believes that with appropriate management, SOPs and training, standardisation can be achieved across centres if the decentralised storage model is used. Importantly, the challenge of achieving standardisation will exist for other aspects of biobanking irrespective of where storage is located; this is because, of necessity, collection will be decentralised. The standards and extensive QC measures described in Chapter 7 must be in place in order for the Biobank to function. Governance within the National Cancer Control Programme would help address these issues. In relation to cost, a solution that delivers the best value for money should be sought. More detailed cost considerations are outlined in Chapter 5; these demonstrate that the most significant cost will be for staff involved in sample collection – irrespective of where samples are stored. Other arguments in relation to costings are presented in Chapter 5, which notes that a detailed cost-benefit analysis should guide any decision in relation to storage locations. Thus, while the Expert Group recommends the decentralised model of sample collection and storage, the extent of decentralisation of storage requires further consideration and should be a priority for the implementation group.

3.2.3 Other considerations

International experience suggests that researcher buy-in is much more likely if a decentralised biobank model is adopted. Those countries (e.g. the UK and Singapore) which have centralised biobanking structures also have decentralised biobanking in their academic centres i.e. a hybrid model. While decentralised storage of tissue is favoured by the Expert Group, the option of storing certain types of samples such as bloods or fluids in a central storage facility might be considered (hybrid model). DNA extraction might then be carried out in a central laboratory. Details in relation to such an approach should be finalised during the implementation phase. Importantly, this may have implications for space provision. For example, unlike the storage of extracted DNA, the storage of fluids will require significant space – particularly if all such samples are stored centrally.

A National Cancer Biobank should strive to achieve full coverage of all cancer cases. The Expert Group recognises that the proposed model will not fully reach that target. While public cancer services are being consolidated under the National Cancer Control Programme, patients continue to be treated in non-designated hospitals. While it is anticipated that the number of such patients will decrease, it will take some time for this to happen. Haematology services in particular will continue to be provided by a

variety of hospitals. With the increased development of private hospitals in Ireland, a substantial number of patients undergo surgery and treatment in these hospitals, and the number of patients is set to rise further in the future. It is conceivable that the eight cancer centres would act as a hub for non-designated public and private hospitals who wish to participate in the National Cancer Biobank. Strict monitoring of adherence to SOPs would be a pre-condition for their participation. Resource allocation to these hospitals should only be considered when the required infrastructure has been established in the cancer centres.

3.3 Recommendations

- The optimum model in an Irish context is **decentralised collection, decentralised storage, centralised and compatible informatics**, with a central point of access for researchers who wish to use biobank samples and data.
- The primary sample collection sites for the National Cancer Biobank should be the eight cancer centres designated under the National Cancer Control Programme and a dedicated national centre for paediatric oncology.
- The number of decentralised storage facilities needs to be determined during the implementation phase.
- The option of including centralised storage for some types of samples should be considered during the implementation phase.
- Adequate infrastructures and dedicated specialist personnel must be located at each sample collection point.
- There must be excellent communication between everyone involved in biobank operations – medical and paramedical staff, hospital and central management, and researchers.
- SOPs must be followed at all sites, and an overarching quality management system will be vital.
- An efficient communications network will be essential for the collection of samples for prospective studies.
- A key objective must be to build trust and maximise buy-in from hospitals, clinicians, nurses, technical staff, researchers and other stakeholders, particularly patients, patient groups, and the public.
- Governance within the National Cancer Control Programme will help address many of these issues.

4.0 Governance, structure and organisation

4.1 Principles for biobank governance

A number of different options exist for the organisation of a biobank: it may be structured as a single agency, managed as a confederation governed by a central body, or managed as a loose confederation of interested parties bound only by mutual agreements²⁰. Irrespective of which option is chosen, a sound governance model covering rules, regulations and legal issues such as liability and intellectual property concerns must be designed. The roles of stakeholders must be defined, and the governance must be capable of establishing and enforcing biobank standards such as those relating to data and sample collection and access. Some key principles to guide biobank governance are outlined in the recent *OECD Draft Guidelines for Human Biobanks and Genetic Research Databases*²²:

- The biobank should be governed by the principles of transparency and accountability.
- The governance structure and management responsibilities applicable to the biobank should be clearly formulated, and information should be made available to participants, stakeholders and the general public.
- The governance structure should ensure that the rights and well-being of the participant prevail over the research interests of the initiators and users of the biobank.
- The biobank should have a mechanism to review applications for access to the human biological materials and/or data.
- It is the shared responsibility of all personnel, researchers and partners to ensure that all activities are carried out in accordance with the highest legal norms and ethical principles. Specific roles and chains of responsibilities should be clearly delineated.
- Oversight mechanisms should be in place to ensure compliance with applicable domestic and international ethical, financial and regulatory legislation, policy and frameworks.
- The individuals involved in the oversight procedure should be drawn from diverse relevant areas of expertise including the scientific, legal, and ethical fields.
- Participants should have access to an independent means of recourse for redressing breaches of the ethical, financial, and regulatory legislation, policy and frameworks.

- The biobank should anticipate that over its lifespan the need to modify its policies, protocols and procedures will arise. A process for undertaking these modifications should be in place.
- An independent audit mechanism should be in place to review uses of the human biological materials and data for consistency with the research uses agreed to by a participant during the informed consent process.

4.2 Governance principles for the National Cancer Biobank

Based on international best practice and guiding principles and consideration of local needs, a number of specific criteria may be outlined in order to guide the establishment of a governance structure for the National Cancer Biobank. The National Cancer Biobank:

1. Must promote stakeholder buy-in and good citizenship.
2. Should be a distinct business unit within the National Cancer Control Programme and therefore also within the HSE. The relationship between the Biobank and non-HSE hospitals should be by way of a specific service level agreement.
3. Must include the eight designated cancer centres and the national centre for paediatric oncology. Other locations where samples are generated might be incorporated later using a 'hub and spoke' model.
4. Must have a structure of governance which allows hospitals and associated teaching universities to cooperate under a common framework, with clear understanding of responsibility and liability.
5. Must be in a position to receive funds from other sources and manage its budget, and have a clear position on intellectual property rights.
6. Must include a director (informed by a strategic advisory group), a central management function, hospital management and medical staff, and the principal investigators who wish to access material. A scientific review board including international experts will be required to assess the scientific merit of applications for the use of material.
7. Representation on the strategic advisory group must be equitable and should include key stakeholders as well as a number of international experts and a member (or members) nominated by the Chief Medical Officer (CMO), Department of Health, Social Services and Public Safety, Northern Ireland (DHSSPSNI).
8. Should integrate a research focus into the clinical environment and foster collaboration between clinicians and scientists. This might be facilitated by

enlisting expertise in the management of research infrastructures by the CRFs, where appropriate.

9. Must execute an identical consent process for samples taken at all sites, even if this has to be agreed by a number of ethics committees operating under the current ethical review structure.
10. Must lobby for a streamlined ethical review process for research applications from different institutions.
11. Decisions regarding access to the National Cancer Biobank must be impartial, and must be seen to be impartial. They must be based primarily on the scientific quality of ethically approved applications. A transparent, independent peer-review process must be executed.
12. As a condition of access, all results (positive and negative) derived from samples from the National Cancer Biobank will have to be deposited as raw data in a central database in order to maximise the scientific gain from each sample and avoid duplication. The timeframe should not interfere with securing peer-reviewed publications or intellectual property rights where appropriate.
13. Must be in a position to gain the trust and confidence of patients, clinicians, researchers, industry and the general public alike, and continue to maintain that trust and confidence.

The process of establishing an appropriate governance structure is complex. The Advisory Science Council *Towards Better Health* report⁶ provides recommendations for integrating governance in relation to research and clinical practice; these recommendations might be applied to the Biobank. Much can also be learned from other biobanks.

4.3 Governance models

A number of existing biobank governance models can be used to inform the design of governance structures for the National Cancer Biobank. While none of these models will provide an exact fit for the Biobank, they do, however, provide an indication as to how the organisational structure might be arranged. The Spanish National Tumour Bank Network and the Wales Cancer Bank are international examples of successful cancer biobanks. Both operate a model of decentralised collection and storage with centralised informatics and co-ordination. Their governance organisation, described overleaf, include structures which might be useful when designing a governance structure for the Irish National Cancer Biobank.

4.3.1 The Spanish National Tumour Bank Network

The Spanish National Cancer Centre (CNIO) was founded in 1998 by the Carlos III Institute of Health under the Ministry of Health. The CNIO is managed through its foundation (Fundación Centro Nacional de Investigaciones Oncológicas Carlos III). Scientific activity is governed through the CNIO by the Director in association with the Scientific Advisory Board¹⁸.

As described in Chapter 3, the SNTBN is co-ordinated by the CNIO's Molecular Pathology Programme. It is a cooperative and co-ordinated network of hospital banks, based on standardised protocols for sample collection, processing and storage. The Central Office at the CNIO co-ordinates the network; it also uses and maintains the database and monitors quality control.

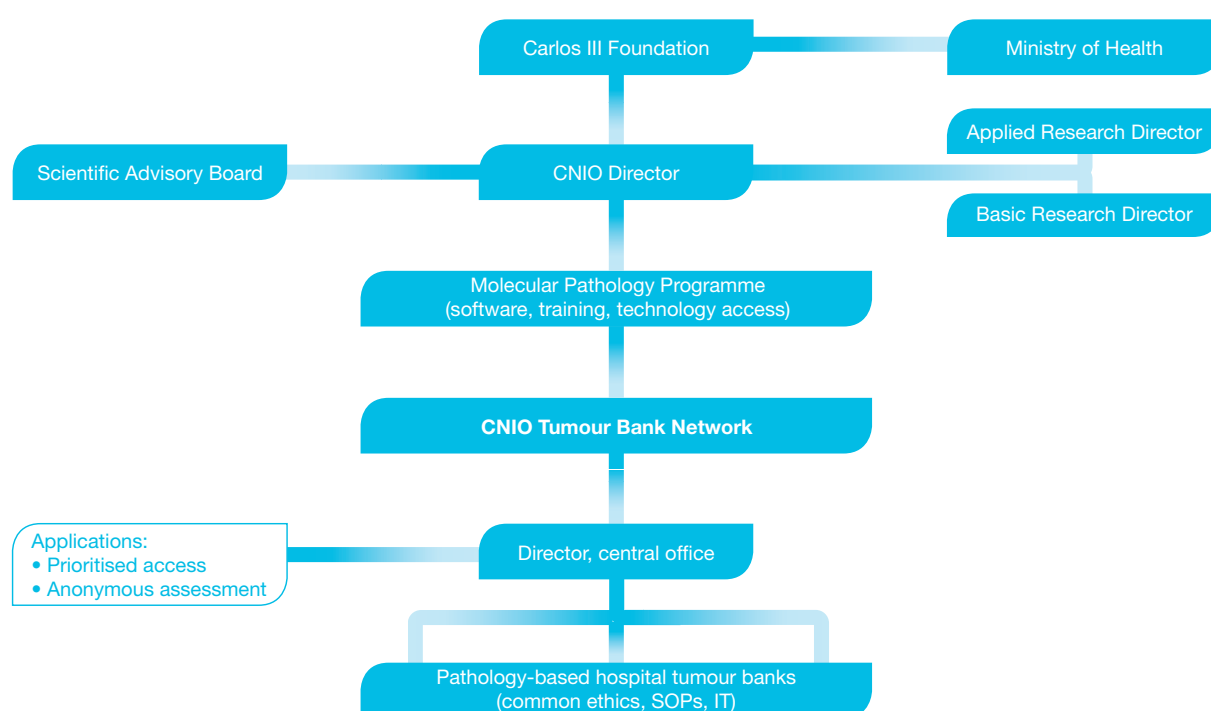


Figure 4.1 Outline of governance structure of Spanish National Tumour Bank Network

The contractual relationship with the associated centres (hospitals) is fundamental to the successful operation of the SNTBN, and it is based on the mutual provision of services. A number of criteria must be met in order for a hospital tumour bank to collaborate with the tumour bank network. These criteria include biobanking activity being accepted as an activity of the entire hospital, with provision of appropriate staff, material resources, premises and infrastructure such as IT resources. The hospitals must guarantee that the network's procedural manual is respected and they must accept the co-ordinating role played by the network's central office, which includes the facilitation of periodic quality controls. The CNIO, in turn, provides the software to the

hospital tumour banks to help them fulfil their IT requirements; it also provides other services such as training and technology access.

4.3.2 Wales Cancer Bank

The Wales Cancer Bank (WCB)¹⁹ was established in April 2003 with initial financial support provided by the Welsh Assembly Government NHS Fund. The WCB is a collaborative project involving higher education establishments, various NHS Trusts in Wales, and the Wales Assembly Government Office of Research and Development (WORD). As described in Chapter 3, the WCB has decentralised sample collection and storage, and is managed by a central office with a centrally co-ordinated IT platform.

The WCB is governed by an *advisory board*, with representatives drawn from WORD, consultant pathologists, professors of clinical and medical oncology, patient and community health council bodies, the Wales Cancer Trials Network, members of the WCB executive group and subgroups. Membership will be expanded to include specialists based outside Wales who can advise on specific areas of the WCB's intended development.

The Executive Group includes the Director of the WCB who is also the HTA licence holder; the Director of Scientific Services; the Human Tissue Authority (HTA)-designated individual and laboratory manager who is responsible for the day-to-day running of the WCB; and the database manager who has responsibility for the WCB's IT infrastructure, including project management and the development of WCB software and integration with NHS clinical information systems.

All applications to the WCB for samples are subject to review. Approval to supply samples is dependent on an external review panel being satisfied with the scientific merit of the proposal. Additional subgroups include the IT group, who are responsible for co-ordinating the central database system; the Sampling Group, which comprises pathologists and technical staff; the Ethics and Patient Liaison Group, which comprises representatives of patient groups; the Collection Management Group, which comprises the IT Manager as well as nurses and technicians employed in local hospitals.

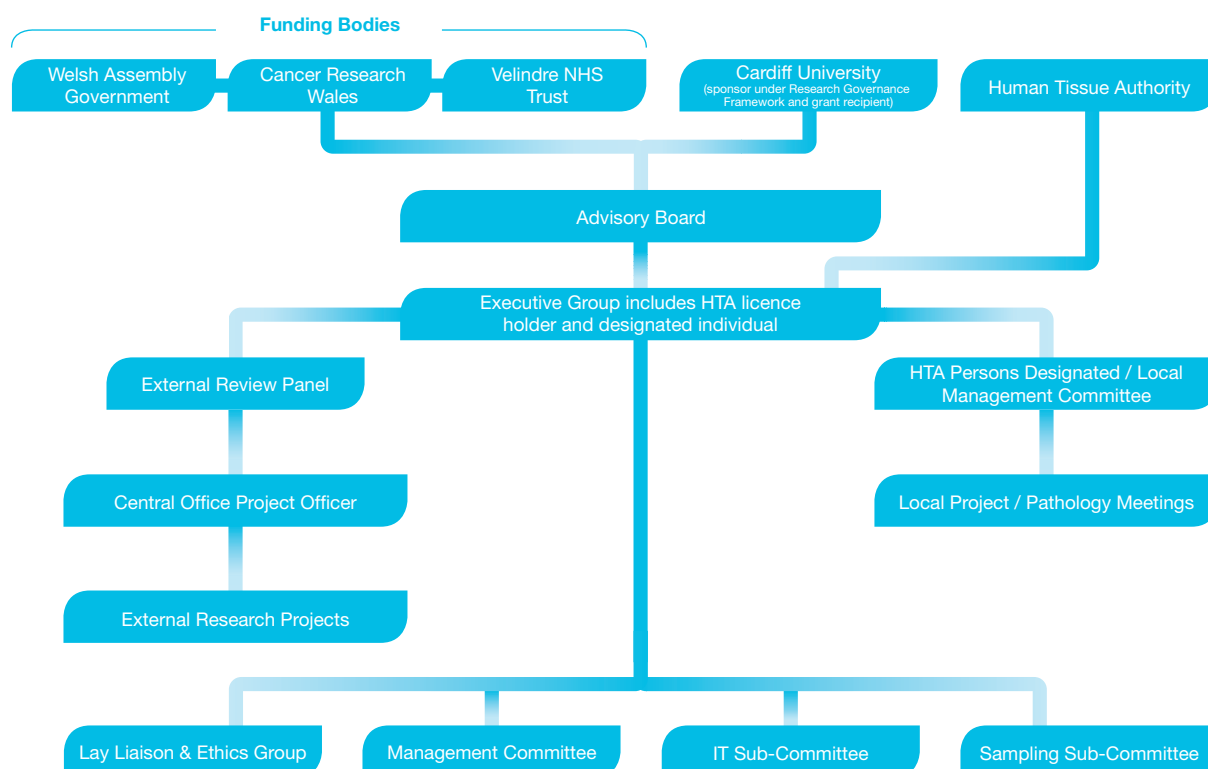


Figure 4.2 Governance structure of Wales Cancer Bank¹⁹

4.4 Proposed governance structure for the National Cancer Biobank

Currently, a number of levels of governance are envisaged within the chosen biobank model of decentralised collection, decentralised storage and centralised informatics.

The *NCCP* has the ultimate, high-level responsibility for the National Cancer Biobank. A *strategic advisory group* including stakeholders, representative(s) nominated by the Northern Ireland CMO, and independent international experts will advise the *NCCP* on the strategic direction of the National Cancer Biobank. The *central management structure* will manage the day-to-day running of the repository, aided by a *scientific review board* who will decide on the scientific merit of applications for access to samples. *Hospital management and medical staff* will be essential for sample collection, data collection and storage. *Principal investigators/researchers* will be the main users of the Biobank and therefore their needs will have to be identified and catered for. An overlap between those contributing to the Biobank and those using the Biobank is to be expected.

Each governance level has responsibility for ensuring that the Biobank is governed effectively, and that optimum use is made of the samples for research purposes. In certain instances, there will be an overlap of responsibilities between governance

levels, with a range of stakeholders involved in developing some of the Biobank's policies and procedures. As a result, feedback between the various levels of governance will be crucial. At all times, communications between the different governance levels will be of paramount importance, in order to maximise the efficiency of the Biobank and also ensure that best practice is followed. Many of the responsibilities which must be assigned to particular groups have been outlined in a table in Appendix A, which also gives some indication as to where these responsibilities may lie.

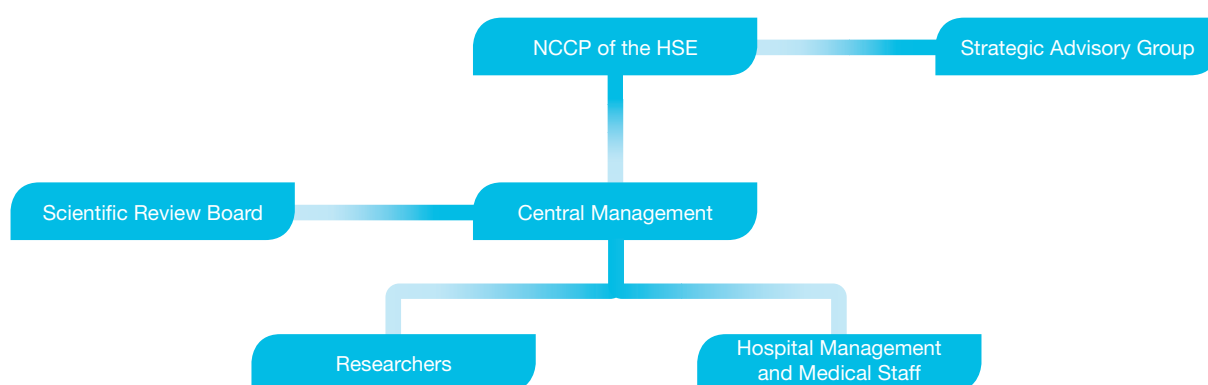


Figure 4.3 Outline of proposed governance structure of the National Cancer Biobank

The central management team, with input from the strategic advisory group where appropriate, must ensure that the requisite standards are adhered to and implemented; they must also ensure that standards are further developed over time. The system must have intrinsic flexibility and it must be responsive to the Biobank's dynamic nature. In addition, access rules must be clarified i.e. rules such as whether those supplying tumour tissue have priority in relation to use, or whether the same rules apply equally to all users of the Biobank. A transparent mechanism for the distribution of the samples will be essential.

At the implementation phase, a coherent proposal as outlined in Appendix D should be developed with the involvement of all stakeholder groups including representative(s) nominated by the Northern Ireland CMO. The proposal should be peer reviewed by international experts, some of whom might be invited to participate in the Strategic Advisory Group. The Expert Group strongly recommends that the Biobank be reviewed periodically by an independent international panel.

4.5 Recommendations

- The governance structure should follow the principles outlined in section 4.2 of this report.
- Governance must be inclusive of a director (informed by the Strategic Advisory Group), a central management structure, hospital administration and clinicians, and the principal investigators who wish to access material. A scientific review board including international experts will be required to assess the scientific merit of applications for the use of Biobank material.
- Feedback between the various levels of governance will be crucial. At all times communications between these levels will be of paramount importance in order to maximise the efficiency of the Biobank and ensure that best practice is followed.
- The Biobank must have the built-in flexibility to accommodate the evolution and changing needs of the Biobank over time.
- Assignment of responsibilities must be finalised/clarified during the implementation phase. A proposal detailing plans for implementation should be peer reviewed. Periodic reviews of the governance and operations of the Biobank should be carried out by an independent international panel.

5.0 Operations and cost estimates

5.1 Introduction

Biobanking costs vary widely from one country to the next. Many cost elements are common to all biobanks but these vary considerably depending on the Biobank model, the individual biobank's purpose, type of activity, maturity, and the type and number of samples acquired and stored there. In addition, the number of salaries, the IT platform, additional sample processing, release and distribution, cost-recovery efforts, lifespan of equipment and management costs all influence annual costs greatly²³. Personnel costs are one of the major costs common to all biobanks. While many of these elements can only be costed accurately once an implementation plan has been finalised, it is possible to gain a number of important insights into cost considerations by examining the operations of established biobanks. The main factors influencing cost are described in detail below and include:

- Sample collection and processing.
- Biobank operations and the associated HR requirements.
- Capital investment for space and equipment.

5.2 Sample collection and processing

Cancer resection or biopsy collection from hospital operating theatres and day wards for research purposes requires individual staffing arrangements in each hospital. Specimens for research sampling may be brought to histopathology by research personnel, hospital porters or medical staff. The time-lag between resection and freezing is a major determinant of RNA and protein preservation; establishing the most efficient way to meet this challenge is of the utmost importance.

In order to assess human resource requirements as well as costings in general, decisions on sample types to be collected and estimates of sample numbers are valuable. For example, sample numbers may be much greater than the number of individual cancer cases. They may be dependent on several factors including cancer types collected; the inclusion of both cancer tissue samples and control tissue samples; sample types to be stored (e.g. cancer tissue, control tissue, blood, urine, etc.); the amount of samples from each case (e.g. single/multiple samples from each case); the number of sample aliquots, and the inclusion of follow-up samples.

While the collection of frozen tissue is the gold standard for a cancer biobank, the first consideration for all patient tumour specimens is that the samples used for research

must not jeopardise full pathology examination for diagnosis and planned further treatment. If the tumour is too small or is not visible a frozen section may be carried out to confirm the existence of a tumour and identify the tumour type. Alternatively, the specimen should not be sampled by the pathologist at all. For each tumour type, a ranking order should be established. This would indicate the type of sample processing that should be available for all cases. In cases where limited tissue only can be procured, the ranking order should indicate which type of sample processing would be preferable. Where sufficient material is available, it should indicate the types of samples that should be collected. It is preferable to collect as many different sample types as possible including paraffin-embedded tissue, frozen tissue, blood (serum) and urine. In order to supply many different research projects, it is also important to collect multiple samples wherever possible. Different sample types e.g. serum, urine and DNA/RNA have different time implications and different cost implications which must be considered. It is preferable to take as many different tumour types as possible so as not to limit potential in the future; this principle should be applied even if there is a risk of some tissue not being used at all. Pilot studies/feasibility studies should be carried out around specific disease areas/sample types in order to ensure that the appropriate and practical standards are applied.

The sample types collected also influence the cost effectiveness of running a collection site. The Wales Cancer Bank performed a cost analysis of samples collected at various sites and found that sites collecting paraffin-embedded samples only are more expensive to run²⁴. This is due to the limited number of useful samples for research purposes that is yielded from such tissue samples. In contrast, frozen tissue samples, once DNA/RNA has been extracted, have the capacity to supply twenty five to thirty research projects.

When a request for access to material is received from a researcher, the extraction of what exactly they require should be carried out so as to ensure that only the material that has been requested (e.g. DNA or RNA) is actually released to the researcher. Using this precautionary measure unnecessary waste of valuable material will be avoided. Researchers should be asked to specify exactly what they need – e.g. RNA of a certain quality and of a particular quantity – for whatever work they are planning to carry out. The relevant laboratory can then perform the extraction, aliquot the extracted material, deliver what is required to the researcher and store the remaining aliquots. These could then be made available to the same researcher (should they require more samples for future applications), or they could be made available to other researchers.

5.3 Biobank operations

5.3.1 HR requirements at sample collection sites

A successful biobank requires significant resources in terms of the number of staff allocated to sample collection sites. Significant staff resources are necessary in order to ensure the smooth operation of sample collection and also ensure that biobanking is integrated into everyday hospital activities but does not interfere with patient care. In order to achieve this type of seamless integration, dedicated **research nurses** are vital members of any biobank operation. These nurses inform patients, co-ordinate consent procedures and ensure that this information is transferred to the relevant departments. They ensure the implementation of SOPs for sample collection and the acquisition of follow-up information; they often oversee the transfer of samples from surgery to pathology, and they are responsible for the collection of patient data or non-surgical samples such as blood and urine.

The collection and storage of appropriate tissue samples, inventory data and pathology minimum datasets is overseen by a **pathologist** and is co-ordinated through the pathology laboratories of the relevant centres. This must be performed in close consultation with and collaboration with clinical researchers/scientists, theatre nurses and the **surgeons** who perform the cancer operations. A commitment by surgical staff to biobanking activities will be required, and there will also be a need for pilot studies/feasibility studies to be carried out in order to ensure that the most appropriate and practical standards are applied. The impact on the diagnostic pathology laboratories of handling these specimens appropriately and complying with uniform SOPs will be critical, and will involve significant time inputs by **medical laboratory scientists** and pathologists alike.

Dedicated pathologist time is essential for the banking of solid tumours. The pathologist specifically assigned to the Biobank examines the pathological specimen and decides which, if any, excess tissue is suitable for biobanking. This ensures the optimum selection and quality of all samples being banked, and it represents the first important QA step in the biobanking process. Subsequent full gross examination of the specimen after formalin fixation, sectioning and microscopic examination provides diagnosis and enables the specimen's stage, grade and margin status to be considered for further treatment. The pathologist is the "gatekeeper" between the surgeon who procures the sample and the researcher who depends on appropriately classified and quality controlled material. While quality control procedures are also carried out after processing – e.g. following RNA extraction – these procedures are worthless and wasteful of time and resources if the original quality assurance method is unreliable. In the event that additional services such as tissue microarrays or laser-capture microdissected samples are provided, pathologists can play a critical role in identifying

and annotating the samples to be used and ensuring that high quality research material is provided. In the pathology laboratory, laboratory personnel will be required to carry out sample processing among other biobank-related tasks.

While the pathologist is a key person involved in the biobanking of solid tumours, other medical professionals will play a role in the banking of other sample types. Diseases such as leukaemia, for example, will require **haematologists** to contribute samples. This is because such samples will pass through the haematology laboratory rather than the pathology laboratory. As a result, provision for the collection of such samples will also need to be made. Here again, research nurses will play a critical role in co-ordinating activities between departments and ensuring that consent procedures and SOPs are strictly adhered to. They will continue to play this role irrespective of who is overseeing the procurement of samples.

Data management and administrative assistance will be important for co-ordinating Biobank staff and ensuring that relevant clinical, ethical and diagnostic information is entered into the Biobank's ICT system. Collaboration with research nurses in relation to consent and clinical information, and collaboration with laboratory staff in relation to diagnostic information will also be important.

In addition, biobank personnel at each collection site and/or storage site will be responsible for sample receipt, storage, retrieval and dispatch. In small-scale operations this could be one of the duties assigned to medical laboratory scientists. However, where demand for samples from each hospital biobank increases, designated persons will be required for the preparation and shipping of samples to other institutions in Ireland and elsewhere. Designated persons will also be required for tasks such as inputting updated information to databases.

International experience

In order to estimate staff requirements, it is useful to consider some international examples. One particularly useful piece of information deals with the number of patients consented per year and the staff complement required to fulfil this function – one that is most frequently carried out by research nurses. The amount of time committed to each consent procedure can vary depending on the context. For example, in British Columbia, in the Manitoba Breast Tumour Bank, one half-time nurse consents between 500 and 750 donors per year, while in the British Columbia Cancer Agency Tumour Tissue Repository (BCCA-TTR), one full-time nurse consents 550 donors per year²⁵. The difference is explained by the fact that in the BCCA-TTR the consent process involves taking bloods and a questionnaire; this is a much more time-consuming process and the spectrum of the clinical system is also more complex. In the Wales Cancer Bank, the nurse/patient ratio is lower, with consents secured from 125 patients

per full-time nurse per year²⁴. However, as well as talking to patients and securing their consent, the nurses take bloods from each patient as well as a corresponding control donor. (Control consents are not counted separately. Therefore if a patient and their spouse each donate blood, it only counts as one donation). WCB nurses also take routine pre-operative bloods and take a questionnaire. They spin and aliquot the serum; do the related paperwork and data entry; retrieve follow-up data on patients who gave their consent in the previous year; attend multidisciplinary meetings for each specialty to identify potential donors; liaise with other staff regarding theatre lists and, in most cases, they also take the tissue to the histology department. The number of consents secured per year is clearly dependent on the range of activities carried out by the individual research nurse.

The consent process accounts for between 20% and 25% of a biobank's costs²⁵. Other functions which must be covered include sample processing, retrieval and dispatch, data entry and follow-up, and co-ordination of the entire process. In Wales, many of these tasks are covered by research nurses, but at least one full-time laboratory technician is also employed at each of the sites where frozen tissue is collected and stored. The WCB has been in operation for only 18 months; therefore, according as the scale of operations increases, the number of additional designated personnel required is also likely to increase. Here again, the experience of some of the longer established British Columbia biobanks provides some useful indicators. A typical bank, with accrual in the order of 500 cases per annum, requires the following²⁵:

- A consent (research) nurse (either half-time or full-time depending on factors described above).
- Tissue manager – one manager can sustain 500 cases accrued per year, if supported by a co-ordinator (see below).
- Data manager (half-time) – one manager can abstract and enter data on >500 cases per annum and sustain follow up on 3,000 cases in a registry/chart setting.
- Co-ordinator (full-time) acts as back-up for all processes, in particular the consent process.
- Pathologist – in the British Columbian experience, this is best incorporated by appointing a pathologist as a director, with that person's commitment to biobank activities being dependent on the scope of the biobank and the duties required. In the Irish model this might mean assigning a pathologist as the local manager at each collection site where appropriate.

In the case of the National Cancer Biobank the exact distribution of tasks at collection centres should be considered during the implementation phase and should allow for the fact that requirements will differ between the different centres. For example,

if a designated data manager and/or a co-ordinator were hired at each centre, this could reduce the burden on research nurses who could then devote additional time to securing consents from patients. In addition, laboratory staff could be given responsibility for sample retrieval and/or data entry in addition to assuming responsibility for sample processing. Irrespective of the distribution of tasks, it is clear from the examples given that a baseline number of staff will be needed at all collection sites in order to cover tasks such as securing consents, obtaining and processing samples, inputting data, information follow-up, sample management/retrieval and dispatch, and overall co-ordination of all of these tasks.

5.3.2 HR requirements for central office

As noted in Chapter 4, the day-to-day running of the National Cancer Biobank will be overseen by a central management structure. Again, this is similar to the situation that applies in the Wales Cancer Bank where decentralised collection and storage are co-ordinated by a central office. The resources employed in the Wales Cancer Bank provide a very useful guide for what will be required in Ireland.

The **Director** of all biobank operations will be the person who will be responsible to the NCCP for the implementation of the strategic direction determined by the Strategic Advisory Group and the NCCP itself. Reporting directly to this individual should be a **central office manager** who will be responsible for the co-ordination of the network's day-to-day activities including tasks such as quality control and SOP implementation. It will be essential to have strong ICT expertise in the form of an **ICT manager** in place from the outset. This particular point has been emphasised by management in a number of existing biobanks. An ICT manager will be required throughout the lifetime of the Biobank.

Other central office functions will include the management of applications for samples, the co-ordination of scientific and ethical review, and liaising with sites on issues relating to sample requests. General administrative support will be required and provision for the functions of finance, communications and IT support will also be required.

5.4 Capital investment for space and equipment

As outlined in Chapter 3, the Expert Group recommends that a decentralised collection and storage model be adopted. Samples have to be taken where cancer surgeries are being carried out, and under the National Cancer Control Programme, eight cancer centres have been designated to carry out the bulk of public patient cancer operations. The volume of surgeries in these specialist cancer centres justifies designating them as collection centres also. It further determines the footprint of decentralisation to eight sample collection centres (nine including a paediatric oncology centre). While ideally all cancer cases should be captured in the Biobank system, the Expert Group recognises that full coverage is not cost effective. Therefore, the Group recommends the roll-out of the sample collection process to the eight/nine designated cancer centres.

The footprint of decentralisation in relation to sample storage is not so obvious. It could coincide with either all or a subset of the collection sites. A number of factors have already been considered in Chapter 3. Below, the financial implications of the different models are discussed. The cost factors to be borne in mind are a) initial set-up costs, b) ongoing staff costs and c) other operating costs.

- a) Capital costs for storage in each hospital (or other location) will need to be assessed, and the size of storage facility determined. If significant storage space is required, a new build may be considered. In this case, the possibility of building biobank storage facilities as part of other major capital projects such as the National Radiation Oncology Centres should be examined, with the aim of minimising additional capital costs. The radiation oncology programme will be rolled out to four different locations. Potentially, this would facilitate decentralised storage at these four locations. Moreover, additional efficiencies of scale could be achieved as a result of housing larger, more cost-effective storage equipment (e.g. larger freezers, storage tanks) in these locations as compared to having nine different storage centres. On the other hand, an opportunity may exist to make use of other facilities at each of the eight centres and the paediatric oncology centre. For example, six of the nine collection centres will be associated with a clinical research facility, and the possibility of housing biobank storage within these or other similar facilities might be considered where space permits. Back-up power and temperature-monitoring systems may already be available in some locations. All collection sites require short-term temporary storage for samples, irrespective of where they will be stored in the long term.
- b) The biggest share of operating costs are staff costs, and, as illustrated in section 5.3.1 of this report (HR requirements at sample collection sites), the biggest share of staff cost relates to sample collection and processing at each collection site. Central office staff requirements remain the same within the potential scope of

the number of storage sites, and are independent of the storage model chosen. The only variable that is dependent on the extent of decentralisation of storage is the need for personnel to cover the function of sample receipt, storage, retrieval and dispatch. The number of staff required will depend on the number of storage facilities, the size of the facilities, the number of samples being stored, and the number of sample requests received from researchers. If, for example, one person was required at each of the eight storage sites, two people might be required per site if there is long-term storage at only four sites, leading to no overall difference in personnel costs. Therefore, such costs will not be a decisive factor when determining the extent of decentralisation of storage.

- c) The number of storage facilities also impacts on other operating costs such as electricity and liquid nitrogen, temperature monitoring services, security, sample transport and tracking costs. While some savings could be made as a result of having fewer centres, additional costs for transport and tracking would be incurred. Before a more detailed cost analysis can be carried out in relation to transport, the preferred method for co-ordinating the collection and distribution of requested samples would first have to be determined. Samples could either be sent to the users directly from all storage sites, or they could be sent to a central location first; final QC procedures could be carried out in this central location and from there the user could also receive all requested samples in a coherent fashion. This second model is used in Wales, where the central office is located on the same hospital grounds as one of the collection centres (Cardiff). In order to assist the decision-making process in this regard, it would be useful to carry out a cost analysis and risk assessment which would judge the benefits of any savings likely to be made by considering efficiencies of scale in relation to storage, and comparing that with the cost of additional transport and costs associated with the tracking of samples.

Costs are a key factor influencing storage location. Every effort should be made to minimise costs without compromising the ability of the Biobank to fulfil its purpose. Issues such as best models of delivery, tapping into existing resources and cost-sharing should be considered. The model of delivery may not be identical for all sites, and may involve a phased roll-out.

5.5 Appropriate funding sources

The 2006 *Strategy for Cancer Control in Ireland* report recommended the establishment of eight cancer centres throughout Ireland³. In relation to research, the report highlighted the need for the establishment of ‘a national tissue biobank to support research and service delivery’. As discussed in Chapter 2, it is recommended that the National Cancer Biobank would be best placed within the new framework of eight cancer centres. While the Biobank would be funded by public finance through the NCCP, the Expert Group clearly found that a number of other funding sources would also be appropriate. When the number of banked samples has grown sufficiently to ensure interest from academia and industry researchers, the organisational structure of the National Cancer Biobank must ensure that it is possible to access these sources to finance the expansion of services in line with demand.

5.5.1 Statutory funding

If the Biobank is integrated into the National Cancer Control Programme, as is recommended in this report, it would be funded through the HSE. This would have to be dedicated funding within the NCCP budget. Similarly, any biobank posts/whole-time equivalents (WTEs) would have to be protected and not subject to recruitment embargos. A biobank cannot be built in a stop-start fashion, and the continuity and reliability of funding will be a cornerstone of its success. It must be operated using a financial structure that allows the Biobank to accept funding from additional sources such as charitable trusts, the pharmaceutical industry and philanthropic bodies. It would require clear governance structures and terms of reference which are in accordance with the requirements of the Office of the Comptroller and Auditor General. It could set up a service level agreement with the NCCP for distribution of NCCP funds. Clear guidelines about the receipt of funding from other sources would have to be established.

5.5.2 Cost-sharing

Initially, it would be expected that the Biobank would be wholly funded by the government through the HSE. Cost-sharing with other government-funded activities such as a capital investment at the initial set-up stage could also be considered. Once a sufficient number of samples have been collected, additional cost-sharing measures should be put in place to supplement Biobank income. The pharmaceutical industry requires a source of good quality samples for research. As the Biobank will be in a position to provide these samples, it should recover costs incurred by sample collection and distribution from commercial users. As well as creating revenue streams from commercial users academic researchers who use samples should be asked to make a contribution to these costs, in particular the cost of sample retrieval. Provision for such

expenses could be covered in researchers' funding applications. The Biobank's cost-recovery measures could also be enhanced by the provision of value-added services such as the construction of tissue microarrays, for which competitive rates might be charged. Before offering such services however, molecular pathology support services may need to be in place. Based on international experience, it is unlikely that the National Cancer Biobank will ever become financially independent even if various revenue-generation measures are implemented. As a result, statutory support will be required for the foreseeable future. It is essential that the Biobank is not under-resourced and a government commitment to this end will be necessary.

5.6 Recommendations

- The Biobank must be an integral part of the culture of clinical practice.
- While frozen tissue is the gold standard, all sample types should be collected where possible. Multiple samples must also be collected.
- For each tumour type, a ranking order should be established. This would indicate which type of sample processing should be available for all cases, and which types of processing should be carried out if sufficient material were available.
- Pilot studies/feasibility studies should be carried out around specific disease areas/sample types in order to ensure that the appropriate and practical standards are applied.
- Sample processing should be performed by the relevant laboratory in order to ensure that only the material that has been requested by the researcher is actually released, thus avoiding the unnecessary waste of valuable material.
- Research nurses are essential to the entire process including the co-ordination of the consent, implementation of SOPs for sample collection, and the acquisition of follow-up data.
- The collection and storage of appropriate tissue samples should be overseen by a pathologist and it should be co-ordinated through the pathology laboratories in close consultation with and in collaboration with surgeons and other relevant clinical teams.
- The local histopathology department should be paid for a service post for laboratory staff. There should be dedicated biobanking sessions for pathologists. There should also be provision of resources to support the collection of samples in other departments such as haematology.
- An initial fund should be allocated for the training and education of surgical/medical and other clinical staff on the requirements of the National Cancer Biobank.

- From the outset, up to five senior posts will be required for the central management office function, with requirements for the IT (minimum one person), finance and communications functions to be finalised during the implementation phase.
- The Biobank should be established within the NCCP and therefore the HSE, using a financial structure that would enable the Biobank to receive HSE funding while retaining the ability to accept funding from other sources such as charities, industry, funding agencies and philanthropic bodies.
- Funding must be dedicated within the NCCP budget. Any Biobank posts must be protected, and not subject to recruitment embargos (derogation from WTE ceilings).
- Once the Biobank is up and running, cost-recovery measures should come into play; these could include administrative charges to industry and academia as well as revenues generated by the provision of value-added services.
- As is the case in other countries, a government commitment to long-term funding is required.

6.0 ICT requirements

6.1 Bioinformatics and data management

Central to the management and utilisation of a biobank is the data management and bioinformatics system. Data management systems are used for tracking the collection, processing and distribution of material; they are also used for the management of pathological and clinical information about the specimens, and for the storage of identifiable and personal patient information. Bioinformatics, which is described as the statistical method for understanding biological data, is used to link the clinical data with the pathological and molecular data which might be generated from the biological samples.

6.2 ICT strategy

The ICT strategy of any large biobank should be driven by the users. Experience in other biobanks has shown that it is important to have an ICT manager in place at the outset. This person would develop an overall ICT strategy in response to the needs of users and as part of the overall strategic management of the Biobank. The ICT manager should have a strong background in the delivery of ICT projects. While lessons can be learned from other, existing biobanks, the detailed specifications for the design of a new biobank need to come from biobank users. In order to plan for appropriate capacity, the number of potential users must be estimated before the system is designed. One of the issues that will have to be taken into consideration is the fact some hospitals will not allow certain technologies on their networks. Again, this is an issue that must be addressed upfront at the design stage of the system. Consultations with all sites involved in the biobanking system are crucial.

In the development of any biobank data management and bioinformatics support system, the following areas must be considered:

- Standardisation of data and common data elements (CDEs).
- Development of workflows and SOPs for data entry and identification.
- Identity management for all users.
- Role-based access to information.
- Ability to interact with all systems.
- Flexibility to develop and expand, according as demand requires (scalability).
- Data-searching and mining capabilities.

- Consent management (to facilitate the destruction of a sample if a participant withdraws consent).
- Accessibility of data.
- Sample tracking.
- Management of formal application process for principal investigators.
- Network security and back-ups.
- Complete audit trail over two years minimum.
- Information technology personnel.
- Staff training.

If the Biobank is also going to be used for outcome measurements, the structure governing information and the back-up security must be even stronger i.e. in line with the higher risk for participants that is associated with giving a sample.

The resulting ICT system should have the capacity to store both raw data and analysed data, thus creating very large file sizes. It will provide the greatest possible benefit to researchers; it will avoid duplication of sample analysis and thus preserve a valuable resource. Where possible, the system should automatically capture data from hospital laboratory information management systems (LIMS) so as to avoid entering data twice into separate systems, with all the associated staffing implications and potential for error. During development of the system, consideration should be given to the possibility of the future incorporation of existing biobanks into the National Cancer Biobank. A practical solution for the integration of existing ICT systems should be in place. A federated structure may be appropriate in such cases.

6.3 Buy or build?

It is not possible at this stage to make a clear recommendation on whether a system should be bought off the shelf and customised, or whether it would be better to develop one specifically designed for the Biobank. Currently, there is no system on the market that is likely to fulfil all the Biobank's requirement for an integrated solution. Therefore, extensive customisation would be necessary and this would tie the Biobank to a specific supplier. It is the experience of other biobanks that a high degree of flexibility is necessary; if provided by a vendor, this would come at a price. On the other hand, developing an in-house solution is very labour-intensive and might be more feasible as a module structure rather than as one large block. If a solution is developed in-house, it is essential that detailed documentation is made available and that succession planning is taken into account from the outset. Having more than one

person familiar with the system is fundamentally important. The decision as to whether the ICT system should be bought or built should rest with the ICT manager and the director/strategic advisory group; it should be addressed in the context of developing the user specifications.

The Data Protection Commissioner should be informed about plans for the Biobank before ethical approval is sought. The application for ethical approval should contain materials as approved by the Data Protection Commissioner. This will help to avoid unnecessary delays.

6.4 Best practices

1. Obtain ethical consent and Data Protection Commissioner approval for the collection and use of data.
2. Maintain communications between bioinformatics system developers, researchers, clinicians and collection personnel.
3. Use either an automated data extraction system or multiple checks of data entry, accepted common data elements, drop-down menus and data range limits.
4. Develop and use bioinformatics systems which are searchable and can be mined, and which will also facilitate easy downloading of data in multiple formats.
5. Employ network security systems and access control in order to ensure that privacy is protected and secure. These should include a second security safeguard such as a biometric identifier so as to ensure that no password sharing takes place.
6. Develop an active user management policy in order to ensure that data access is on a need-to-use basis.
7. Establish mechanisms for a complete audit trail of data entry and retrieval.
8. Upload of “omics” research data for general access by other groups.

6.5 Recommendations

- An ICT manager with a strong background in the delivery of ICT solutions should be appointed from the outset to ensure that the ICT system fits within the overall strategy.
- There must be strong user input into the design of the ICT system, taking into account both the relevant issues outlined above and best practice.
- The system must be compatible with hospital networks and should aim for automatic data capture from other hospital information systems.

- Data Protection Commissioner approval must be obtained before applying for ethical approval.
- It must be possible for all relevant raw data and analysed data to be entered and retrieved easily, and the system must be scalable.
- Strong security systems and a complete audit trail for all data entries and retrievals will be required.

7.0 Standards and quality assurance

7.1 Background

There are many biobanks in existence throughout the world and some of these have been established for decades. A major drawback with many of these biobanks is that samples have been collected and stored under varying conditions. As such, when they use these samples, it is difficult for researchers to compare results from different studies. Similarly, the amount of clinical information collected with samples varies widely, as do the associated levels of consent. In an effort to standardise biobanks, a number of international organisations have, in recent years, produced detailed guidelines in relation to standards for biobanking. Each of these documents covers biobanking considerations to varying degrees. When taken together, they provide a detailed reference source of biobanking best practices which can be applied to biobanks in all countries once local legislative considerations are taken into account. In the case of the National Cancer Biobank, the recommendations for standards and quality assurance are based on the best practice guidelines outlined in the *National Cancer Institute Best Practices for Biospecimen Resources*²⁶, and the *ISBER 2008 Best Practices for Repositories*²⁷, as they cover the areas to be addressed by the terms of reference in relation to standards in detail. Importantly, guidelines produced by other organisations such as the OECD should also be considered as these guidelines address complementary issues which are particularly relevant for international co-operation. Ensuring compatibility with the OECD guidelines will facilitate co-operation with, and integration into, BBMRI; this is because BBMRI will be based on OECD best practice guidelines.

7.2 Data coding, classification, storage and protection

The way in which data is obtained, classified and stored must be clearly defined in order to protect the privacy of the individual and, at the same time, obtain the most value from a particular sample. Data must be obtained through the appropriate channels of consent, and it must be recorded in a way that enables it to be compared with other data. Data collection, including follow-up information, should be co-ordinated between centres, and a minimum clinical dataset should be defined. At the same time, the security of the data in relation to coding patient information must be ensured, while simultaneously maintaining the necessary links to facilitate information follow-up. Furthermore, it is essential that samples can be tracked at all times. While several documents produced by international experts outline best practices for data collection and management, the Expert Group recommends that the Biobank should base its standards for data collection on the guidelines set out in the *National*

Cancer Institute Best Practices for Biospecimen Resources (7–8 and 11–15)²⁶ which are summarised briefly below.

Best practice dictates that, where possible, all relevant clinical data associated with samples is collected in a manner that is in keeping with the relevant regulations. In Ireland, such regulations include the Tissue and Cells Regulations (2006)²⁸ and data protection legislation. The use of a ‘uniform vocabulary’ and common data elements (CDEs) is recommended, and the Biobank must employ an appropriate method to validate data collection. Data associated with a sample should be coded, and a secure link should be maintained in order to facilitate the identification of a participant for follow-up; this must be in keeping with consent and privacy regulations. Each sample should be assigned a unique identifier or a combination of identifiers e.g. a barcode. Each division of the sample or extraction should be considered a new sample and would thus require a unique identifier.

Data management is very labour intensive and must be properly resourced. As discussed in Chapter 6, the informatics system which underlies data management must be robust, reliable, scalable, and it must be capable of interfacing with other systems for data exchange. The system must be able to support all biobank operations. At biobank level, the system must, in compliance with the regulations, have the capacity to track all aspects of collection, processing and distribution up to the point where unused samples are returned; it must also have the capacity to document all identifiers and link information on labels to information in the system. Fields should be available to add quality assurance data and research results from users, thus ensuring that the bank evolves both dynamically and interactively. The database must be on a secure site and there must be appropriate plans in place for data storage and retrieval. In addition, it should be able to facilitate monitoring and reporting on sample quality. Permissions and roles must be defined so as to ensure proper access to data and biospecimens. The system must be able to integrate with local, national and international systems including caBIG.

Ideally, follow-up information should be collected from each patient. Clinical follow-up, such as responses to therapy and a set of outcomes, should be included in the dataset wherever possible. Clinical follow-up might also involve obtaining further bloods and other fluids, as appropriate. With the changes that are taking place in the delivery of cancer care under the National Cancer Control Programme, it is currently not entirely clear as to how clinical follow-up can be achieved since much of the current follow-up procedures will be handed over from hospitals to the community. That said, links to the National Cancer Registry will provide an important source of follow-up in relation to outcomes. This issue should be considered in detail during the initial Biobank implementation phase.

7.3 Sample collection, handling, and storage

If samples from different collection sites, or indeed from the same site, are to be comparable, they must be collected in a standardised fashion, and they must be processed and stored according to the same protocols as far as possible. The *ISBER 2008 Best Practices for Repositories* document (40–46)²⁷ sets out detailed guidelines for sample collection, handling and storage; it is recommended that the Biobank's standards should be based on those guidelines.

All sample types should be collected where possible (see Chapter 5). With each sample type come considerations for collection. These include the timings incurred at each stage of specimen collection and processing, up to the point of storage. The ISBER guidelines recommend that pilot studies or feasibility studies be carried out to identify any problems associated with the collection and processing of particular sample types. However, it is impossible to predict all future requirements.

All assessments of quality should be adequately recorded both in relation to the methods employed and the results obtained. The QA process for sample collection, processing and annotation must be standardised; this should include recording the time from actual cancer resection to the freezing of samples in the Biobank. Appropriate QC such as Haematoxylin and Eosin (H&E) staining of sections and/or immunostaining must be performed for each specimen. Where possible, a H&E section should be taken from an adjacent (paraffin) block, to confirm that a lesion is present and to determine what percentage of the sample it accounts for. DNA and RNA integrity should be tested on a defined percentage of samples, as is the practice in the Spanish National Tumour Bank Network and the Wales Cancer Bank.

It is important to maintain diagnostic integrity and, as such, a pathologist should supervise tissue procurement. A pathologist must review all patient tissue specimens to determine what material can be made available for research and the optimal samples and number of aliquots to be taken. Bloods and other body fluids not required for diagnosis can be collected in accordance with approved protocols and do not require pathologic review.

Importantly, where samples are to be aliquoted, there are a number of standards to be considered in relation to freezing and thawing (e.g. the rate of cooling, storage, handling and reconstitution). In addition, the retrieval of specimens from storage must adhere to strict protocols for sample inventory and tracking. There should be an appropriate inventory system and SOPs for sample retrieval along with checklists and other forms which are specifically designed to document the process.

7.4 Safety, security and appropriate back-up for physical samples

Best practices for safety, security and back-up are again outlined in *ISBER 2008 Best Practices for Repositories* (13–22 and 27–30)²⁷. This notes that knowledge of materials to be stored, processing requirements, length of storage and application are necessary when assessing the Biobank's safety and security requirements. As the purpose of the Biobank is the safekeeping of the materials, many aspects of facility design which may affect the quality of the samples must be considered; these would include fire protection, temperature, air flow and lighting. In addition, monitored security systems should be employed, and provision should be made for alarms to be responded to on a 24-hour/seven-days-a-week basis. The systems must be designed in such a way that a series of responsible individuals will respond to an alarm in a timeframe that either prevents or minimises loss or damage to the collection materials.

Access systems should ensure that only those with the appropriate clearance are able to access samples, and alarms should monitor unauthorised entry. Best practice recommends a hierarchical system of security – one that employs multiple levels of physical, electronic and procedural controls. For example, the repository material may be in a restricted area which is operated using key-coded access or which employs electronic sensors when the area is unoccupied; the freezers in this restricted area would be locked and the freezer keys would be kept in a cabinet which would also be locked.

As power cuts are inevitable, it is essential that a back-up power supply is in place. Best practice recommends that computer systems and electronic systems such as freezer controllers should be protected by an uninterruptible power supply (UPS) system. Where the back-up power is run by a motor generator, the system should be tested regularly. Freezers and fridges should also be monitored daily. Ideally, an automatic system should be employed; this should continually monitor all temperatures and critical parameters, create logs, generate alarms and notify personnel to take action.

Back-up storage of sufficient capacity should be available in the event of equipment failure. In the case of liquid nitrogen storage, a supply should be available, and the system should be monitored and alarmed. Relevant personnel safety measures would also be key. Protective wear and oxygen sensors should be provided. Procedures for maintenance, repair, and calibration of equipment should also be in place.

In relation to personnel safety, national guidelines for health and safety in the workplace should be adhered to (Safety, Health and Welfare at Work Act, 2005)²⁹. In order to develop an appropriate safety programme, the Biobank must assess which areas of safety affect its employees. This would include issues such as fire, electrical and physical safety which are standard in all organisations. In addition, safety measures

in relation to handling human material will have to be put in place, together with considerations for specific roles such as handling sample retrieval from liquid nitrogen, as noted above. The development of safety plans and the appointment of a designated individual responsible for safety are recommended, and appropriate training measures should be put in place.

7.5 Quality assurance and quality control

As outlined by ISBER best practices (23–30)²⁷, it is essential that systems are in place to track all events in relation to a sample and to confirm that samples are handled correctly at all times. In order to facilitate this, an effective quality management system must be in place; this system should incorporate appropriate SOPs and levels of quality checking and audit. The Biobank should have a quality assurance programme/quality management system (QA/QMS) and, in the case of the National Cancer Biobank, it is envisaged that at least one dedicated individual would be employed in a central office for this purpose. Appropriate training and SOPs would also be in place in each centre.

Detailed policies and procedures should be outlined in a SOP manual in order to ensure that all samples are collected and stored in a standardised manner. It is recommended that biobanks share their quality practices so as to ensure similarity of the shared samples. For this reason, when it is drawing up its SOPs, the Biobank should look at practices in other national and international biobanks. These SOPs should be compiled by individuals who have experience in performing the practices described. Several topics should be covered by these manuals and these include specimen handling and processing, legal and ethical issues such as consent, access and sharing procedures, shipping and receipt, records management, procedures in relation to equipment, safety, accident response, and training. Policies should be in place for review and modification of SOPs and for associated training.

In addition, the Biobank should, where appropriate, aim to attain quality standards such as Current Good Practices (CGP), and ISO (ISO9001:2000, ISO/IEC 17025). There is currently no clear international standard specific to biobanking activities. However, the French national normalisation authority (Association Française pour l'Assurance de la Qualité/Association Française de Normalisation – AFAQ/AFNOR Certification), supported by the INSERM (Institut National pour la Santé et la Recherche Médicale) are aiming to create a national standard for biobanking which may form the basis of a new ISO standard. Based on existing ISO standards and the *OECD Best Practice Guidelines for Biological Resource Centres*³⁰, the document aims to create a set of standards which are specifically aimed at quality management issues affecting research biobanks. This move is supported by other biobanking groups such as the Marble Arch International Working Group on Biobanking for Biomedical Research.

7.6 Recommendations

- Best practices for data coding, classification, storage and protection as outlined in *National Cancer Institute Best Practices for Biospecimen Resources* should be followed including:
 - All relevant data associated with samples collected where possible.
 - Use of uniform vocabulary and CDEs.
 - Data should be coded, and a secure link to the patient should be maintained.
 - The data management system must be able to track all aspects of data/sample collection, processing, and distribution.
 - Permissions and roles must be defined.
 - Procedures regarding patient follow-up must be defined during the implementation phase.
 - Data collection, including collection of follow-up data, should be co-ordinated between centres, and a minimum clinical dataset should be defined.
- Sample collection, handling and storage procedures should adhere to *ISBER 2008 Best Practices for Repositories*. These would include the following:
 - Pilot studies/feasibility studies should be carried out in order to identify any problems associated with the collection and processing of particular sample types.
 - A pathologist should supervise tissue procurement.
 - Appropriate inventory systems and SOPs for sample inventory and tracking are needed.
- Recommendations for safety, security and back-up as outlined in ISBER guidelines as follows:
 - Security systems should be in place and monitored 24 hours a day, seven days a week.
 - Access systems should prevent unauthorised entry. A hierarchical system of security should be in place.
 - A back-up power supply in the form of uninterruptible power supply (UPS) or generators will be required.
 - Back-up storage of sufficient capacity will be required.

- An appropriate safety programme should be developed; a safety officer should be designated, and a training procedure should be implemented.
- Implementation of the QA standards and QC standards outlined in ISBER guidelines including:
 - An effective QMS should be developed which incorporates appropriate SOPs and quality checking.
 - A dedicated Quality manager should be in place.
 - Detailed policies and procedures must be outlined in a SOP manual, and appropriate training should be provided and monitored.
 - The Biobank should aim to attain quality standards where appropriate.
- Irish biobanks will have to meet certain requirements in order to participate in European biobanking initiatives such as BBMRI. As such it is important that the National Cancer Biobank ensures that it is compatible with the best practice guidelines, such as the OECD guidelines, used by the BBMRI.

8.0 Ethical issues

8.1 Introduction

The collection of samples and data from individuals must adhere to the highest ethical standards and ensure informed consent, patient confidentiality and protection. While Ireland currently has no specific legislation pertaining to biobanks, in terms of ethical guidelines the *Human Biological Material: Recommendations for Collection, Use and Storage in Research*, which was produced by the Irish Council for Bioethics in 2005³¹, covers many of the important questions related to biobanking including consent, confidentiality, and commercialisation.

In relation to biobanking in Ireland the main ethical issues are³²:

- Ownership of tissue.
- Consent.
- Privacy/confidentiality – access to data.
- Feedback of research results.
- Ethical oversight of research.
- Benefit-sharing and commercial uses.

In particular, ownership, consent and privacy issues will be addressed here in detail³²:

8.2 Ownership

Historically, human tissue has been regarded in law as *res derelicta*, with no value and therefore no ownership. Most countries with legal systems based on the British Common Law traditionally prohibited human tissue having a property value. The intention was to treat the human body as beyond commercial value, and therefore incapable of being owned, sold, bought or stolen.

Due to rapid changes in science and medicine, and the frequent use of human samples in the discovery and development of new drugs and treatments, it is now recognised that the human body or parts thereof potentially have both personal informational and commercial value. This raises the question as to whether the old law is still tenable and whether a patient should now have rights over tissue. Also, does a patient still have rights to his or her tissue or organ if they 'sell' it to the Biobank? One of the most relevant cases in relation to ownership rights was *Moore v Regents of the University of California* (1988)³³. In this case, a patient took legal action against the university for

using his tissue, without his knowledge, to commercial advantage. The court ruled in favour of the university in relation to ownership, concluding that once tissue is excised, the patient loses legal interest, but it ruled in favour of the patient in relation to informed consent. The decision was based on the need to protect research. If patients had ownership rights, researchers would be unduly restricted and inhibited. It is not clear whether this ruling would also apply in Ireland as no similar cases have come before the Irish courts to date.

Ownership Theories of abandonment, donation or gift

Abandonment: Applying this theory raises a number of issues. First, if the patient does not know that they are relinquishing their rights, the term ‘abandonment’ may not accurately describe the situation. Second, if they do not own the tissue legally, the person logically cannot abandon his/her tissues. In the case of biobanking, the right of a donor to revoke consent to the use of their tissue would cause problems in relation to the concept of abandonment.

Donation: There are some analogies with organ donation and blood donation. However, with blood donation, for example, restrictions are not attached by a donor. This is not necessarily the case with tissue donation; in some cases the donor may stipulate that the donated material may be used in certain types of studies only. There is some confusion between organ donation and tissue donation, and it may not be useful to compare the two. Currently, family members have the option to override a consent given for organ donation. How would this apply in a biobank context?

Gift model: With the gift model, difficulties may arise around feedback and withdrawal. In order to address this, the *conditional gift* model may be the most appropriate. In this model, there is a recognised relationship between the biobank and the donor, with ethical considerations. While the donor has relinquished control of the tissue, certain conditions may apply (e.g. use only for certain identified studies, or types of studies), and the donor maintains the right to withdraw the sample at any time.

8.3 Consent

There is currently no international consensus in relation to consent. Informed consent is the gold standard in medical and research applications; however it is impossible to specify all future uses of material in biobanks, and therefore fully comply with traditional theories of informed consent. Classical research ethics would mandate that fresh consent must be obtained for each use. However, this would severely limit the potential use of samples since a number of disadvantages are associated with this approach including cost, delays, and loss of some participants through lack of response, inability to contact them, or death.

A number of guidelines for consent are available. In Europe, the Council of Europe produced recommendations for research on bio-materials of human origin³⁴. They recommend that future uses be *as specific as possible*. Many guidelines used by EU countries permit general or broad consent for ‘unspecified future research use’; such countries include Germany, the UK, Sweden, Iceland and Estonia. This is seen as acceptable if two conditions are met: approval of research by an ethics committee, and the right of participants to withdraw at any time. This is a less strict standard of consent than traditional informed consent, but it is counterbalanced by the optimum use of samples (maximising research outputs and minimising the need to collect more samples in the future, with its attached ethical advantages).

In the US, the prevailing opinion has been in favour of the classical standard of informed consent. Similar to the recommendations of the Irish Bioethics Council³¹ there may be a multi-layered consent whereby different choices are presented on a detailed form. Alternatively, there may be limited consent relating to specific diseases or research projects. A major disadvantage of this is the considerable administrative burden for research associated with tracking the different layers of consent and the costs involved. Another proposed solution is a system of waivers if there is no risk for the participant, as defined by federal regulations. The Office for Human Research Protections (OHRP) changed the definition of non-identifiable data in 2004³⁵ so that it is not necessary to obtain informed consent or seek Institutional Review Board (IRB) approval (see below).

8.4 Privacy/anonymisation

In relation to privacy/anonymisation, it is essential to clearly define the terms being used. Currently, a confusing array of terms is used throughout the biobanking sector, leading to communications barriers. Examples of European terms include anonymous, unlinked anonymisation, linked anonymisation, coded, identified. Terms such as ‘anonymous’ might, strictly speaking, only be appropriate for archaeological data, as opposed to prospective samples. ‘Anonymised’ on the other hand refers to samples which have data associated but have been stripped of identifiers, while coded samples may be linked back to the patient, but not by the researcher. The OHRP in the US have defined ‘not identifiable’ as referring to researchers being unable to access the participant’s identity under any circumstances³⁵. It is therefore not considered ‘research on human subjects’; this is because the subject from which it was derived (although human) cannot be identified, and therefore neither informed consent nor ethical approval is needed. This enables researchers to avoid regulations, avoid costs, delays, IRB approval etc. The advantage of enlarging the definition in this way is that researchers can escape regulations by signing legal documentation which prevents access to the code under any circumstances. However, problems may arise in that a

link still exists, and it is therefore theoretically possible to trace a donor, especially where clinically relevant information exists. This approach also makes it impossible for the donor to withdraw a sample, since the sample cannot be identified. Also, the basic assumption that any sample of human origin is in fact human, and therefore subject to ethical guidelines and regulations, should apply to the National Cancer Biobank.

8.5 Feedback, ethical oversight and benefit-sharing

Other issues to be considered in relation to operating a biobank include:

Feedback: The right to know, and the right not to know must be considered, particularly in the context of population biobanks where clinical interest, genetic counselling and the interpretation of results may be issues. There is a requirement for comprehensive information for study participants prior to their participation in any large-scale population biobank. Where appropriate, and as determined by the relevant ethics committee, study results impacting on individual donors should be fed back to the donor in an appropriate way e.g. through the donor's GP or through a medical geneticist. Examples might include the risk of reoccurrence as well as studies entirely unrelated to the original disease of the donor. This will be study-specific and it should be part of the submission for access to samples. Confirmation of research results from an accredited diagnostic laboratory, as well as peer review of the interpretation of the results, would also be needed before feedback is given. Generic, non-individualised information on the result of a study might also be fed back. This question is not unique to biobanks; it also relates to clinical trials and translational research studies involving human materials.

Ethical oversight: In line with efforts already underway, the Biobank should lobby for a single streamlined ethical review process for research. There must be adequate scientific and ethical oversight during the period when the Biobank is being established; in addition, ongoing monitoring by an appropriate committee will be required for the duration of the project.

Benefit-sharing: This is a policy issue which has to be conceptualised during the implementation phase. Access to samples has to be regulated in an appropriate manner. Possible models include broad access or restricted access – either for national researchers only, or for international researchers, who are coming from a clinical background, an academic background or a commercial background.

At the other end of the research process, the results arising out of the use of samples from the National Cancer Biobank (both in the form of raw data and analysed data) have to be disseminated in a way that best serves the public interest. Thus, it will be necessary to oblige all researchers accessing samples to deposit their raw data

and their analysed data in shared data repositories which are accessible to other researchers. The depositing of data must be done in such a way that it does not hinder the publication of scientific papers or the filing of patents. This will prevent the use of scarce samples for repeat experiments by other researchers, and it will maximise the benefit per sample and the research output per sample. In addition, there is a need to elaborate benefit-sharing policies that take into account the potential commercial uses of the data.

8.6 Irish context

Currently, there is no legislative framework in place in Ireland to deal with these issues. The Tissues and Cells Regulations (2006) only cover tissues and cells used for human application²⁸. The current Department of Health and Children proposals for Human Tissue legislation cover the retention and use of tissue for research, but only in the case of post-mortem tissue; it is unclear whether tissue from living donors will be included in the legislation. So, while this will have some relevance to biobanking, additional legislation will probably be needed in relation to tissue from living donors. It is important that the Biobank becomes actively involved in any discussions around proposed legislation relevant to biobanking, and that it highlights the requirement for legislation to underpin biobanking. For example, any developments in relation to the proposed Health Information Bill will have implications for the National Cancer Biobank.

In relation to issues such as consent and privacy it is considered that an approach in line with other European countries, with provision for broad/general consent, linked anonymisation and ethical oversight, would be the most valuable. Linked anonymisation would add great scientific value to the Biobank by making it possible to follow up individuals for outcomes and long-term history while protecting the individual donor from being identified. This is particularly relevant in the context of a cancer biobank where donors are, by definition, ill and therefore the potential to follow up would be extremely valuable.

While the initial time commitment necessary for obtaining layered consent is essentially the same as that which applies to obtaining other types of consent, the issue of tracking different uses of consent is one that creates a considerable burden. It also reduces the number of samples available for a given research study, and it adds a layer of complexity to the process of predicting how many samples would be eligible for a given study. In order to reach the same statistical significance for studies, the Biobank's samples size would have to be increased in line with the number of participants limiting the use of their sample. Layered consent requires IT specifications for compliance which are beyond the reach of most biobanks. A

more practical approach might be a general consent, whereby the situation is fully explained to patients who then have a simple opt in/opt out choice for their samples. In other words, they might consent to have their samples included in future unspecified research studies on condition that ethical approval has been granted to the study and on condition that they can withdraw their samples at any time. Any patients who are uncomfortable with this should not consent to submitting their samples to the Biobank. Studies in Ireland and in other countries show that a majority of people would prefer general consent and do not wish to take on the burden of being re-contacted for their consent^{36,37}.

The issue of consent by proxy is unresolved and will have to be revisited during the implementation phase. Legal advice may be needed, and new legislation governing this area may be required. From an ethical standpoint, not allowing proxy consent would exclude children and incapacitated adults, and would therefore exclude paediatric oncology patients and people suffering from neurodegenerative conditions among others. This in itself is potentially unethical. Advice on this issue could be sought from those already involved in the banking of paediatric tissue. Our Lady's Children's Hospital, Crumlin currently deposits patient samples in a Scottish biobank as part of its involvement in a large clinical trials network. Transparent, accepted consent procedures are in place for children, and these may be used to inform the National Cancer Biobank's operations in this area. Contingency for retrospective consent in special circumstances should be considered, as should procedures around the use of archival histopathology paraffin blocks in research. In the latter case, it is considered inappropriate to encroach on patient/family sensitivities years after surgery as this is analogous to re-consenting. The Biobank offers an opportunity to define the most appropriate way to include such material in research studies if desired.

A generic, national consent process must be enacted. This will require input from clinicians, and patients under legal guidance, and it must be agreed by the various ethics committees. The process of seeking consent from patients should not take place immediately before surgery/biopsy, when patients may be vulnerable. Consent should be sought in the context of a discussion between the surgeon/physician and/or the research nurse and the patient about the procedure that the patient will be undergoing. There is a distinction to be made between a consent being obtained in order to perform a surgical procedure and consent required in order to obtain a sample for research purposes. Consent forms for surgery and tissue procurement should be separate, with the latter providing an explanation of the tissue sampling and handling procedures as well as potential use for the tissue. It should state that consent or refusal will not influence treatment.

8.7 Recommendations

- Legislation to underpin biobanking is required. This might be discussed in the context of the proposed human tissue legislation and the Health Information Bill.
- An approach in line with other European countries towards issues such as consent and privacy is preferable.
- In terms of ownership, the 'conditional gift model' is the most appropriate.
- In relation to privacy/anonymisation, linked anonymisation should be used, as it is the most valuable.
- Consent should be given in the form of general consent or broad consent for 'unspecified future research use'.
- A generic, national consent process must be enacted.
- The Biobank should lobby for a single streamlined ethical review process for research.
- The issue of consent by proxy must be addressed during the implementation phase.
- Contingency for retrospective consent in special circumstances should be considered.
- Consent forms for surgery and tissue procurement should be separate.
- Seeking consent from patients should not take place immediately before surgery, as this is a time when patients may be vulnerable. Consent should be sought in the context of the discussion between the physician/research nurse and the patient regarding the procedure that the patient will be undergoing.

9.0 Relationships and links

As clearly demonstrated by a consultation process that involved input from diverse groups (Appendix C), many different groups have a stake in the National Cancer Biobank. These include hospital management and staff, academia, the HSE, funders, industry, patient groups, counterparts in Northern Ireland, other clinical research initiatives, and other biobanks in Ireland, Europe and globally. Many of these groups have expertise in areas relevant to biobanking; this ranges from implementation of SOPs and gaining approval from the Data Protection Commissioner to enacting peer review processes and appropriate education initiatives. The Biobank should seek to draw on the expertise available and take advantage of the significant resources already in place. It should collaborate with and cooperate with existing infrastructures and it should initiate mutually beneficial relationships with stakeholder groups.

9.1 North/South collaboration and the potential for an all-island biobank

There is a high level of interest in establishing a biobank in Northern Ireland. A working group was set up to consider the potential for a tumour bank in Northern Ireland which would, in the first instance, support local healthcare research in both academic and NHS environments. However, during the course of this work, the need for further consideration of the wider application of biobanking beyond cancer has emerged. Links have already been developed with cancer biobanks elsewhere in the UK through preliminary membership of the NCRI-supported Confederation of Cancer Biobanks (CCB). It is anticipated that, once formally established, the informatics used by a biobank in Northern Ireland would link directly with other CCB members including onCore UK. The Department of Health, Social Services and Public Safety has noted that collaborative links with the developing National Cancer Biobank in the Republic of Ireland are welcome and are considered valuable – particularly in the context of the Ireland-Northern Ireland-NCI Cancer Consortium.

Formal arrangements would be envisaged whereby researchers could access Northern Ireland/Republic of Ireland tissue samples as well as clinical data. Future co-operation in biobanking from an all-island perspective may require a specific agreement between the two Departments of Health. Both the Department of Health Social Service and Public Safety in Northern Ireland and the Department of Health and Children in the Republic of Ireland are interested in an all-island approach to biobanking within the context of a wider feasibility study on North-South co-operation in health and social care which is currently being undertaken by the two Departments of Health.

As inferred in section 4.4 of this report, it is proposed that the Chief Medical Officer of Northern Ireland be invited to nominate a representative or representatives from NI to the strategic advisory group.

9.2 Academia/industry partnerships

The focus of health research is currently on translational research i.e. turning basic research into novel diagnostic and therapeutic tools. This 'bench to bedside' approach requires collaboration between basic researchers, drug development companies and clinicians. The commercialisation of research is necessary to ensure that novel findings make it to clinical trials and, ultimately, to the patient. For this reason, partnerships between academia and industry are essential. The cancer biobank can build on such partnerships by:

- Providing standardised, high-quality samples for use in basic and translational research.
- Recognising the importance of industry in bringing therapeutics to the patient.
- Creating a framework for collaboration.
- Creating clear access policies.
- Developing clear IP policies.

Enterprise Ireland has acknowledged the importance of biobanking to both the healthcare sector and industry in the CIRCA report of 2007³⁸. The importance of biobanking as a tool for industry is also recognised by the fact that the number of industry clinical trials which include a biobanking component has increased over the last number of years. This might present a conflict in some cases. The well-being of the patient must always be the decisive factor in clinical decision making. If it is in the best interest of a patient to be offered participation in a clinical trial which requires banking surgical material as a condition to participation, then this must be the first offer made to the patient. In such cases the Biobank would attempt to negotiate upfront agreements with industry (particularly with companies that are carrying out a high number of trials in Ireland) about possibilities for sharing samples where appropriate.

There are mutual benefits to be had as a result of co-operation between clinical trials and biobanks. For the Biobank, one of the benefits will be cost recovery through administrative charges to industry and the rapid generation of data relating to samples which will go back into the system and will benefit all other users. The existence of a high-quality biobank will benefit industry-based research and development and will ultimately generate more clinical trials. Furthermore, the ability of basic researchers to investigate why trials either fail or have unexpected outcomes will be facilitated by

samples from clinical trials being made available through the Biobank – a move that will be of benefit to all parties.

Without the involvement of industry, any discoveries and developments made with material sourced from the National Cancer Biobank will not reach patients. While a relationship between industry and the National Cancer Biobank will be mutually beneficial, it should also be made clear to all stakeholders, including the general public, that industry access to samples and information adheres to the same principles as those that apply to researchers. In other words, a study must be scientifically sound, it must be ethically approved, and data must be made accessible to other researchers. Access cannot be 'bought'.

It is important to take on board industry concerns about the establishment of the National Cancer Biobank. Consultation with industry, or involvement of industry representatives during the implementation phase, will help to pre-empt potential blocks to maximum use of materials.

9.3 Incorporation of existing biobanks, and linkages with other Irish biobanks and clinical research facilities

A number of cancer biobanks already exist in Ireland. These range from small collections of samples, to highly organised cross-institutional collaborations such as the Prostate Cancer Biobank. A clear remit of the Expert Group is to envisage how other biobanks might be linked with the proposed National Cancer Biobank. In principle, there are two options available (i) the decision as to whether an existing biobank can be incorporated is taken on a case-by-case basis, based on a clearly defined set of standard requirements, against which the Biobank is measured to guarantee the quality of all samples and data under the cancer biobank umbrella. This decision must be based on careful evaluation of existing biobanks and the intentions of current owners. (ii) A decision is made upfront that the quality of samples and associated information can only be guaranteed prospectively, not retrospectively, and no existing biobanks are incorporated.

If the decision is taken to incorporate existing biobanks into the National Cancer Biobank, each case will need agreement from both partners. A critical factor will be the wishes and intentions of the owners of existing biobanks. All materials incorporated into the Biobank will be accessible under the National Cancer Biobank rules. Current owners would have to balance the loss of complete control over their current collection against the benefits of being part of a much larger internationally recognised biobank.

From the perspective of the Biobank, a number of considerations will have to be made:

- The quality of the samples involved – is there information available on sample collection? Do they meet the standards of the Biobank?
- Associated clinical data available.
- Type of consent obtained for the samples.
- Ability of IT interface between the biobanks.

A decision must also be made around the incorporation of archival histopathology paraffin blocks as part of the Biobank inventory. While a number of additional ethical and consent issues exist around the use of this material, the establishment of the Biobank provides an opportunity to address these concerns not only in relation to biobanking but also for research in general.

Importantly, the National Cancer Biobank should also be compatible with non-cancer biobanks such as the proposed 'GeneLibrary Ireland', which will contain important population health and genetic information and, potentially, will act as a source of control samples for research. During the consultation process, the possibility of expanding the Biobank to other disease areas was brought up repeatedly, and there is a strong interest among members of the clinical and research community to do so. While it is outside the remit of this Expert Group to make any specific recommendations for other disease areas, the implementation of the National Cancer Biobank should be carried out in such a way that it can act as a model for future developments in other disease areas.

The development of new clinical research facilities on campuses at St James's Hospital Dublin, University College Hospital Galway and Cork University Hospital offers a new opportunity to expand and co-ordinate biobanking efforts. These facilities complement existing clinical research facilities at Beaumont Hospital, the Mater Misericordiae Hospital and St Vincent's University Hospital. Each of these sites corresponds to a dedicated cancer centre, as outlined in the implementation document for the National Cancer Strategy¹¹.

For the last few years, major efforts to co-ordinate clinical research in Ireland have been underway. The Dublin facilities are already co-ordinated as the Wellcome Trust – Health Research Board Dublin Centre for Clinical Research (DCCR); they share decision-making, structures, procedures and personnel. This cohesive approach was a major factor in ensuring the success of their application in a very competitive process, and it has led to significant investment from the HRB and the Wellcome Trust. The new facilities in Galway and Cork are co-funded between the HRB and the HSE, and they

demonstrate recognition by the HSE that clinical research is essential for excellence in the delivery of clinical care. The new facilities are aligned with the Dublin facilities through the Irish Clinical Research Infrastructure Network (ICRIN), which in turn links into European activities such as the Irish arm of the European Clinical Research Infrastructure Network (ECRIN).

As part of their remit, all clinical research facilities are involved to a greater or lesser extent in biobanking studies. Although not all biobanking will be for cancer research, the same basic system will apply – logistics, procedures, databases and so on can be modified accordingly. The National Cancer Biobank must work harmoniously with the clinical research facilities, and vice versa, and there should be no duplication of facilities. Expertise in the CRFs around the management of infrastructures should be leveraged where possible.

9.4 Linkage with existing international cancer biobanks

In order to ensure that research efforts are not duplicated, collaboration not only within Ireland but also internationally should be promoted. However, despite the European Data Protection Directive, a number of regulatory and ethical difficulties with regard to exchange of tissue and data remain; this has been highlighted by the TuBaFrost group³⁹ and others. Efforts such as the European Bio-Banking and Biomolecular Resources Research Infrastructure (BBMRI), which was recently funded as a European infrastructure for a two-year planning phase under FP7, are aiming to harmonise and co-ordinate existing infrastructures, develop new tools and technologies, and facilitate studies of unprecedented statistical power by bringing together fragmented collections in over 20 different countries¹⁴. The National Cancer Biobank should clearly link in with this initiative. It will be very important in the initial set-up phase, in order to ensure that future collaboration is as straightforward as possible. BBMRI includes disease-specific biobanks as well as population-based biobanks. Currently, it has two Irish partners, the HRB and ICRIN. BBMRI is carrying out a survey of existing biobanks in Europe in 2008. The results for Ireland will help to identify potential national candidates for collaboration or integration.

The Public Population Project in Genomics (P3G) is a not-for-profit international consortium which aims to promote collaboration between researchers in the field of population genomics⁴⁰. Its P3G Observatory contains a wealth of scientific information and tools aimed at facilitating the development, realisation and harmonisation of research projects carried out using biobanks.

Similarly, the International Society for Biological and Environmental Repositories (ISBER) has been instrumental in providing information and guidance on the safe and effective management of specimen collections⁴¹.

Resources such as these should inform the implementation phase of the National Cancer Biobank, in order to ensure that international best practice is followed and also ensure that the National Cancer Biobank can easily become part of initiatives such as the BBMRI.

Many of the cancer clinical trials carried out in Ireland are part of international studies which will benefit patients in many countries. A biobank is ideally placed to promote such collaboration and there are many benefits to be had from links to international biobanks e.g.:

- Avoid duplication of research projects.
- Obtain samples not available in Irish banks.
- Provide samples to external studies that might otherwise go unused.
- Increase critical mass for statistical studies, especially for rare medical conditions where only small sample numbers are available.
- Collaborative international effort will greatly increase speed from 'bench to bedside'.
- Platform for networking.

The Biobank can achieve this through:

- Clear policies on access and intellectual property rights, appropriate material transfer agreements.
- An ICT system that is compatible with outside systems.
- Legal and ethical policies in line with international best practice where possible.
- Linking in with international organisations such as BBMRI and ISBER, which will facilitate compliance with emerging standards.
- Ensuring that researchers at an international level are aware of the resource.

9.5 Appropriate linkages with research programmes and potential for collaborative initiatives, including cancer clinical trials

The National Cancer Biobank is not an end in itself, and only fulfils its potential if the samples collected are widely used for high-quality research with ultimate diagnostic, therapeutic or prognostic benefits to patients in Ireland and worldwide. While it is clear that the cost of the Biobank (in particular the core costs) should be state-funded, additional activity-based funding of research projects must be provided for research programmes which use the Biobank's resources. Where large-scale cancer research programmes with a biobanking element are funded, the exchange of samples and data between the National Cancer Biobank and such research programmes should be expected.

The Biobank should collaborate with existing networks such as ICORG (All-Ireland Cooperative Oncology Research Group)⁴². ICORG co-ordinates cancer clinical trials units in 17 hospitals (16 in Ireland, one in Northern Ireland), and it also provides training, raises hospital standards, and operates according to Good Clinical Practice using SOPs. The importance of cancer clinical trials for the delivery of an excellent cancer service for patients has been recognised in the *Strategy for Cancer Control in Ireland* (2006); this strategy also recommends the setting up of a National Cancer Biobank. ICORG receives significant funding from the HRB and the ICS, and is strongly supported by the Department of Health. In 2007, more than 1,300 cancer patients in Ireland participated in clinical studies under the ICORG umbrella and, currently, a number of studies that are underway include a biobanking element. The National Cancer Biobank should collaborate with ICORG, where appropriate, to obtain samples and clinical data. Similarly, the resources of the National Cancer Biobank will be available to the clinical researchers affiliated to ICORG.

9.6 Collaboration with the National Cancer Institute under the Consortium

The National Cancer Biobank will be ideally placed to facilitate the mission of the Ireland-Northern Ireland-NCI Cancer Consortium⁴³ as outlined below:

- *'Improve the infrastructure necessary for the island of Ireland to further cancer research and clinical investigations.'* The National Cancer Biobank is a critical part of the infrastructure required to further cancer research on the island of Ireland.
- *'Facilitate interactions among US, Irish, and Northern Irish cancer research communities.'* The governance and operation of the Biobank will be based on international best practice and it will thus be able to interface with other systems. In particular, it is recommended that the Biobank should be compatible with initiatives in Northern Ireland and the US e.g. caBIG. The Consortium could provide a platform for increasing awareness of the Biobank, while the Biobank could provide samples and data for national/international collaborative research projects.
- *'Develop joint programs to enhance the cancer research environment in Ireland, Northern Ireland and the US with the anticipated outcome of improved cancer care.'* A number of joint research programmes have been set up by the cancer consortium. The Biobank will provide a much needed resource for research, and it will reduce the time taken for findings to reach the clinic, thereby improving patient care.
- *'Develop educational exchange programs for cancer professionals.'* Many important hospital personnel and laboratory personnel will contribute to the Biobank, and the need for research nurses cannot be overemphasised. Without adequate provision for research nurses, biobanking initiatives will fail. The Consortium already funds the training of cancer clinical trials nurses. A similar initiative, either implemented by the Consortium or using their expertise, might be applied to the training of research nurses for biobanking.

The Biobank will also have added value if it can link in with the cancer registries. The potential for the National Cancer Biobank database to link with the National Cancer Registry (NCRI) should also be explored. In this way, it may be possible to leverage further (de-identified) data, such as disease stage, age and survival – data which would not necessarily be available in the Biobank database.

The NCI has extensive experience in biobanking, including the recent publication of the Best Practice Guidelines for Biobanking. The Biobank would benefit greatly from continuing access to this expertise and to the expertise of NCI grantees, particularly during the initial set-up phase, but also on an ongoing basis.

9.7 Recommendations

- Collaborative links between the National Cancer Biobank and the evolving biobank in Northern Ireland should be developed, with further consideration being given to developing an all-island biobank.
- The National Cancer Biobank should provide access for industry using a clear governance and administrative charging structure. Industry is a key partner, and potential concerns from both sides should be explored during the implementation phase in order to develop a resource that will deliver maximum benefit to all stakeholders.
- If existing biobanks are to be incorporated, decisions should be taken on a case-by-case basis to determine whether they meet the quality requirements of the National Cancer Biobank and whether their owners should be invited to incorporate these biobanks into the National Cancer Biobank.
- The National Cancer Biobank must work harmoniously with the CRFs, and vice versa. Expertise in the CRFs around the management of infrastructures should be leveraged where possible.
- Collaboration with the ICORG cancer clinical trials initiative should be encouraged where appropriate.
- The option of linking with the National Cancer Registry should be explored.
- The National Cancer Biobank should develop close links with international organisations such as ISBER, BBMRI, P3G and the Marble Arch Group, and in particular the NCI through the Ireland-Northern Ireland-NCI Cancer Consortium. These links will be important during the implementation phase and when the National Cancer Biobank is fully operational. Much can be learned from these organisations, and collaboration with them should be the norm.

10.0 Patient education and awareness

10.1 Introduction

“Today’s health research is tomorrow’s healthcare.” This often-quoted statement sums up the enormous importance of research. While it takes many years before findings of basic research benefit patients, without it we would not have many of the treatments that we currently rely on for treating cancer and other diseases. Recent discoveries such as Herceptin and Glivec, drugs which fall into the category of personalised medicine, could not have been developed without the relevant research and the essential resource of patient samples.

If we wish to continue translating the rapid advancements in our understanding of the molecular basis of cancer into new treatments, then more and better research is needed. This will require better resources, including the National Cancer Biobank. Patients and the general public are key to the success of such a major initiative. Patients contribute the samples on which current and future research is based, and importantly, both patients and the general public have a major role to play in relation to influencing public opinion as well as influencing government opinion and the opinions of those who provide funding for research. Therefore, one of the Biobank’s essential roles will be to ensure that people understand how their contributions, together with the development of research excellence, will be of benefit to all in the future.

In an effort to ensure public awareness of biobanking activities, an assessment of the public viewpoint on research and related issues represents an important starting point. In their landmark report *Public Perception of Biomedical Research in Ireland*, Cousins *et al.* found that, when properly informed, the general public are in favour of the use of tissues for research purposes. A majority of those surveyed (86%) would be willing to allow their ‘excess’ surgical tissue to be used in a research study³⁶. There were many factors influencing this, ranging from education and awareness to a sense of duty to future patients. However, a most important finding was the favourable view of research. Despite this, the report also clearly demonstrated a need for further engagement with, and the provision of information to, the public.

10.2 Outreach and information

In its 2006 report, the Advisory Council for Science recognised the need for outreach initiatives to raise awareness among the general public about the importance of health research in Ireland⁵. It recommends that “outreach initiatives (to) be introduced to raise awareness of the importance of research in improving health service delivery, patient care and population health and the role of industry in timely translation of research outcomes to innovative products and therapies.” Similar initiatives are required to introduce the concept of biobanking to the public.

Patients need to be informed in such a way that they will have the knowledge and competency to handle decisions about contributing to a biobank. A clear and explicit definition of what is meant by a biobank in this context is necessary before beginning to inform patients. The definition (purpose) of the Biobank is of use to the patient in understanding the global framework of their involvement. In addition, definitions in relation to identifiability are important; they must clearly understand what is meant by terms such as ‘identifiable’, ‘linked’, ‘coded’ and ‘anonymous’. Understanding the terms used is essential so that each person can assess the consequences of their participation. Importantly, of those consenting to the use of excess tissue for research, it was found that on receipt of additional information as to what was meant by ‘linked’ storage of samples, the number of people agreeing to storage of their samples using a linked model rose from 50% to 89%³⁶. This underlines the importance of fully informing and educating people.

As well as involving patients, education and awareness should involve families, patient organisations and the general public. Increasingly, the public, including patient-support groups, is recognised as an active participant in the development of large-scale projects. Patient organisations can ensure that information materials are appropriate for target groups. They can communicate with participants, and they can also offer a sounding board in relation to issues such as consent. Patient organisations can put pressure on government and research funding councils; in Wales, they played an important part in helping to bring the Biobank into existence. In addition, patient organisations can participate in ethics and advisory committees; they can support researchers, not only by way of fundraising, but also by providing a platform for the communication of research goals and results to the public (e.g. Irish Platform for Patients’ Organisations, Science and Industry (IPPOSI)). Already, this issue is beginning to be addressed; for example, on 3 December 2007 the Faculty of Pathology of the Royal College of Physicians of Ireland hosted a public meeting on cancer biobanking. This meeting made a valuable contribution towards increasing public awareness and media awareness of the issue of biobanking.

10.3 Requirements and approaches

It is necessary to engage with a number of different target groups including Patients, Families, Patient organisations and Politicians. Table 10.1 outlines some of the approaches and actions that could be taken.

Table 10.1

Suggested actions
Increase awareness by encouraging and facilitating
<ul style="list-style-type: none">• Public debate around issues of consent and the identification of patient's samples.• Public consultation on choices and directions for scientific (including medical) research.• Information about research that is taking place in Ireland.• General information on who provides funding for studies, and their motives for doing so (including pharmaceutical industry).• A sense of duty as citizens to donate excess surgical tissue for research to help future patients.• Exploration of different attitudes towards on the one hand people being favourably disposed to donating their own excess surgical tissue and on the other hand being anxious about excess tissue from a deceased relative being used³⁶.
Provide clear definitions
<ul style="list-style-type: none">• What is a biobank?• What is an ethics committee?• What is 'excess' surgical tissue?• What are the different types of consent?• What is meant by anonymous, de-identified, linked etc.?
Provide transparent explanations
<ul style="list-style-type: none">• Research is largely motivated by altruism.• Doctors at the forefront of their disciplines see research as being important.• Blood samples and tissue samples are often stored as part of a person's medical record and for that person's future care and treatment.• The benefits of being able to link tissue samples to medical records.• What is retained and what is not retained after post-mortem.• The role of the pathologist – what they do in various settings and why their work is important.• The link between biobanking and organ donation (the majority of people would be willing to donate their organs after death for transplantation purposes³⁶).• The safeguards that have been put in place since the Dunne Inquiry into Organ Retention.• Genetic research and the distinction between adult stem cells and embryonic stem cells.• The link between family risk assessment and genetic testing.

Table 10.1 continued

Approaches
Potential education and awareness initiatives
<ul style="list-style-type: none">• Public and patient education through information campaigns.• Provide information to patients and families during hospital stays.• Patient organisations should be represented in the Biobank's governance.• Annual presentation of report to the Dáil Health Committee.• Research organisations must work together to address the deficit of knowledge among the public on who conducts research and who decides what gets researched in Ireland.• Routine procedures e.g. blood donation provide an opportunity for education. Build on the fact that many people engage with the health service for blood tests and tissue tests as inpatients.• Targeted and sustained public information campaigns.• Regular survey to gauge public opinion and, more importantly, to gauge a shift in public opinion.• Evaluation of the effectiveness of these campaigns.• Access to a well-resourced communications function - use media opportunities to generate informed debate.• Issues such as attitude to donation should be teased out through media opportunities e.g. discussion programmes, TV and radio.• People will naturally recall the most recent controversial issue. It is important to point out what we have learned from previous organ-related public inquiries.
Website and information leaflets
<p>Any information provided in a leaflet or via the web must be in plain English.</p> <ul style="list-style-type: none">• Develop a website with comprehensive definitions and information.• Tailor all information to suit all population groups.• Distribute information leaflets which deal with biobanking and related issues in a sensible way.• Explain and feature the work of pathologists, other professionals involved in biobanking and the research projects being carried out in information literature and on the website.

10.4 Recommendations

- A website which provides comprehensive definitions and information tailored to all population groups is required.
- Comprehensive information must be provided to patients and families in a hospital setting.
- Patient organisations should be represented in the Biobank's governance.
- An annual report should be presented to the Dáil Health Committee.
- The Biobank requires a well-resourced communications function in order to create opportunities for public debate as well as media (TV and radio) discussions.
- Public information campaigns to highlight the important roles of the public, researchers, funders etc. are essential. Evaluation of the effectiveness of these campaigns and surveys to gauge public opinion should be carried out regularly.
- Communication of research to the public must be facilitated.
- The importance of the pharmaceutical industry's role in furthering the development of new drugs must be communicated.
- The preparation of guidelines for consent and the collection of tissue should involve patients/public.

11.0 Conclusion

The Expert Group concludes that the establishment of a National Cancer Biobank is not only desirable but feasible and essential for the future of cancer research and patient care in Ireland. With the roll-out of the National Cancer Control Strategy, the opportunity now exists to implement the best possible model for a National Cancer Biobank. The long-term value of this initiative cannot be overemphasised. The development of the biobank has the potential to make an invaluable contribution to patient care and research excellence, with additional benefits accruing to education, training and the national economy for many years to come. The question should no longer be whether a biobank should be established, but how soon this can be done. A planning phase will be necessary in order to provide detailed costings, and in order to agree policies for dealing with ethical, legal and other considerations. Implementation of the project should follow swiftly after that. A high-level implementation strategy is set out in Appendix D. It is recommended that action is taken now so to ensure the delivery of future benefits to the population of Ireland.

References

1. National Cancer Registry of Ireland at <http://www.ncri.ie/ncri/index.shtml>
2. National Cancer Registry (2006) *Trends in Irish cancer incidence 1994–2002 with projections to 2020*. Ireland: National Cancer Registry. http://www.ncri.ie/pubs/pubfiles/proj_2020.pdf
3. National Cancer Forum (2006) *A Strategy for Cancer Control in Ireland*. Dublin: Department of Health and Children.
4. Daly H, Collins C (2007) Detection of cancer: general practitioners needs' assessment. *Irish Med J*, 100: 624–626.
5. Gaffney EF, Flanagan C (2005) The cancer biobank network: essential infrastructure for basic and clinical translational research in Ireland. *Cell Preserv Technol*, 3: 126–127.
6. The Advisory Council for Science, Technology and Innovation (2006) *Towards better health: achieving a step change in health research in Ireland*. Dublin: Forfás.
7. National Dialogue on Cancer (NDC) Research Team Forum, March 2002.
8. Dr Anna Barker, Deputy Director NCI, Biobank Summit II, New York, November 2004.
9. Bonavida B (2007) Preface: antibody therapies for cancer. *Oncogene*, 26: 3592–3593.
10. Dublin Molecular Medicine Centre at <http://www.dmmc.ie>
11. HSE Managed Cancer Control Networks and Centres Working Group (2007) *National Cancer Control Strategy: Establishment of Managed Cancer Control Networks and Designation of Eight Cancer Centres*. Retrieved 27 February 2008 from <http://www.hse.ie/text/en/NewsEvents/News/NationalCancerControlStrategy/FiletoUpload,8420,en.pdf>
12. Majumdar SR, Roe MT, Peterson ED, Chen AY, Gibler WB, Armstrong PW (2008) Better outcomes for patients treated at hospitals that participate in clinical trials. *Arch Intern Med*, 168(6):657–62.
13. Nason, E., Janta, B., Hastings, G., Hanney, S., O'Driscoll, M., Wooding, S. (2008) *Making an Impact – The Economic and Social Benefits of HRB-Funded Research*. Dublin: Health Research Board.
14. Biobanking and Biomolecular Resources Research Infrastructure <http://www.biobanks.eu/>

15. Eiseman E, Bloom G, Brower J, Clancy N and Olmsted SS (2003) *Case studies of existing human tissue repositories: "Best Practices" for a biospecimen resource for the genomic and proteomic era*. California: RAND.
16. Hainaut P, Vozar B, Rinaldi S, Riboli E and Caboux E (2008) The EPIC biobank (European Prospective Investigation into Cancer and nutrition). In Vineis P, Garte S and Wild C (eds) *Methods in Molecular Biology Book Series: Methods in Biobanking*. The Human Press Inc. (in press)
17. onCORE UK at <http://www.oncoreuk.org/>
18. The Spanish National Tumour Bank Network (SNTBN) at <http://www.cnio.es/ing/grupos/plantillas/presentacion.asp?grupo=50004308>
19. Wales Cancer Bank at <http://www.walescancerbank.com/>
20. Friede A, Grossman R, Hunt R, Li RM, and Stern S, (eds) (2003) *National Biospecimen Network Blueprint*. Durham NC: Constella Group, Inc.
21. Prostate Cancer Research Consortium (<https://pcrc.tchpc.tcd.ie/pcrc/home>)
22. *OECD Draft Guidelines for Human Biobanks and Genetic Research Databases* available at: <http://www.oecd.org/dataoecd/47/28/40405918.pdf>
23. P Geary, Marble Arch Group, personal communication.
24. Dr Alison Parry Jones, Manager, Wales Cancer Bank, personal communication.
25. Dr Peter Watson, Director, TTR, BC Cancer Agency, personal communication.
26. NCI, NIH and DHSS (2007) *National Cancer Institute Best Practices for Biospecimen Resources*. US: National Cancer Institute.
27. International Society for Biological and Environmental Repositories (2008) 2008 Best Practices for Repositories: Collection, Storage, Retrieval and Distribution of Biological Materials for Research. *Cell Preserv Technol*, 6: 3-58.
28. Statutory Instrument SI No 158 of 2006, European Communities (Quality and Safety of Human Tissues and Cells) Regulations 2006 available at: http://www.dohc.ie/working_groups/tissues_cells/
29. Safety, Health and Welfare at Work Act, 1989. Retrieved 27 February 2008 from <http://acts.oireachtas.ie/zza7y1989.1.html>
30. Organisation for Economic Co-operation and Development (2007) *OECD Best Practice Guidelines for Biological Resource Centres*. France: OECD.
31. The Irish Council for Bioethics (2005) *Human Biological Material: Recommendations for Collection, Use and Storage in Research*. Dublin: Irish Council for Bioethics.

32. From a presentation by Dr Deirdre Madden (UCC) to the Expert Group on the 29 November 2007, HRB Offices.
33. Moore vs Regents of the University of California, 793 P.2d 479, 271 Cal. Rptr. 146 (1990).
34. Recommendations Rec (2006) 4 of the Committee of Ministers to member states on research on biological materials of human origin. Retrieved 27 February 2008 from http://www.coe.int/t/e/legal_affairs/legal_co-operation/bioethics/texts_and_documents/Rec_2006_4.pdf
35. The Office for Human Research Protections (OHRP), Department of Health and Human Services (HHS) (2004) Guidance on Research Involving Coded Private Information or Biological Specimens Retrieved 27 February 2008 from <http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.htm>
36. Cousins G, McGee H, Ring L, Conroy R, Kay E, Croke D and Tomkin D (2005) *"Public Perceptions of Biomedical Research" A survey of the general population in Ireland*. Ireland: Health Research Board.
37. Hoeyer K, Olofsson BO, Mjörndal T, Lynöe N (2004) Informed consent and biobanks: a population-based study of attitudes towards tissue donation for genetic research. *Scand J Public Health*. 32(3): 224-9.
38. Circa Group Europe (2007) Enterprise Ireland Panel on Clinical Support.
39. van Veen EB, Riegman PH, Dinjens WN, Lam KH, Oomen MH, Spatz A, Mager R, Ratcliffe C, Knox K, Kerr D, van Damme B, van de Vijver M, van Boven H, Morente MM, Alonso S, Kerjaschki D, Pammer J, Lopez-Guerrero JA, Llombart Bosch A, Carbone A, Gloghini A, Teodorovic I, Isabelle M, Passiukov A, Lejeune S, Therasse P, Oosterhuis JW (2007) TuBaFrost 3: regulatory and ethical issues on the exchange of residual tissue for research. *Eur J Cancer*, 42(17): 2914-23.
40. The Public Population Project in Genomics (P3G) at <http://www.p3gconsortium.org/>
41. International Society for Biological and Environmental Repositories (ISBER) at <http://www.isber.org>
42. All-Ireland Cooperative Oncology Research Group (A-ICORG) at <http://www.icorg.ie/>
43. Ireland-Northern Ireland-NCI Cancer Consortium at <http://www.allirelandnci.org/index.shtml>

Appendix A

Assigning responsibilities within governance structure

The table outlines many of the responsibilities which must be assigned to different groups/individuals, and the potential allocation of those responsibilities within the governance structure of the Biobank (as described in Chapter 4).

Table A1 Assigning responsibilities within governance structure

Responsibility	Director and Strategic Advisory Group	Central management structure	Hospital management and medical staff	Principal investigators
Strategy, planning, budget				
Plan Biobank infrastructure	X			
Estimate annual costs of acquisition, storage and dedicated staff		X		
Approve budgets	X			
Choose and administer bioinformatics and data management platforms		X	X	X
Approve data management system	X			
Determine criteria for sample access	X			
Approve study design and feasibility	X	X		
Approve applications for access to samples	X	X		
Develop best practice (BP) sample acquisition and storage protocols		X	X	
Develop BP sample annotation system		X	X	
Develop disaster recovery plans		X	X	
Develop transport logistics policy		X		
Create sample shipping and material transfer agreements		X	X	
Day-to-day management				
Conduct QC reviews		X	X	
Provide education and staff training		X		
Manage workflow in pathology laboratories			X	
Ensure that BP is used in pathology laboratories		X	X	
Supervise sample acquisition and storage			X	

Table A1 continued

Responsibility	Director and Strategic Advisory Group	Central management structure	Hospital management and medical staff	Principal investigators
Manage 24-hour monitoring system		X	X	
Manage sample shipping and logistics		X	X	
Apply for access to samples				X
Return unused samples to Biobank				X
Legal requirements/ethical considerations				
Advise on current ethical and legal issues	X	X		
Decide on legal and ethical issues	X			
Enforce data protection legislation	X	X	X	X
Code protected data			X	
Ensure compliance with all legislation and data protection regulations	X	X	X	X
Develop/tailor patient consent forms	X	X	X	X
Inform and advise patients on consent			X	X
Ensure staff safety procedures are implemented		X	X	
Inform principal investigators of legislation and guidelines relating to biomaterials		X		
Seek ethical approval for research				X
Communications				
Promote the National Cancer Biobank and develop and maintain links with other biobanks, both nationally and internationally	X	X	X	X
Create a communications strategy		X		
Give feedback to hospitals and central management	X			X
Put out calls for prospective studies	X	X		
Request and monitor feedback from principal investigators		X		
Develop feedback questionnaire for patients		X	X	

Appendix B

National Cancer Biobank Meeting, 10–11 December 2007

1. National Cancer Biobank – Mini-symposium

10 December 2007

Durkan Lecture Theatre, Trinity Centre for Health Sciences, St James's Hospital, Dublin

Presentations:

Professor Donal Hollywood, Academic Unit of Clinical and Molecular Oncology,
Trinity College Dublin

Welcome

Dr Carolyn Compton, Office of Biorepositories and Biospecimen Research,
National Cancer Institute

Evidence-based Standards for Biobanks: The Foundation of Personalized Medicine

Professor Eoin Gaffney, St James's Hospital and Trinity College, Dublin

A Cancer Biobank Network for the Island of Ireland

Professor William Watson, Prostate Cancer Biobank and University College Dublin

Prostate Cancer Research Consortium: Bioresource Overview

Professor Kurt Zatloukal, Institute of Pathology, Medical University of Graz, Austria

European Biobanking and Biomolecular Resources Research Infrastructure (BBMRI)

Daniel Naeh, Wales Cancer Bank

Biobanking Informatics: the Wales Cancer Bank – a case study

2. National Cancer Biobank – Workshops

11 December 2007

Health Research Board, Knockmaun House, 42-47 Lower Mount Street, Dublin 2

Participants:

Models of delivery and governance

Eoin Gaffney* (Chair), St James's Hospital and Trinity College Dublin

Joe Harford*, National Cancer Institute

William Watson, University College Dublin and Prostate Cancer Biobank

Kurt Zatloukal, Institute of Pathology, Medical University of Graz, Austria

Peter Doran, Clinical Research Centres, Mater and St Vincent's hospitals
Ciara Heeney, Beaumont Hospital

Operations and costings

John McCormack* (Chair), Irish Cancer Society
Brian Moulton*, ICORG
Tony O'Grady, Beaumont Hospital
Alison Parry-Jones, Wales Cancer Bank
Nicola Miller, National University of Ireland, Galway
Peadar MacGabhann, Biostor Ireland

Ethical Issues

Elaine Kay* (Chair), Beaumont Hospital/RCSI
Carolyn Compton*, National Cancer Institute
Ailis Quinlan, state Clinical Indemnity Scheme
Margaret Cooney, ICRIN

ICT requirements

Anne Cody*, Health Research Board
Jackie James*, Queen's University Belfast
Jane Grimson (Chair), HIQA
Dougie Beaton, HSE
Peter Hamilton, Queen's University Belfast
Daniel Naeh, Wales Cancer Bank
Geoff Bradley, Prostate Cancer Biobank and Trinity College Dublin

*Member of the Expert Group

Workshops were facilitated and co-ordinated by Bernadette Herity (Chair of the Expert Group) and Catherine Gill (Secretary to the Group).

Appendix C

Consultation process

Background

Any expert group has to be limited in size if it is to be effective. While the 13 members of this Expert Group represent a range of stakeholders, it was not possible to include representation from all relevant professions and organisations; neither was there representation from all regions in Ireland. The Group clearly recognised these limitations and, because input and buy-in from all stakeholder groups is key to the success of any biobank, it was agreed that an extensive consultation process should be carried out prior to finalising the Group's report. The Group considered a targeted stakeholder consultation to be the most valuable; by adopting this approach, it was hoped to engage with the various communities who will play a role in either setting up or using the National Cancer Biobank.

Scope

In March 2008 the first draft of the Expert Group's report was emailed to more than 1,000 stakeholders throughout the island of Ireland. They included surgeons, oncologists, pathologists, nurses organisations, patient organisations, government agencies, researchers, hospital management, the HSE and NCCP, stakeholders in Northern Ireland, industry representatives and many others.

In addition to inviting written submissions, regional stakeholder meetings were held in Dublin, Cork and Galway in order to give people an opportunity to discuss their views with members of the Expert Group. Representatives from many of the aforementioned organisations attended these meetings. The format of the meetings included a brief presentation by the Expert Group covering the key recommendations contained in the first draft of their report; this was followed by extensive discussion of issues related to these recommendations. The majority of the time at these meetings was given over to discussion and debate.

Response

The response to the report was overwhelmingly positive. As well as several general expressions of support, the Expert Group received 18 detailed submissions from organisations including Enterprise Ireland, Our Lady's Children's Hospital, Crumlin; the Office of the Data Protection Commissioner; BBMRI; Irish Medicines Board; IDA; RCSI; CMO of Northern Ireland; Molecular Medicine Ireland; Biostor Ireland; patient

organisations including IPPOSI, as well as individuals in diverse disciplines such as surgery, biobanking, pathology, haematology, research and general practice.

The content of these submissions, together with extensive and valuable feedback from the regional meetings held in Dublin, Cork and Galway, is summarised below.

Summary of feedback

Model

It was agreed during the consultation process that the Expert Group's recommended model of decentralised collection and storage, with centralised informatics and management, was appropriate. However, it was noted that the national centre for paediatric oncology (currently Our Lady's Children's Hospital, Crumlin) should be included as the 'ninth cancer centre'. It was also suggested that an Irish example of biobanking – the Prostate Cancer Research Consortium Bio-resource – should be included among the examples of biobank models provided. In relation to decentralised storage, it was noted that QC measures, SOPs and regular checks would be required and, importantly, that the Biobank would need to have the capacity to recover samples for diagnostic purposes if necessary. Other suggestions included that the designated cancer centres might act as hubs for small private/non-designated centres located nearby, and that it may be desirable to have a central archive storage facility in which to deposit back-ups of some samples for disaster recovery purposes and to protect the collection. The centralised storage model was suggested in only one of the submissions received.

Governance

Structure

Clarification was sought around the issue of governance of the Biobank e.g. should it operate as part of the HSE? It was suggested that the criteria for biobank governance should be set out in the Expert Group's report and that the governance structure should be designed around these criteria. Within this structure, a data controller should be appointed to ensure compliance with data protection legislation. Representation on the Board* must be equitable and it must include the key stakeholders. The proposed governance structure would have to be peer reviewed. Organisations such as ICRIN

* In the first draft of the report, it was envisaged that the Biobank would have a board of directors. In the current proposals i.e. where the Biobank would sit within the NCCP, this suggestion has been removed. It is now recommended that the Biobank would have a director who would be informed by a strategic advisory group

could support this development of the Biobank. A number of suggestions relating to the proposed governance structure were put forward:

- The Board of Management should be wholly independent, and could operate in a similar manner to ICORG, with all stakeholders represented.
- Organisational structure must be independent. It can be associated with other organisations, but it must be separate.
- Independent governance – free-standing both administratively and scientifically.
- Potentially, it could be housed within ICRIN (as they are involved in co-ordinating CRFs).
- Model should be somewhat independent, but should be embedded within an existing structure such as the HSE.

Access and scientific review

Clarity on the role of the Board* in approving research study design and feasibility was requested and it was noted that procedures for determining user access would have to be defined. There was a concern that conflicts could arise around issues relating to the delivery/release of samples depending on who has the authority to approve access to Biobank samples. This is a particular issue in the Irish context given the size of the Irish research community. Requests for access to samples would have to be reviewed in a completely impartial manner. With a decentralised system, it is important to provide good access for all researchers and not just for those associated with the centre housing the samples. It is also important not to make the seeking of access to samples an excessively complex, bureaucratic process. The Biobank should have a clear policy on the expected lead times for securing project approval. The importance of independent peer review was highlighted, and clarity around the review process is needed.

Motivation for involvement in sample collection

It was suggested that motivating medical staff to participate in the sample collection process would be important. Providing resources for pathology departments is one option; this is the system used in the Wales Cancer Bank. One submission contained the suggestion that incentives for medical professionals who contribute to the National Cancer Biobank should be considered during the implementation phase to encourage participation and a quicker build-up of samples.

Standards/QA

Data collection

Data collection, including collection of follow-up information, must be co-ordinated between participating centres. A minimum clinical dataset must be defined. Researchers should feed information, including raw data and analysed data, back to the Biobank in order to avoid the duplication of experiments. This is particularly important in circumstances where the number of samples available is limited.

Access

An active user management policy should be implemented in order to ensure that physical access to the Biobank and access to the Biobank's internal IT system are on a need-to-use basis. A second security safeguard, such as a biometric identifier, should be used to ensure that no password sharing takes place.

Follow-up

Recommendations as to how patients will be followed up subsequently are required.

Guidelines

Consideration of the OECD best practice guidelines was recommended, as these guidelines address complementary issues which are particularly relevant for international co-operation.

ICT

Consideration of a federated architecture, which combines advantages of centralised and decentralised solutions, was suggested as a possible alternative.

Operations/cost

Sample collection

As many different types of samples as possible should be collected, as this will increase the value of the resource. Biofluids (serum, plasma, urine and other biological fluids) and DNA must have equal standing and must be treated with the same importance as tissue samples. The collection and storage of appropriate tissue samples should be overseen by a pathologist, and it should be co-ordinated through the pathology laboratories in close consultation with and in collaboration with surgeons and other relevant clinical teams. The procurement of samples from surgical patients should

be supervised by appropriately trained surgeons. There may be a need to carry out pilot studies/feasibility studies in order to ensure that the appropriate and practical standards are applied.

It was suggested that a ranking system be created e.g. obtain paraffin-embedded tissue in all cases, followed by, for example, RNA extraction, DNA extraction and finally, if sufficient material is available, samples for proteomic analysis. The methods by which samples are taken will differ depending on the disease and so disease-specific protocols must be established. The format of tissue types, number of samples etc. must be considered. While the Expert Group's report notes that frozen tissue is the gold standard, the importance of determining single nucleotide polymorphism (SNP) and proteomic profiles of host tissue, as well as tumour tissue should be noted. Such samples may be easier to obtain than tumour samples. There is also a need to be able to source samples (e.g. peripheral blood, bone marrow samples) which are being processed in haematology laboratories because these laboratories operate independently of histopathology laboratories, where most of the biobanking activity is likely to be focused.

In order to get maximum use out of each sample, the amount of sample material to be released to individual projects should be the precise amount required by the researcher and no more than that. The processing of samples has an important role to play in this regard. Extraction should be performed by the relevant laboratory in such a way that the unnecessary waste of valuable material is avoided.

Human resource requirements

The Biobank must be an integral part of clinical practice culture. The involvement of a research nurse is essential for the co-ordination of informed consent, the implementation of SOPs for sample collection, and the follow-up of patients through outpatients departments or through the patient's GP. While the pathologist is central to tissue collection, the research nurse is central to both the procurement of biofluids and DNA and the co-ordination of their appropriate processing and storage. Similarly, scientists may be central to the supervision of bio-materials collection, processing and storage. Within the Biobank, significant medical laboratory scientists' time and pathologists' time will be required. Samples such as blood or bone marrow from haematological cancers are not processed in pathology departments; this means that haematologists may have to take on the role of collecting such samples for biobanking purposes. Resources will be needed in order to support sample collection in haematology departments and to support co-ordination of biobanking activities between the different laboratories.

An approach to maximising the resources for the pathology laboratory was suggested. While funding might be provided for one post, elements of biobank duties might be incorporated into the job descriptions of a number laboratory staff in addition to other duties. This would ensure that a number of staff are trained in the relevant duties, and can cover for each other. Alternatively a designated person could take on this role, perhaps in association with a deputised back-up person. It was also suggested that consideration would have to be given to allocating resources to pathologists who are working in private hospitals and are involved in tissue collection for the Biobank. While such pathologists would be happy to store samples at a designated centre, funding would be needed to cover the pathologists' time, sample shipping costs and so on. The problem with HSE recruitment policy was noted on a number of occasions during the consultation process. For example, when independently funded staff go on maternity leave, often they are not replaced. As far as possible, provision should be made to protect biobank posts from erosion due to service demands.

A communications resource needs to be included in the list of staff required for the Biobank's central management office.

Costings

A number of contributors suggested that the draft report had understated the requirement for the adequate and appropriate funding of salary costs for support staff; it was also suggested that the overall costs of the Biobank may be understated.

An initial fund should be allocated for biobanking-related training and education of surgical/medical and other clinical staff. Concerns were expressed about the Biobank being run exclusively under the auspices of the HSE; Biobank budgets would have to be ringfenced and, more importantly, WTEs would have to be protected.

Funding options need to be explored further. For example, the HSE (via NCCP) or the DoHC (via HRB) could commission a biobank. Irrespective of which model is finally chosen, there should be a commissioning/tendering process for the Biobank based on competition and international peer review. The importance of the Biobank maintaining its scientific independence – even if it is funded by the HSE – was noted.

Ethical issues

Consent

The predominant view is that a generic and national consent process will be required. However the Data Protection Commissioner did suggest that it is possible to strike a balance between the provision of general, broad consent and the capture of layered

and future consent. It was also suggested that legal advice may be required, as the possible extent of future research use cannot currently be envisaged and may therefore prevent truly informed consent.

Distinctions are to be made in relation to the consent that is obtained from a patient to allow a surgical procedure to be carried out and the consent that is required in order to obtain a sample from a patient for research purposes. Different types of consent may be needed. For example, for samples that wouldn't normally be taken during surgery, explicit consent would have to be secured. Consent forms for surgery and for tissue procurement should be separate, with the latter providing a clear explanation of the Biobank's tissue harvesting and handling procedures and the potential use that is envisaged for the sample taken. It should state that patient consent or refusal will not influence their treatment.

It was suggested that apart from the practical difficulties that would arise, it might cause more harm than good to seek re-consent from patients for future studies that might use their samples. A move to providing a simpler approach than that used currently is supported by many patients. Education is key, and consent needs to be streamlined and standardised. Resources such as research nurses/designated nurses are needed on the ground. From the research nurse perspective, it was noted that patients like to have relevant information in advance of surgery in order to give them time to think about the related issues and talk them over with family.

Ethical review

In order for access to samples to be workable in the context of using a decentralised biobank model, as is proposed by the Expert Group, a single streamlined ethical review process must be put in place. This would ensure more straightforward access to samples with agreed common procedures for accessing such material.

Feedback

A mechanism must be in place to deal with issues including how relevant information such as risk of recurrence is fed back to the physician but not directly to the patient. Protocols around feedback will be study-specific and proposals relating to feedback should form part of the submission that accompanies requests for access to samples. Confirmation of research results from an accredited diagnostic laboratory, as well as peer review of the interpretation of the results, would also be needed before feedback can be given to the physician. Information might be fed back through the original peer review committee. Generic, non-individualised information on the results of a study might also be fed back. The issue of feedback of results to patients is not unique to biobanks; it also applies to clinical trials and other translational research studies.

Legislation

The absence of human tissue legislation in Ireland means that the legal framework within which biobanks currently operate remains unclear. It will be important to ensure that what is put in place now by way of governance and operation of the Biobank is robust enough to comply with future legislation and/or regulation. It was suggested that the Expert Group's report should highlight gaps in the current legislation and advocate a legal framework that would underpin biobanking best practice. Discussions on the absence of legislation governing the use of tissue from living donors for research should be undertaken in relation to the current DoHC proposal for human tissue legislation. The biobanking of children's tumour samples could be considered within the same framework.

Relationships and links

Industry

This report contains very little reference to links with the industrial sector. There was no industry representative on the Expert Group, and the report makes little reference to the importance of making provision for industry access to the Biobank collections other than to say that this issue will be important in the future. Industry should be involved in this initiative at many different levels – possibly including having a representative on the Board of Management, but at a minimum, being involved in consultations about the establishment of the collections.

The Biobank could be a very important resource by way of supporting the development of indigenous industry and attracting multinational companies to Ireland. It was suggested therefore that input should be sought from industry – both pharmaceutical companies and indigenous Irish companies which are involved in conducting clinical trials.

In contrast, it was also suggested that there is a need to create access limitations – particularly access by industry. The Biobank's *raison d'être* should be to support research; access by industry-based researchers should only be permitted if they team up with a non-industry research group. Patients who are considering donating samples may also have a problem with industry access. However, it was also noted that, in practice, industry must have access to the Biobank. In the past ten years there has been availability of great drugs, and in order for this to continue, companies will need to be able to carry out translational research. There should be no problem with industry access once it is regulated. Otherwise there may be a conflict between samples being sent to a biobank and being diverted for use in clinical trials.

Various submissions emphasised the need for partnership and clear-cut co-operation. It must be accepted that industry also needs access to samples for patient benefit. It is important to communicate to the public the important role that the pharmaceutical industry plays in medical research; communicating this positive message is important because, as one submission noted, the public has a dim view of this industry. Patients may object if they think the purpose of a biobank is merely to enable companies to make money. Industry access must be understood to be given on the basis that research results are made public. Information and results must be freely available – this should also be the case for academic research. Like the clinical trials registries, all data should be registered. Both negative and positive research results must be registered in order to prevent duplication of studies.

Clinical trials

There may be some conflict of interest in terms of access and some samples may not be eligible for biobanking due to other activities taking place within the pharmaceutical industry. Other procedures such as genomic testing will take priority over biobanking as they offer more immediate benefit to patients. Prioritisation should be considered with the interests of the patient in mind e.g. diagnosis first, participation in clinical trials second, and biobanking third.

Northern Ireland

The structural relationships that will exist with activities in Northern Ireland will need to be explored further in order to achieve the scale-up that will be facilitated as a result of all-island collaboration. The Expert Group's report needs to recognise the structural relationships that exist within both health services and ensure that the relevant institutions in Northern Ireland are kept informed. There will also be a need to develop the appropriate governance arrangements, giving due regard to security and ethical aspects. All stages of implementation should consider the widest range of potential users; sourcing advice and input from those stakeholders, and using language that will ensure dissemination of the various roles of the Biobank and the many benefits that will accrue from it.

Cancer biobanks

The Biobank will not dictate to existing biobanks. In time, users of smaller biobanks will realise the advantages of being involved with a large internationally recognised biobank. If the National Cancer Biobank does its job properly there will be no need for additional cancer biobanks.

During the implementation phase SOPs and other operational decisions should be informed by existing biobanks e.g. the Prostate Cancer Research Consortium bio-resource and NUIG Department of Surgery Cancer Biobank, and input should be sought from these biobanks. A clear quality assurance scheme would need to be developed in order to ensure that samples stored retrospectively meet current requirements. If biobank samples are well annotated with clinical data, participation in the Biobank will be attractive both to those accessing samples and those wishing to deposit their samples in a reputable facility.

Trans-disease biobanking

The door should be left open to enable the creation of future links with other non-cancer biobanks e.g. BBMRI is looking at biobanking across disease. It would be important for the National Cancer Biobank to keep pace with developments in BBMRI and ensure that the proposed biobank complies with international best practice in Europe so that links with European biobanks can be facilitated.

It was suggested that the inclusion of non-malignant tissues from chronic diseases with undoubted genetic bases should be considered. Similarly, it was suggested that a trans-disease model be developed. While the model should be such that it can be adopted for other disease areas in the future, it was clarified during the consultation process that the development of proposals for a trans-disease model was outside the remit of the Expert Group.

Other

It was suggested that the National Cancer Biobank should be linked with the National Cancer Registry. It may be possible to leverage data such as stage/age and survival – data that would not be available from the pathology laboratory.

In future-proofing the Biobank, consideration should also be given to sample types to be stored there in order to cater for advances in new technologies.

Patient education and awareness

The definition of ‘excess’ surgical tissue will require detailed discussion, explanation, definition and agreement with patients and the public in order to avoid future misunderstandings. It will be necessary to ensure that samples, in excess of what is normally required for diagnosis, are not taken for the purpose of biobanking without securing specific consent from the patient.

A large-scale public information programme on biobanking will be required. With the Dunne Report fresh in people's minds, questions about biobanking must be answered in plain language. Security systems must be so that patients are assured that in no way can their information be accessible to any outside source.

This role is incredibly important and needs to be carried out by some organisation that the public trusts. It should not involve just one organisation such as the Irish Cancer Society; it must extend wider than that in order to be effective. It will also be important to demonstrate that industry is a necessary partner. The aim is to bring public awareness to the stage where biobanking is considered normal and for the public good. Simple information will be required upfront in order to achieve this aim. More detailed information will be required in the hospital setting. However, it is necessary to separate treatment from biobanking, so as not to overburden patients; it should also be emphasised that when a patient is deciding whether or not to agree to donate a sample to the National Cancer Biobank that this will in no way influence their treatment. The Biobank should disseminate a simple, broad-based message to familiarise the general population with the concept of clinical research and biobanking. As a result, when people find themselves faced with the question of whether or not to donate to a biobank, they have already had the opportunity to consider the issue. Communications programmes should contain a trans-disease message. Groups such as IPPOSI could play an important role in communicating this message. They could also play an important role in other advocacy functions, and they should be involved in the implementation phase of the Biobank.

Appendix D

Implementation strategy

Introduction

The first step going forward will be the presentation of the Expert Group's report to the Minister for Health and Children, and the acceptance of the report. As soon as possible, the Minister must appoint a group who will prepare an implementation plan for the Biobank. Further development of the recommendations of the Expert Group will be required. Some of the key areas to be addressed during the planning phase include:

- Footprint of decentralisation.
- Governance structure.
- Details of samples to be collected – types, processing, QA.
- Legal, ethical, and consent issues.
- Staffing – ensuring that provision is made for a sufficient number of posts.
- Ensure appropriate and secure finance.

Who should be involved at the implementation stage?

- HSE/NCCP representatives.
- Pathologists from the proposed centres.
- Surgeons from the proposed centres.
- Oncologists, haematologists.
- Hospital management.
- Local representatives from each centre who can co-ordinate consultation not only within that centre but also in local non-designated hospitals, both private and public.
- Researchers.
- Representatives of existing biobanks e.g. PCRC Bio-resource, NUIG Department of Surgery Cancer Biobank, Our Lady's Children's Hospital, Crumlin.
- Research nurses.
- CRF representation/ICRIN.
- Legal, ethical experts.

- IT experts.
- Financial advisor.
- Enterprise agency (Enterprise Ireland and/or IDA).
- Department of Health and Children.
- Research funders' representative.
- Representatives from DHSSPSNI.
- International experts.
- Communications expert
(from any of the groups involved, or from an agency such as ICS).
- IPPOSI and/or other patient representatives.

NB: There may be overlap amongst some of the above e.g. some surgeons/pathologists may also be researchers, researchers involved in existing biobanks etc.

In addition, consultation with a number of additional groups is recommended; these would include MMI, the Health Research Group, patient organisations, university representation.

How to proceed?

A number of areas must be addressed in detail. Representatives of all stakeholders who have expertise in various areas related to biobanking should be invited to join the implementation group (as outlined above). It is recommended that a number of subgroups be formed. Each would have the task of addressing the individual work packages outlined below. It is important that the recommendations of the Expert Group be used as a starting point for the development of an implementation plan, as these recommendations have been derived from extensive discussions and consultations with stakeholders nationally.

The chair of each subgroup will report back to a main committee responsible for overall co-ordination of the process. Some groups will need to cooperate from the outset on particular areas e.g. decisions in relation to the biobank model will require input from the group who are costing the Biobank. The findings of the working groups should be assembled into a single coherent proposal, to be peer-reviewed by a panel of international experts. The review panel should remain in place and should periodically review the Biobank against a set of performance criteria. The implementation group may recommend that roll-out of the Biobank should be via a phased approach. As a first step, a complete implementation and costing of the fully operational biobank (i.e. nine

collection centres) should be outlined, which could then be rolled out on a phased basis.

Work packages and working groups

1. Model and governance

- One of the first decisions to be made relates to the organisational structure of the Biobank as this will influence all other decisions in relation to the model of delivery and the Biobank governance. For example, will it be part of the HSE and specifically the NCCP? Who will have ultimate responsibility for the Biobank?
- A decision must be made in relation to the storage decentralisation footprint. This will require close consultation with the group who are given the task of costing the Biobank. Areas to be explored as follows:
 - Possibility of making use of existing facilities at collection sites.
 - Possibility of aligning the capital requirements with other capital programmes under the NCCP in order to maximise value for money.
 - Detailed analysis of the pros and cons of partially decentralised storage versus fully decentralised storage.
 - Decision as to the most suitable method of collecting and distributing requested samples.
- Policies and procedures relating to the inclusion of samples from private and non-designated hospitals should be outlined.
- A decision must be made as to the necessity for some centralised back-up storage and whether some sample types should be stored at only one of the decentralised storage sites. This decision should be made in consultation with work package 3.
- Detailed plan of the governance structure should be made and peer reviewed. Issues to cover:
 - Criteria for selecting and appointing the Strategic Advisory Group.
 - Assignment of responsibilities, including liabilities in relation to legal issues and data protection legislation.
 - Development of strategy for ethical review and approval of sample requests, including selection criteria and terms of reference for the Scientific Review Board.
 - Clearly define access rules, authorship policy.
- Develop plan for staff training in consultation with work package 3.

Minimum membership of this group: HSE/NCCP representatives, clinicians and hospital management from the proposed centres, representative from DHSSPSNI, legal/ethical experts, financial expert, and external advisor.

2. ICT strategy

- Appoint an ICT manager to lead on the 'buy or build' decision.
- Consult with other biobanks and similar ICT initiatives to identify best practice.
- Consult with Data Protection Commissioner regarding development of ICT system.
- Consult with users regarding design of ICT system; draw up extensive user requirements.

Minimum membership of this group: ICT experts including those already involved in biobanking, Data Protection Commissioner representation or individual to co-ordinate with the Data Protection Commissioner's office, user groups including researchers, research nurses and pathology laboratory staff.

3. Sample and data collection, standards and QA

- Define services to be provided.
- Define what will be collected, and prioritise sample types/formats.
- Plan pilot studies for sample collection methods.
- Adapt SOPs for sample collection, processing, etc. from established best practice documents.
- Determine minimum dataset.
- Establish procedure for patient follow-up.
- Develop training plan for staff collecting samples.
- Agree protocols for quality assurance and quality control.
- Agree design for sample storage and back-up facilities in consultation with work packages 1 and 6.
- Define criteria for inclusion of established biobanks in consultation with work package 5.

Minimum membership on this group: Pathologists, researchers, surgeons, research nurses, and representatives from existing biobanks.

4. Ethical, legal and societal issues (ELSI)

- Establish consent procedures in consultation with the Irish Bioethics Council, legal experts, Data Protection Commissioner and patients.
- Develop consent forms in consultation with patients.
- Actively seek clarification of legal issues such as consent and ethical approval.
- Identify procedures for de-identification of samples and patient information.
- Develop SOPs for the exchange of samples and data in order to comply with the legislation and ethical standards of EU member states.
- Aim for harmonisation with ethical and legal frameworks within Europe.
- Develop a detailed communications strategy.
- Plan public information campaign.
- Initiate survey of public opinion.

Minimum membership on this group: Legal and ethical experts, IPPOSI, patient representatives, Department of Health and Children, communications expert, surgeons and research nurses.

5. Relationships and links

- Define role/access to industry.
- Communicate with conductors of clinical trials regarding any potential conflicts.
- Identify how to make best use of facilities/infrastructures already in place e.g. CRFs.
- Liaise with relevant organisations such as the National Cancer Registry with regard to establishing links.
- Aim for harmonisation of rules (quality, IT, instruments, samples, ethics etc.) in line with international initiatives.
- Liaise with DHSSPSNI, NCI, BBMRI.

Minimum membership on this group: Representation from DHSSPSNI, CRFs/ICRIN, HSE/NCCP, IPPOSI, ICRG, NCI, academic researchers, industry, and Irish representatives on BBMRI (from HRB and/or MMI).

6. Implementation: costing and financing

- Detailed assessment of staffing requirements.
- Identify training requirements.
- Identify infrastructural requirements.
- Detailed financial model.
- Accurately determine costs of collecting, processing, storing and distributing samples.
- Develop a financial plan which considers long-term sustainability of the Biobank when it is operating at capacity (i.e. all nine collection centres).
- Clear outline of government commitment required.
- Policies for budget and financial management, and HR requirement for finance function.
- Policies around receipt of funding from non-government sources e.g. philanthropic bodies.
- Identify potential for cost-sharing and cost-recovery.

Minimum membership on this group: Finance, DoHC, HSE/NCCP and input from biobank staff (e.g. research nurses, pathologists).

