Future Investment in Clinical Research
## Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>3</td>
</tr>
<tr>
<td>Steering Committee Members</td>
<td>4</td>
</tr>
<tr>
<td>Vision</td>
<td>7</td>
</tr>
<tr>
<td>Executive Summary</td>
<td>8</td>
</tr>
<tr>
<td>Key Recommendations</td>
<td>10</td>
</tr>
<tr>
<td><strong>Chapter 1</strong> Economic and Health Impacts of Clinical Research in Ireland</td>
<td>11</td>
</tr>
<tr>
<td>1.1 Economic Impacts</td>
<td>12</td>
</tr>
<tr>
<td>1.2 Health Impacts</td>
<td>14</td>
</tr>
<tr>
<td><strong>Chapter 2</strong> Clinical Research Strategy and Policy</td>
<td>18</td>
</tr>
<tr>
<td>2.1 Clinical Research Strategy and Policy</td>
<td>19</td>
</tr>
<tr>
<td>2.2 Strategic Leadership and Coordination</td>
<td>22</td>
</tr>
<tr>
<td>2.3 Legal Mandate for Health Research</td>
<td>23</td>
</tr>
<tr>
<td>2.4 Governance</td>
<td>23</td>
</tr>
<tr>
<td>2.5 Patient Engagement</td>
<td>24</td>
</tr>
<tr>
<td>2.6 Regulation and Legislation</td>
<td>25</td>
</tr>
<tr>
<td>2.7 Insurance</td>
<td>26</td>
</tr>
<tr>
<td>2.8 Information and Communications Technology</td>
<td>27</td>
</tr>
<tr>
<td>2.9 Quality Management Systems</td>
<td>27</td>
</tr>
<tr>
<td>2.10 Outcomes based Clinical Research</td>
<td>27</td>
</tr>
<tr>
<td>2.11 Investment in Clinical Research</td>
<td>28</td>
</tr>
<tr>
<td>A Patient’s Experience of an Irish Clinical Trial</td>
<td>29</td>
</tr>
<tr>
<td><strong>Chapter 3</strong> Coordination of Clinical Research in Ireland</td>
<td>30</td>
</tr>
<tr>
<td>3.1 National Coordination</td>
<td>32</td>
</tr>
<tr>
<td>3.1.1 Clinical Research Development Ireland</td>
<td></td>
</tr>
<tr>
<td>3.1.2 HRB Clinical Research Coordination Ireland</td>
<td></td>
</tr>
<tr>
<td>3.1.3 HRB Trials Methodology Research Network</td>
<td></td>
</tr>
<tr>
<td>3.1.4 Cancer Trials Ireland</td>
<td></td>
</tr>
<tr>
<td>3.1.5 Irish Platform for Patient Organisations, Science and Industry</td>
<td></td>
</tr>
<tr>
<td>3.1.6 Medical Research Charities Group</td>
<td></td>
</tr>
<tr>
<td>3.2 European and International Coordination</td>
<td>38</td>
</tr>
<tr>
<td>Ireland’s Involvement in International, Multicentre Stroke Research</td>
<td>40</td>
</tr>
</tbody>
</table>
Contents

Chapter 4  
Ireland’s Clinical Research Infrastructure and Resources  41

4.1  Clinical Research in the Health System - Hospitals and the Community  42
    4.1.1  Paediatric Clinical Research

4.2  Academic Clinical Research  45
    4.2.1  Universities - Clinical Research Facilities and Centres
    4.2.2  Translational Research Laboratories
    4.2.3  Clinical Research Networks

4.3  People involved in Clinical Research  49
    4.3.1  Patients and Public
    4.3.2  Clinical Research Staff
    4.3.3  Protected Time for Clinical Research
    4.3.4  Clinical Research Nurses

4.4  Commercial Clinical Research  52
    4.4.1  Pharmaceutical industry
    4.4.2  MedTech Industry
    4.4.3  Bodies
    4.4.4  Contract Research Organisations

4.5  Training and Education  58

4.6  Information Management and Technology Infrastructure  61
    4.6.1  Challenges of IMT Infrastructure for Clinical Research
    4.6.2  Virtual Trials

4.7  Regulatory and Ethics Infrastructure  61

4.8  Biobanking  62

4.9  Patient Registries  64

4.10  Bioresource Facilities  66

4.11  Funding and Development Agencies  66

Focus on Paediatric Clinical Research in Ireland  67

Chapter 5  
Future Investment in Clinical Research  68

Conclusion  72
Appendices  74
Glossary  88
Introduction

Clinical research generates the knowledge essential for understanding human disease, preventing and treating illness, promoting health and improving care.

It is universally accepted that a well-resourced and functioning clinical research system is an essential part of any national infrastructure which benefits all stakeholders including patients, the healthcare delivery system, the life sciences industry and academia. It facilitates discovery and adoption of essential advances in health care provision for the benefit of the population and contributes to economic growth and prosperity.

We are fortunate in Ireland to have a very significant and flourishing life sciences sector and a well-developed healthcare delivery system. However, this has not yet been reflected in the development of our national clinical research capacity and capability. With due regard to the valuable efforts and funding investments made over recent years, significant opportunity exists to further enhance clinical research here.

Accepting the challenges posed by the present reality, a group of interested parties from across many of the stakeholders, including patient groups, clinical research facilities and academia, funding and enterprise agencies, industry representative bodies, healthcare delivery and Clinical Research Development Ireland (CRDI), convened as a Steering Committee to strategically examine and define the optimal future clinical research infrastructure, support, capacity and capability for our population and economy.

This report is the output from that Steering Committee. The report provides a summary of the current landscape and the opportunities that exist for the strategic development of clinical research in Ireland. The report presents the evidence to support the needs identified and provides high level recommendations for the future.

I thank all those who have contributed to the development of this report. I commend the report to you the reader and look forward to further engagement with stakeholders and policy makers in actioning the various recommendations to the benefit of our people and economy.

Prof Pat O’Mahony
Chair
Future Investment in Clinical Research Steering Committee
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<table>
<thead>
<tr>
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<th>Job Title</th>
<th>Organisation</th>
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<tbody>
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## Steering Committee Members

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<th>Organisation</th>
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Vision

An integrated Irish clinical research system that drives excellence and innovation to further advance patient health and economic prosperity

Mission

1. To develop an integrated clinical research system that meets best international standards
2. To integrate clinical research within the national Irish Health Service for the benefit of Irish patients
3. To support innovation in the Irish Life Sciences Sector
4. To attract, develop and retain a skilled workforce
5. To support the development of clinical research so that it becomes a key component of the knowledge economy, and
6. To support economic development and prosperity.
Executive Summary

Health care delivery is an essential part of any national infrastructure and the quality of health care available has a direct impact on health and wellbeing, at the individual and population level.

Clinical research is a fundamental part of the overall health care system. It is clearly demonstrated internationally that outcomes for patients are always better in countries where clinical research is better developed, and a more active clinical research system also provides substantial economic benefits to the national economy.

Ireland's life sciences sector has grown rapidly since the 1960s to a point now where it has global significance. A large number of pharmaceutical, biotechnology, medical devices and diagnostics companies, both indigenous start-ups and major multinationals, have enabled this remarkable growth, reflected in substantial employment, export earnings and tax receipts to the Irish Exchequer. However, this stellar performance in the manufacturing sphere has not been matched with growth in our clinical research infrastructure or performance. In fact, many life sciences companies operating in Ireland conduct all of their clinical research activity overseas because Ireland's clinical research system and infrastructure cannot meet their needs. This gap represents an opportunity to develop a fit-for-purpose clinical research system for Ireland. Delivering on this opportunity would align with the Government's Future Jobs Initiative whilst underpinning further potential for networked research and collaboration between industry and academia that could leverage international research funding opportunities.

A large group of experts, representative of all stakeholders involved including patients, health care delivery, funding agencies, academia and industry, convened in an initiative titled “Future Resourcing of Clinical Research”, since renamed as “Future Investment in Clinical Research” to share insights and expert knowledge, assemble the facts of the matter, and to strategically examine the optimal future clinical research infrastructure, support, capacity and capability for Ireland. In July 2018, the Steering Committee agreed a Mandate and Terms of Reference for their work and this is attached at Appendix I. This Mandate has been delivered on by the Steering Committee members. In addition to expert contributions from the Steering Committee members, an additional range of interested parties contributed to the work. These colleagues are listed at Appendix II. The process involved written submissions, development of a SWOT analysis by all contributors, discussion and analysis of all the inputs, and distillation to a vision and mission for clinical research in Ireland and recommendations for how to achieve the desired outcome.
The findings from the process are presented in a series of recommendations across five chapters:

Chapter 1: Economic and health impacts of clinical research in Ireland
Chapter 2: Clinical research strategy and policy
Chapter 3: Coordination of clinical research in Ireland
Chapter 4: Ireland’s clinical research infrastructure and resources
Chapter 5: Future investment in clinical research

Expanding clinical research in Ireland by a factor of four with the delivery of an additional 3,000 direct and indirect jobs is proposed. This level of growth would generate gross value added of some €200 to €300 million per annum. In addition, expanded clinical research activity would generate a wide range of additional economic, health and academic value and benefits.

The report sets out what is now needed to significantly scale up and place clinical research at a new level so that it becomes a core feature of Ireland’s health care delivery system and knowledge economy. The report recommends the creation of a new national strategy lead for clinical research at central Government level and a national coordinating entity which would have oversight of all clinical research and would provide a vehicle for coordination of the additional investment proposed. The additional investment called for is foreseen as being delivered through an Exchequer and industry matched co-funding model.

The report provides a range of detailed recommendations for the infrastructure and resources required including investment in core infrastructures, both facilities and staff; career structure for research staff; protected time for investigators; Information and Communications Technology systems; and coordinated approaches to biobanking and patient registries.

Finally, the report quantifies the investment required to support the enhanced clinical research delivery foreseen and presents a proposed phasing for the investment.
Key Recommendations

A wide range of recommendations are made throughout this report.

These appear throughout the chapters and adjacent to the chapter content on particular issues. The full list is referenced in Appendix III.

The key recommendations are listed below:

1. Appointment of a senior strategy lead at cross-departmental level.

2. Provision of funding for and establishment of a national coordinating entity and an office at HSE/Service Delivery Level to coordinate all aspects of clinical research and the application of the additional Exchequer and Industry co-funding proposed in this report.

3. Additional investment in clinical research infrastructure and staffing, co-funded by Exchequer and industry, while maintaining all existing funding.

4. Enhancing patient involvement and patient centeredness in clinical research.

5. Delivering the required changes and enhancements to the clinical research system and health care delivery system.

6. Legislative changes recommended to develop clinical research in Ireland.
Chapter 1

Economic and Health Impacts of Clinical Research in Ireland
This chapter describes the economic and health impacts of the clinical research activities supported by this report. The health and economic benefits of clinical research have been well documented in countries making more significant national investments. In the UK, patients treated in research active health trusts have been found to suffer reduced mortality and morbidity\(^1\).

In Australia, an economic evaluation of investigator-initiated clinical trials conducted by networks found that clinical trials had the potential to provide $2 billion in health benefits from better health outcomes and reduced health service costs. It also found that reduced healthcare costs alone easily exceeded the government’s investment in clinical research networks\(^2\).

### 1.1 Economic Impacts

Evidence from the implementations of similar strategies in other countries shows that implementing this report’s strategy and recommendations will expand clinical research in Ireland by a factor of 4 and will result in an additional 3,000 direct and indirect jobs, generating Gross Value Added (GVA) of €200-300 million per annum. On average, each patient participating in a trial will generate a benefit of approximately €13,500. In addition, expanded clinical research activity will generate a wide range of significant but difficult to quantify economic, health and academic benefits.

In 2017, clinical research in Ireland employed an estimated 600 people in supporting the conduct of clinical trials of medicinal products, medical devices and novel diagnostic tests, as well as, non-interventional observational studies involving Irish patients. Clinical research is a labour-intensive activity undertaken by a highly skilled and educated workforce. It has the potential to become a key feature of Ireland’s knowledge economy.

Patient participation in clinical trials generates revenues and cost savings to the health service. On average, clinical trial sponsors pay the health service an estimated €7,481 (£6,658\(^3\)) for each patient participating in a clinical trial. In addition, the health service receives medicines worth an average of €5,899 (£5,250) per patient for patients participating in clinical trials. In 2018, an estimated 500 patients\(^4\) were recruited into clinical trials of medicinal products for an average of 24 months, representing estimated revenues and savings to the health service of €7.5 million and €5.9 million, respectively.

A study of 25 high impact, networked clinical trials in Australia found that if the results of these trials were implemented with 65% of eligible patients for one year, there would be a benefit worth AUS$2 billion in terms of health outcomes and reduced health service costs. The estimated reduction in health service costs of AUS$ 580 million more than offsets the running costs of the clinical trial networks supporting these trials. The study found large and compelling leveraged economic returns from the government’s funding of clinical trial networks.

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\(^{3}\) Exchange rate used was the rate that prevailed at the time of writing this report (Spring 2019)

\(^{4}\) According to Cancer Trials Ireland May 2016 Report, over the three years between January 2013 and December 2015, 2,151 Irish patients were recruited into clinical studies with 3.5% (753), or 250 per annum, being enrolled into drug trials. If we assume that haematology/oncology accounts for 50% of clinical trial patients, then some 500 patients are recruited into clinical trials annually and assuming that each patient participates for an average of two years, at any one time, 1,000 patients are actively involved in a clinical trial with many more being followed up for five years or more.
The Irish economy can also benefit from the centralised coordination of activities, rendering the clinical research system more effective and efficient. Such coordination, as detailed in Chapter 3, increases the profile of Irish clinical research and attracts activity to Ireland. A coordinated and well managed clinical trial infrastructure improves study set-up times and processes, leading to lower study set-up costs and faster completion of clinical trials. Training provided to clinical research staff and the sharing of best practice makes clinical research more cost competitive with other jurisdictions and improves quality and safety.

In 2014, the global market for clinical research was estimated to be €45.5 billion (£38 billion)\(^5\). In the UK, the National Institute for Health Research (NIHR) commissioned a study by KPMG published in September 2016 that found that the economic impact of the UK’s clinical research network in 2014/15 had a GVA to the economy of £2.4 billion and 39,500 jobs. If Ireland were to adopt a similar investment approach to that of the UK, Ireland could realistically achieve 5% of this impact within five to ten years, generating a GVA of almost €200 million per annum and added employment of 2,000 people in Ireland. This only takes into account regulated clinical trials; we estimate that a further 1,000 people and €100 million in GVA would be accounted for by those conducting other forms of clinical research not regulated by the Health Products Regulatory Authority (HPRA), including biobanking, observational studies and the maintenance of patient research registries.

Up-scaling clinical research activity in Ireland will create a range of benefits for the Irish economy. Clinical research is a labour-intensive activity offering high quality jobs in the knowledge economy. Furthermore, based on the 2016 KPMG study, each direct clinical research job creates a further 0.34 jobs from indirect and induced employment impacts. Other indirect outputs include the development of patents and outputs that foster the development of intellectual property.

Currently, Ireland’s clinical research sector provides employment in the following areas:

- Clinical Research Organisations (CROs)
- Clinical Research Facilities and Centres (CRF/Cs) funded by the Health Research Board (HRB) and other research funding agencies
- Government agencies that support clinical research, such as, the Health Products Regulatory Authority and National Standards Authority of Ireland supporting trials of Investigational Medicinal Products (IMP) and medical devices
- Universities undertaking clinical research, and many of which work in healthcare service settings, and
- Research charities undertaking their own research or funding research on which approximately €7 million\(^6\) per annum is spent.

Ireland has a vibrant medical technology sector. IDA Ireland data on the development of the medical technology sector found that the number of companies grew from 75 in 2000 to 450 in 2016 and these now employ a workforce of +37,000 people. Whilst a significant proportion of this growth is attributed to multinational companies (MNCs), making Foreign Direct Investment (FDI) in Ireland, another strong driver is the 60% who are innovating and scaling their businesses to compete at a global level. In 2017, the Irish medical technology sector exported €11.2 billion worth of products and spent €282 million on Research and Development (R&D). This has resulted in €3.1 billion direct expenditure in the economy.

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\(^5\) NIHR Clinical Research Network: Impact and Value Assessment, KPMG, September 2016
Enterprise Ireland (EI) supports 269 small-to-medium sized enterprises (SMEs) in the life sciences sector in Ireland and estimates that these companies employ 4,833 people. Currently, many of these companies seek to carry out clinical trial activity overseas because Ireland’s health research system and infrastructure cannot meet their needs.

This represents an opportunity to develop a fit-for-purpose clinical research system for Ireland. Investment in a fit-for-purpose clinical research system would not only benefit SMEs in the life sciences sector, but such an initiative would align with the Irish Government’s Future Jobs Initiative\(^7\) and also underpin further potential for networked research and collaboration between industry and academia that could leverage international research funding opportunities (e.g. EU, Wellcome, USA’s NIH (National Institute for Health).

### 1.2 Health Impacts

A well-resourced and fit-for-purpose clinical research system also has positive and potentially life enhancing impacts for patients and their families. New clinical practices and treatments often reduce the costs of disease treatment and prevention.

#### CASE STUDY

**Palbociclib Trial**

Palbociclib Trial demonstrated increased progression free survival for women with a particular type of breast cancer

The Palbociclib international clinical trial, which included 18 Irish patients, demonstrated that a combination of palbociclib plus letrozole extended progression free survival by approximately 50% in patients with metastatic oestrogen receptor-positive HER2-negative breast cancer. For patients, this led to longer survival and additional Quality Adjusted Life Years (QALYs) and longer term follow-up studies may reveal further patient benefits from this medicine.

For the 18 Irish women participating in this trial, it was estimated (DKM, 2016) that the value of the additional QALYs was €340,000, or more than €22,000 per patient.


Research leads to the adoption of disruptive technologies and processes that can make dramatic improvements to the provision and efficacy of healthcare services. It also enhances the structure and performance of the life sciences sector and examples include:

- New healthcare delivery models
- Serving emerging markets found in less developed countries
- Technology and Information Communications Technology (ICT)
- Cost containment
- Evolving regulatory frameworks across key jurisdictions, and
- Discovery of new treatment approaches that avoid unnecessary and sometimes costly treatment.

**CASE STUDY**

**Reducing the Costs of Treating Hard to Heal Wounds**

Hard to heal wounds are hard to manage and incur a cost burden on the health system through extended treatment periods, resource use and patient quality of life. In the UK, it is estimated that hard to treat wounds cost £3.2B (€3.6B) per year.

An audit in seven hospitals in the Republic of Ireland and Northern Ireland compared normal treatment with single use Negative Pressure Wound Treatment (sNPWT), which involves a medical device being used to create negative air pressure around the wound to improve and accelerate tissue healing and viability.

It found that hard to heal wounds treated with sNPWT had, on average, a more successful healing outcome in terms of lower treatment costs, faster healing, strength and quality. These improvements led to an estimated potential cost saving of 21% in the Republic of Ireland and 25% in Northern Ireland.


Strategic investment in clinical research would ultimately lower the cost of recruiting and retaining health professionals into the health system making the Irish healthcare system more attractive. This added attractiveness of Ireland for world class academic clinicians and allied health professionals would in turn encourage more investment in research in Ireland. Clinical research capacity building will develop an Irish community of clinical research excellence that will also increase capacity and expertise within the regulatory bodies.

Clinical research aligns with and supports national research and health policy, for example, innovation in service provision makes access to healthcare services easier for patients, carers and family members (e.g. medical monitoring in the home and eHealth). Clinical research also leads to less invasive treatments and faster recovery times.
A research active health service can improve the survival and quality of life for patients participating in clinical trials\(^8\). Research conducted in the UK has also confirmed that patients in research active healthcare trusts had lower mortality and morbidity than those cared for in less research active trusts\(^9\).

New advances in the medical and life sciences arena benefits the economy by sustaining a healthier workforce. In principle, healthy people are more productive at work, resulting in higher productivity. Increasing lifespans means more long-term benefits from workforce training and development. Increased labour force participation by people who may otherwise be off work with long term sickness/disability also improves national productivity. This is important to Ireland in the context of current shortages of skilled labour.

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\(^8\) Health & Economic Impacts of Cancer Trials – Final Report for Cancer Trials Ireland, 18th May 2016, DKM Economic Consultants

The TAILORx study showed how a new diagnostic test, known as Oncotype DX and developed by an Irish company, can reduce treatment costs and improve patient outcomes.

690 women from Ireland participated in the TAILORx Study which demonstrated that chemotherapy can be avoided for 70 per cent of women, with the most common type of early stage breast cancer (HR-positive, HER2-negative, node-negative breast cancer). The findings suggested that chemotherapy may be considered for the remaining 30 per cent of women.

TAILORx is one of the first large-scale trials to examine a methodology for personalising post-operative cancer treatment. The trial involved 10,273 women with early-stage breast cancer across 1,182 research units in Ireland, United States, Australia, Canada, New Zealand and Peru.

The Irish arm of the trial was conducted by Cancer Trials Ireland and led by Professor Maccon Keane, Consultant Medical Oncologist at University Hospital Galway, as the Chief Investigator.

“Not only did the trial provide great relief for women in Ireland who participated and avoided three months of chemotherapy, it delivered considerable cost savings to the HSE”

Cancer Trials Ireland.


The next chapter addresses the strategy and policies required to enhance clinical research activity in Ireland that will stimulate further economic and health benefits for the Irish population.
Chapter 2

Clinical Research Strategy and Policy
Chapter 2
Clinical Research Strategy and Policy

Introduction

Strategy is generally understood as the statement of a plan of action designed to achieve a long-term or overall aim. Strategy can be seen as a grand design, a master plan, a plan of action, a policy, or a proposed action programme.

The Vision set out in this report is for an integrated Irish clinical research system that drives excellence and innovation to further advance patient health and economic prosperity.

The Mission is:

1. To develop an integrated clinical research system that meets best international standards
2. To integrate clinical research within the national Irish Health Service for the benefit of Irish patients
3. To support innovation in the Irish life sciences Sector
4. To attract, develop and retain a skilled workforce
5. To support the development of clinical research so that it becomes a key component of the knowledge economy, and
6. To support economic development and prosperity.

An expansion of the current quantum of clinical research in the order of 400% within a 5 to 10 year time frame is considered feasible by any international comparison. Therefore, the Strategy to be adopted should focus on enabling this development and expansion to be realised. A wide range of recommendations are made throughout the report and here we concentrate on the high-level strategic issues and factors that influence success.
2.1 Clinical Research Strategy – to date
As discussed in the Clinical Research Roadmap 2010\textsuperscript{1}, Ireland has the potential to be:

• A leading country for quality clinical research including clinical trials,
• A partner of choice in multi-national clinical trials, and
• A generator of innovative products to improve health and reduce disability.

Successive Irish Government reports have recognised the need and economic importance of developing an integrated Irish national clinical research system. This commitment has led to investment in recent years in facilities and expertise, and to policy commitments such as in the Renewed Programme for Government, the Action plan for Health Research 2009-13 and the prioritisation of clinical research for funding in the HRB Strategic Business Plan 2010-14.

The current HRB Strategy 2016-2020 entitled Research Evidence Action focuses on:

• Supporting healthcare interventions,
• Addressing the research needs of the Irish health and social care system, and
• Building a strong enabling environment for health research in Ireland.

In the Report entitled, Innovation 2020\textsuperscript{2}, Government reviewed the priority areas set out in the 2012 Research Prioritisation report to ensure that they were still valid and to refresh and revise them, if necessary, in the light of changed circumstances.

For the 2018 to 2023 period, Health and Wellbeing is one of the five main priority areas highlighted. The priorities for research and innovation in Health and Wellbeing are set out under the following four headings:

1. Connected Health and Independent Living;
2. Medical Devices;
3. Diagnostics; and
4. Therapeutics.

The research prioritisation report states that Government policy will continue to focus on improved health and well-being outcomes for all whilst ensuring that healthy lives and well-being for all are recognised as essential to sustainable development, as per the United Nations Sustainable Development Goals.

This report addresses the area of clinical and translational research which is prioritised under the Health and Wellbeing category.

Commenting on research and innovation, the European Commission states that research and innovation are key components in securing Ireland’s economic future and at the heart of the European Commission’s policies to boost jobs, growth and investment. Successful research and creative innovation not only have huge potential to stimulate economies, but also improves health, transport, security and the environment for Europe’s citizens.

\textsuperscript{1} See https://www.crdi.ie/wp-content/uploads/2015/09/MMI_Clinical_Research_Roadmap.pdf
Furthermore, the European Commission states that Ireland has transformed itself over the past 40 years into one of Europe’s top innovation nations and credits IDA Ireland with helping to attract billions of Euro in Foreign Direct Investment (FDI) from companies in hi-tech sectors including pharmaceuticals and medical devices.

Regarding funding and research and development (R&D) expenditure, figures from Eurostat show that, as a percentage of Gross Domestic Product (GDP) in Ireland, it fell from 1.20% in 2006 to 1.18% in 2016. This compares to the EU average for 2016 of 2.03% and the Horizon 2020 target of 3%.

The Health Service Executive’s (HSE) National Service Plan 2018 ³ states that:

• R&D in health research is essential to generate new knowledge to inform evidence-based practice, and
• Knowledge and learning are also key requirements for effective change and transition planning for the health services in Ireland.

The HSE’s National Service Plan 2019 ⁴ reaffirms this importance and states that:

• A strong research culture and data-driven, evidence-based practice in health service planning and delivery is essential for the effective functioning of a health and social care system.

The HSE 2019 plan also provides details of a research benchmarking exercise conducted in 2018 by the HSE which highlights that:

• Research governance mechanisms are required to safeguard public confidence in research, ensure good use of resources and encourage public and patient participation in research.

The HSE proposes the following key priorities and actions (among others):

• Continue to pursue the development of a framework for research governance and provide stronger national support to grow research at provider level that is better aligned to strategic priorities and focused on improved and more effective patient care.
• Develop a national framework for research governance for the health service in the context of new health service structures.

It is now widely accepted that healthcare organisations with a strong research culture deliver better care and are associated with better organisational performance.

Academic-led clinical research and the activities of the university-based Clinical Research Facilities and Centres (CRF/Cs) (see Appendix VI) provide a significant contribution to clinical research in Ireland. Along with academic support, the universities also provide financial support to clinical research and are an essential part of the strategic leadership and development of clinical research.

Finally, Government strategy as outlined in the Sláintecare Action Plan⁵ includes the following recommendations:

• Consolidate and invest in data and R&D infrastructure and capabilities to ensure that evidence is at the core of routine decision making, and

• Establish an R&D forum in health and social care to input into the development of a new national health research strategy.

From the above, it is clear that the benefits, and indeed imperative, of increased health research are acknowledged. For focused expansion, maximum impact and return on investment, a nationally coordinated model is required to provide for support, oversight and efficient deployment and activation.

2.2 Strategic Leadership and Coordination
Strategic leadership is needed for clinical research and this leadership needs to be positioned at the highest level nationally. This function needs to be appropriately funded.

**RECOMMENDATION 2.1**
A Strategy Lead for clinical research should be appointed at a senior cross-departmental level. This appointee should have a well-funded support office.

Effective coordination is required across all sectors, stakeholders and institutions involved in clinical research.

In making this recommendation, the excellent work that is already being delivered by a range of bodies is acknowledged. In particular, the Department of Health (DoH), provides very substantial support, coordination, and indeed funding to the Health Research Board (HRB). In the Department of Business, Enterprise and Innovation (DBEI), Science Foundation Ireland (SFI) and Enterprise Ireland (EI) provide excellent supports and funding. IDA Ireland are also heavily involved in life sciences supports but less so in direct supports to clinical research.

An overarching national coordinating entity is required to have oversight of all clinical research and to provide the vehicle for the coordination of the additional Exchequer and industry co-funding proposed in this report. This entity would also provide the national IT-based registration, approval and management system for clinical research recommended below.

The multi-stakeholder Steering Committee for the Future Investment in Clinical Research Initiative, which has overseen the development of this report, could serve as a readymade part of the governance arrangements for this national coordinating entity.

A second agreed entity is required at the HSE/Service Delivery Level which would be responsible for coordinating all the activities within the HSE/Service Delivery institutions (public and private) to manage the additional Exchequer and industry co-funding that would be channelled to these managed centres.

**RECOMMENDATION 2.2**
A National Coordinating Entity and an Office at HSE/Service Delivery Level should be established to coordinate all aspects of clinical research and to coordinate the additional Exchequer and industry co-funding proposed in this report.
2.3 Legal Mandate for Health Research
There is no legal mandate for Health Research in Ireland. Such a mandate exists in a number of countries including the UK and Australia and it is an effective mechanism to develop and foster enhanced clinical research. It was only with the recent introduction of the Health Research Regulations 2018 that for the first time ever in Irish law the meaning of health research was defined.

A legal mandate for health and clinical research is required to give government bodies and health service providers the necessary impetus to make health and clinical research a key priority and a key performance indicator in their delivery of health care.

**RECOMMENDATION 2.3**
A legislative mandate for health research should be created in law, which places a positive obligation on the State to carry out evidence-based health research.

2.4 Governance
Despite the interdependence of their roles, Irish hospitals, Community Healthcare Organisations (CHOs) and universities do not have a joint governance and management plan and as a result undertake clinical research separately. The governance of clinical research activities at the university-based CRF/Cs and clinical research networks is generally provided through institutional oversight.

Irish hospitals, Hospital Groups and CHOs are not resourced to take on the role of sponsorship and when universities do so, they accept sole responsibility for the governance of clinical trials. On a case-by-case basis, they may contractually delegate some of their responsibilities to the hospitals and CHOs but they take sponsorship decisions and deal with escalation issues independently.

In the absence of ongoing consultation between the sectors, when contracting with funders, universities are therefore required to make commitments to deliver on clinical research activities over which they may not have full control.

At present there is no contractual framework that sets the terms and conditions of the engagement of HSE consultants and staff with universities in research. Likewise, there are no agreed terms and conditions for the placement of academic employees in hospitals and/or access to hospital patients, facilities and resources. This creates regulatory, legal and insurance gaps for universities, hospitals and clinical investigators and a potential exposure for all parties involved, including patients.

In the case where clinical investigators have a joint affiliation to a hospital/CHO and an academic institution, it is also not always clear whether they are acting in their clinical or academic capacity, and therefore where the institutional responsibility and liability rests. Clarity on terms of affiliation, activities, institutional responsibilities and ongoing engagement with the State Claims Agency (SCA) would help identify and address any insurance/indemnity gaps.
Many of the issues involved have been the subject of discussion at the CRDI-coordinated Corporate Enabling of Clinical Research (CECR) initiative which has involved participation from across the sector. The final report from the CECR initiative is in preparation and, when published, should provide clear guidance on the possible solutions. The collaboration efforts made by all the parties involved to agree streamlined processes must be maintained and the required solutions implemented.

**RECOMMENDATION 2.4**
Each Hospital Group-affiliated university should be funded to deploy a Clinical Research Facility/Centre that facilitates the conduct of clinical research within the Hospital Group and Community Health Organisations as an essential core clinical service. This should also be seen as a significant step towards the establishment of academic health sciences centres/systems.

**RECOMMENDATION 2.5**
The Clinical Research Facilities/Centres should operate under a combined governance of both the university and Hospital Group/Community Health Organisations with appropriate comprehensive legal agreements in place between the parties.

**RECOMMENDATION 2.6**
Clinical Research Facility/Centre staff should be joint staff of both the university and affiliated hospital/Community Health Organisation.

**RECOMMENDATION 2.7**
Universities should engage with and educate healthcare staff as to the importance of their role in clinical research.

2.5 Patient engagement
Engagement of patients, their families and carers is essential to advancing the participation of patients in clinical research so that the benefits of clinical research can extend to a broader group of individual patients and to the healthcare system. Encouraging patient engagement will this ensure that the patient voice is heard, it will also help to inform study protocols with the potential to improve patient outcomes.

**RECOMMENDATION 2.8**
A combined and coordinated information campaign should be in place to inform patients, their families and carers of the benefits involved in participating in clinical research. This should also extend to healthcare staff.
2.6 Regulation and Legislation
The regulatory framework for the conduct of clinical research is an essential element to ensure patient protection and the development of the sector.

There are a number of regulations which govern clinical research. Clinical trials are conducted in accordance with EU Clinical Trial Directive 2001/20/EC. This directive will be repealed by the Clinical Trial Regulation 536/2014 upon its application in 2020. Clinical investigations on medical devices must be conducted in accordance with the Medical Device Regulation (MDR) 2017/745 and In-Vitro Device Regulation (IVDR) 2017/746. The MDR and IVDR represent a significant strengthening of the existing regulatory system and replace the Medical Device Directive 93/42/EEC, the Active Implantable Device Directive (AIMD) 90/385/EEC and the In-Vitro Diagnostic Medical Device Directive 98/79/EEC. The MDR and IVDR will have a staggered transitional period with some aspects becoming binding within six months, full application of the MDR after three years and full application of the IVDR after five years.

The General Data Protection Regulation (GDPR) came into effect across Europe on 25 May 2018. GDPR replaces the Data Protection Directive 95/46/EC. GDPR was transposed into Irish law via the Data Protection Act 2018. GDPR will harmonise the data protection laws across Europe and will strengthen the data protection principles. There are seven principles of GDPR which include lawfulness, transparency and fairness, purpose limitation, data minimisation, data accuracy, storage limitation, integrity and confidentiality and accountability. The Data Protection Commission (DPC) is the supervisory authority for Ireland and is responsible for overseeing compliance with GDPR.

Under Article 9(2) of GDPR, the processing of special categories of personal data (including health data) is subject to “suitable and specific measures”. GDPR does not define what the suitable and specific measures should be, however, the suitable and specific measures for processing personal data for the purposes of health research are provided for in the Health Research Regulation 2018, which came into effect on 7 August 2018.

The Health Research Regulation also provides a definition of health research; it provides the possibility of applying for a consent declaration for new research; it provides transitional arrangements in respect to the granting of consent declaration for health research which is already underway; and provides for the establishment of the consent declaration committee.

It is imperative that the application of the GDPR supports and does not impede clinical research or patient care delivery.

RECOMMENDATION 2.9
The Health Products Regulatory Authority, which is tasked with approval and monitoring regulated clinical trials and clinical investigations, should be adequately resourced so it can continue to monitor and support clinical research.
2.7 Insurance
In addition to approvals, insurance and indemnity provision is required for clinical research in Ireland. This is particularly detailed for clinical trials and regulated investigations of medical devices in ICH GCP E6 R2 which requires a sponsor to indemnify the institution and investigator in respect of claims made on behalf of the trial subjects. When a commercial sponsor such as a pharma company sponsors a clinical trial in an Irish site, that sponsor will procure insurance cover for that trial site. Additionally, the commercial sponsor will indemnify the trial site and the SCA against claims relating to the clinical trial. The commercial sponsor will provide that indemnity to the trial site in the form of the Clinical Trial Indemnity Form which is usually appended to the Clinical Trial Agreement. This Clinical Trial Indemnity Form sets out a number of conditions to be met in order to satisfy the indemnity. The SCA will in turn cover claims relating to the care of the patient by the trial site outside of the clinical trial via the Clinical Indemnity Scheme (CIS).

The Clinical Trial Indemnity Form also refers specifically to Irish Pharmaceutical Healthcare Association (IPHA) guidelines and to an Investigational Medicinal Product (IMP) clinical trial. There is no deviated indemnity form for clinical investigations of medical devices, or for non-interventional clinical research. As the indemnity requirement differs for each category, it would be of benefit to have an indemnity per category, to ensure the “authority” is protected.

Currently, academic institutions are not covered “authorities” for the purposes of the SCA and state indemnity. Academic institutions are becoming more and more involved in sponsoring clinical trials in Ireland. Most of the academic institutions with CRF/Cs have a clinical trials insurance policy which allows them to sponsor clinical trials. The CRF/Cs are not currently designated as “authorities” in Ireland and therefore do not officially have the cover of the CIS. This is currently being reviewed by the CECR group in conjunction with the SCA.

Academic-led clinical research studies often lead the way on research which represents a high risk from an insurance perspective. This type of research could be covered by the SCA on a case by case basis, if supported.

RECOMMENDATION 2.10
The academic institutions be supported in providing academic-led clinical research to participants where commercial insurance is unavailable.

RECOMMENDATION 2.11
All academic-led research conducted under the auspices of the Clinical Research Facilities / Centres should be covered under the provisions of the State Claims Agency Clinical Indemnity Scheme and all Clinical Research Facilities/Centres and subordinate sites should be designated as “authorities” for the purposes of the state indemnity.
2.8 Information and Communications Technology Frameworks and Systems

Appropriate Information and Communications Technology (ICT) systems are required to support the delivery of clinical research. This topic is detailed elsewhere in the report. Ideally, the planned Individual Health Identifier (IHI) and the Electronic Healthcare Record (EHR) would be in place. In advance of this, a number of limited IT based system are in place in individual institutions. These need to be enhanced and developed and managed at a national level.

**RECOMMENDATION 2.12**
Implement a national IT-based registration, approval and management system for clinical research.

2.9 Quality Management Systems

All clinical research must be conducted in accordance with the relevant regulations and with the principles of Good Clinical Practice (GCP).

A Quality Management Systems (QMS) provides a mechanism for embedding the requirements of GCP and the relevant regulations. The QMS sets out the standards the centre is operating to, the roles within the centre which fulfil each task and the oversight of the QMS. The QMS pertaining to the CRF/Cs includes a mechanism for internal audit which allows for continuous improvement and ensures that the research conducted at the facility is compliant with all relevant regulations. HRB CRCI has implemented a programme of Mutual Recognition of QMS across the CRF/Cs.

**RECOMMENDATION 2.13**
Adequate support to be provided to endure appropriate Quality Management Systems are implemented across all clinical research.

2.10 Outcomes-based clinical research

Traditionally, funding and reimbursement programmes often focused on activity-based measures and output-based measures. It is now accepted that it is value, not cost, that is the essential metric and that outcome-based measures are more important.

Failure to apply outcome-based funding and reimbursement measures is a disincentive to conducting clinical research into improved clinical outcomes.

Standardised outcomes measurement across the public health system would drive clinical research to determine the interventions which achieve the best outcomes as well as understanding how biopharmaceuticals and medical technology (medtech) products are contributing to achieving these desired outcomes.

**RECOMMENDATION 2.14**
Outcome-based measures should be applied to all clinical research and to funding and reimbursement programmes.
RECOMMENDATION 2.15
Clinical research within the healthcare delivery system should have a well-defined research translation plan. This should be linked to the clinical programmes.

2.11 Investment in clinical research
This report, and the extensive fact-finding and analysis undertaken by the Steering Committee of the Future Investment in Clinical Research initiative has not presented an in-depth analysis of every element of current funding of clinical research. The recommendations for advancing clinical research in Ireland are firmly based on the maintenance of all existing funding streams, from whatever source. The recommendations for development, and the additional funding required, are made on the basis that this is supplementary funding and is not in any way to be seen as supplanting or replacing any existing funding. Any proposals that might emerge for any changes to existing funding will need to be looked at separately and this report calls for all existing funding supports to be maintained.

RECOMMENDATION 2.16
The additional funding supported by the recommendations in this report is additional, incremental long-term funding to enable clinical research to develop at the pace and to the scale identified. It does not replace any existing supports and funding provided from all sources.
In June 2016, I was in a changing-room trying on some clothes when I noticed something unusual about one of my breasts. Having recently turned 40, I put this odd change in my breast down ‘to my age’, but in hindsight there were other clues that I had largely ignored – a hug would leave my chest aching for days afterwards and my bras were all uncomfortable and tight fitting for no apparent reason. Then there was the fact that I felt exhausted all the time, but I blamed my busy lifestyle for the tiredness as a working mother with three young children.

Breast cancer had never been on my radar up until a couple of weeks later when I found a lump in my left breast.

I immediately sought advice from my GP who referred me to the Triple Assessment Unit in Beaumont Hospital. Within 10 days, I was diagnosed with stage two, grade 3 invasive ductal carcinoma (IDC) breast cancer.

I had a partial mastectomy and full axillary node clearance. A few weeks after surgery I commenced chemotherapy, (4 AC and 12 Taxol) over a 5 month period, followed by 20 sessions of radiotherapy.

After the treatment ended I was told to go off and live my life, and there would be no further interventions until my next annual mammogram. So I got busy living and doing my best to get back to the old me and back to normal. But it played over and over in my mind that I could be doing something else; that something else could be done to prevent others going through what I had just come out of.

Initially, I didn’t know anything about cancer trials until I stumbled across an article in the newspaper about Cancer Trials Ireland. I began to research what trials were taking place in Ireland and my potential eligibility to participate in one. Having found one I thought would ‘suit’ my form of cancer, I had a meeting with my Oncologist. In discussion we hashed out the pros and cons and I went away to think about it for a short time. Although I had some apprehensions, I was actually delighted when I was accepted to participate in the PALLAS trial. (PALLAS aims to see if a targeted medication can decrease the reoccurrence of breast cancer).

My regime is quite straightforward. I take one dose of tamoxifen daily and one palbociclib tablet for 21 days, and then I have a week off the palbo. I keep a meds diary which I give in when I attend the hospital for bloods every 3 months and the trial Nurse checks in on me by phone every 21 days. Other than occasional low energy levels, there have been no major side effects of the drugs. My reasons for joining the trial are two-fold: I wanted to help others and to give myself better odds of the cancer not returning. If just one person didn’t have to go through what I went through as a result of trials like this, it’s job done as far as I’m concerned.

I am also acutely aware that I mightn’t have had the opportunity to avail of the treatment options that have helped my recovery if other people had not trialled those drugs before me. I was surprised to learn that many people consider cancer trials to be a ‘last resort’ treatment option. To me it’s the opposite.

It’s an ongoing process to find new, innovative ways to fight cancer and to enable people with incurable, but treatable cancer, to continue to live productive, happy lives.

Being a participant in a cancer trial also gives me hope for the future. As a ‘cancer patient’ you are often times helpless and feel you have no control over the situation you’ve found yourself in. Being on a trial gave me a sense of purpose and in some ways a sense of control in dealing with my health.

I have never once felt like a ‘human guinea pig’ which can be a common misconception, I feel that by participating in this research I am making a valid contribution towards a better standard of treatment and care for those coming down the cancer conveyor belt behind me.
Chapter 3

Coordination of Clinical Research in Ireland
Chapter 3
coordination of clinical research in ireland

Introduction
A common theme in jurisdictions outside of Ireland is in the integration of research as a fundamental component of the health service provision. Health service providers in countries, such as, the UK, Denmark and France have for many years supported and directly invested in research staff, facilities and networks out of their core budgets, with many having invested extensively in research centres and disease specific networks.

In essence, they work to promote harmonised research procedures by reducing bottlenecks in administrative processes, whilst also providing centralised services aimed at enhancing the visibility and competitiveness of both academic and industry clinical research for their countries.

As part of the infrastructural investment in Ireland over the last 10 years, the HRB has invested in the centralised coordination of clinical research to reflect the functions of some of the organisations described above. Investment in, and integration of research as a fundamental component of the health service provision has yet to be developed. Details on the resources required to do this are detailed elsewhere.

Cancer Trials Ireland is an example of a national coordinating entity for the centralised coordination and management of oncology trials. In more recent years, the HRB has also invested significantly in additional national coordination services in clinical research, namely, HRB Clinical Research Coordination Ireland (HRB CRCI) and HRB Trials Methodology Research Network (HRB-TMRN) detailed later in this chapter. While this investment is significant and delivers a high return, long-term, core funding is required to further develop the centralised coordination services that are necessary to support a world class national clinical research system in Ireland.

RECOMMENDATION 3.1
Long-term, core funding is required to further develop the centralised coordination services that are already in place and necessary to support a world class national clinical research system in Ireland.

Strategic leadership is also needed for clinical research. This leadership needs to be positioned at the highest level nationally and should be funded in the long-term.

RECOMMENDATION 3.2
A Strategy Lead for clinical research should be appointed at a senior cross-departmental level. This appointee should have a well-funded support office.
An overarching national coordinating entity is required which would have oversight of all clinical research and would provide the vehicle for management of the additional Exchequer and industry co-funding proposed in this report.

**RECOMMENDATION 3.3**

*An National Coordinating Entity and an Office at HSE/Service Delivery Level should be established to coordinate all aspects of clinical research and the management of the additional Exchequer and industry co-funding proposed in this report.*

### 3.1 National Coordination

A number of national coordinating entities currently exist in Ireland, each providing important elements required to support clinical research at different levels. These entities include:

#### 3.1.1 Clinical Research Development Ireland

Clinical Research Development Ireland (CRDI) is a not-for-profit research partnership comprising NUI Galway, Royal College of Surgeons in Ireland, Trinity College Dublin, University College Cork, University College Dublin and University of Limerick, their medical schools, associated academic hospitals and clinical research facilities.

CRDI’s mission is to advance patient care and health service delivery by supporting the development of clinical and translational research across its partner academic institutions, their medical schools and associated hospitals.

CRDI builds on the achievements of Molecular Medicine Ireland (MMI) which was established in 2008 by five of the aforementioned universities, together with its predecessor the Dublin Molecular Medicine Centre (DMMC), a partnership initiated by UCD and Trinity College Dublin in 2002, with the inclusion of Royal College of Surgeons in Ireland in 2005. The University of Limerick is the sixth member of the partnership, having joined in June 2018.

Since 2002, CRDI and its partner institutions have succeeded in securing funding from a number of research enablers including; Enterprise Ireland, EU FP6 & 7, HEA PRTLI Cycles 1-5, HRB, HSE, Irish Cancer Society/Movember, SFI and the Wellcome Trust, for cross-institutional initiatives. These comprise for example the Clinician Scientist Fellowship Programme and Clinical and Translational Research Scholars PhD programmes, Irish Clinical Research Infrastructure Network, Dublin Centre for Clinical Research, iPROSPECT and IPCOR prostate cancer research programmes, HRB Clinical Research Co-ordination Ireland, CÚRAM (SFI Centre for Research in Medical Devices) and the Irish Clinical Academic Training (ICAT) programme.
3.1.2 HRB Clinical Research Coordination Ireland

HRB Clinical Research Coordination Ireland (HRB CRCI) is an integrated national clinical research network, providing centralised support for the conduct of multicentre clinical trials (both commercial and academic) across Ireland. It is funded by extramural grants from the HRB and EI, supported by the six largest Irish universities and is hosted by CRDI.

HRB CRCI’s mission is to advance healthcare by enabling a coordinated system with the specialist skills, expertise and infrastructure to design, conduct and analyse clinical trials and other intervention studies in Ireland, undertaken by networked clinician investigators and/or industry.

HRB CRCI became operational in May 2015. Its central office provides overarching support and coordination of clinical trials involving pharmaceuticals, neutraceuticals or clinical care pathways, as well as, the clinical investigation of medical devices. It has developed a range of services and activities to help address the unmet needs in clinical research and acts as a central point of contact, nationally and internationally.

CRDI provides corporate support services to the central office. The eight partner CRF/Cs have over forty years of combined research experience. The partner CRF/Cs provide the infrastructure, physical space and facilities, experienced research and specialist support staff and the necessary quality management and oversight of programmes that are critical for the successful conduct of world-class clinical research.

A central coordinating hub is required to facilitate the conduct of multicentre research in the form of HRB CRCI. This takes ownership of shared activities such as coordination, enhancing visibility, business development activities and the oversight of specialty specific working groups. Without such coordination, the CRF/Cs would fail to become an effective network for clinical research.

**RECOMMENDATION 3.4**

A central coordinating hub is required to facilitate the conduct of multicentre research in the form of HRB Clinical Research Coordination Ireland.

3.1.3 HRB Trials Methodology Research Group

The HRB Trials Methodology Research Group (HRB-TMRN) is a collaborative initiative between a number of Irish and international higher education institutes and methodology centres. It was established with the recognition that the conduct of randomised trials needs to become more efficient and effective for successful and effective patient care and to do this, the right trials need to be chosen, implemented and reported in the best way.

The mission of HRB-TMRN is to strengthen the methodology and reporting of trials in health and social care in Ireland, so that they become more relevant, accessible and influential for patients and other service users, practitioners, policy makers and the public. The network operates under four main pillars of activity: Research and Innovation; Training and Education; Support Services and Public Engagement, with each offering a suite of services.
The HRB-TMRN is actively involved in primary trial methodology research projects and also directly funds network members to carry out studies within a trial (SWATs) which are specifically related to improving the conduct, analysis, reporting and dissemination of randomised trials. The network also expands its research portfolio by developing new collaborations to strengthen grant applications and is named in several grants as a research support infrastructure, where primary trial methodology has been embedded.

**RECOMMENDATION 3.5**

Post-graduate training and exposure to clinical trials for all clinical staff should be a basic component of continuing professional development.

3.1.4 Cancer Trials Ireland

Cancer Trials Ireland is a not-for-profit registered charity involved in planning, opening, coordinating, supporting, monitoring and auditing activities of cancer trials in Ireland. It is partly funded by the Irish Cancer Society and the HRB as well as donations from members of the public. In addition, it generates over half of its income from the cancer trials services it provides through sponsoring its own investigator-initiated studies funded by pharmaceutical companies and working with international research groups to bring their studies to Irish patients.

Cancer Trials Ireland provides training, facilitates cooperation between all professionals working in the area and supports the development of cancer trials research units around the country. There are 45 research staff in the general central office of Cancer Trials Ireland, managing cancer clinical trials across a number of disease areas, eg, breast, gastrointestinal, genitourinary, gynaecology, haematology/lymphoma, and lung cancers. Almost all of the cancer treating specialists in Ireland are members of the group which works closely with many international collaborative groups.

Some 15,000 patients have participated in over 350 cancer trials in the 20-year period since Cancer Trials Ireland was established. In 2018 alone, it supported and oversaw the running of over 130 trials in Ireland with some 1,200 cancer patients participating. In addition, its members published 14 articles in peer reviewed journals and 28 abstracts and addressed some of the most highly regarded international cancer conferences.

Cancer Trials Ireland manages accrual numbers for cancer trials in Ireland annually and reports these numbers to the HRB. In 2014, 3% of cancer patients were recruited to trials involving IMP. In 2018 this number fell to 1.5% for the following two reasons:

1. In 2016, the HRB funding to Cancer Trials Ireland was cut by €750,000 per year which had a direct impact on the general central office and hospital cancer units’ ability to open new trials, and

2. The landscape of clinical trials is changing, as we move away from treatments based on tumour site of origin and more towards targeted studies in small numbers of patients, spanning disease types but sharing common mutations. In this context, the numbers of patients required for these types of trials are lower because they are more specific.
The overall objective for Cancer Trials Ireland is to prepare for the challenge of a two-fold increase in the incidence of cancer on the island of Ireland over the next twenty years. In order to do this, core long-term funding is needed at hospital sites and in the organisation’s general central office. Undoubtedly, the implementation of the National Cancer Strategy 2017 – 2026\(^1\) would take Cancer Trials Ireland significantly closer to finding successful treatments for all types of cancer. However, as yet there are no budgetary commitments to implementing the research-related KPIs in this strategy.

**RECOMMENDATION 3.6**
The target (KPI 20) set in the National Cancer Strategy 2017 – 2026 to double the number of people with cancer on Investigational Medicinal Product trials from the 3% to 6% by 2020 will not presently be met. Commitment is needed to fund core teams at hospital cancer units and Cancer Trials Ireland’s general central office.

**RECOMMENDATION 3.7**
Implement an integrated system between Cancer Trials Ireland and HRB Clinical Research Coordination Ireland with specialist staff sharing experience and learnings in a combined working group with their Clinical Research Facility/Centre counterparts, e.g., in pharma-covigilance and biostatistics.

3.1.5 Irish Platform for Patient Organisations, Science and Industry (IPPOSI)
Engagement of patients, their families and carers is an essential part of clinical research. This allows and advances the participation of patients in clinical research so that the benefits of clinical research can extend to a broader group of individual patients and to the healthcare system.

The Irish Platform for Patient Organisations, Science and Industry (IPPOSI) is a patient-led organisation that works with patients, Government, industry, science and academia to put patients at the heart of health policy and innovations. IPPOSI seeks to build consensus among member groups on existing and emerging health issues and policies and is seen as a key influencer in the development of patient-centred health policies in Ireland.

IPPOSI has been co-funded by the Health Research Board on behalf of the Department of Health since 2007. The remainder of IPPOSI income is generated from leveraged EU and national public grants as well as industry members’ subscriptions and sponsorships. As a public-private partnership, IPPOSI aims to maintain an equal public-to-private funding ratio.

IPPOSI membership includes over 100 patient organisations and medical charities, over 250 individuals from a scientific/clinical and healthcare background and 22 healthcare industry companies.

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\(^1\) See https://health.gov.ie/healthy-ireland/national-cancer-strategy-2017-2026/
In the area of clinical research, IPPOSI has conducted a number of public attitude surveys on the value of clinical research\(^2\) public information campaigns on clinical trials\(^3\) and patient experience focus groups and workshops to discover the kind of healthcare service patients would like to experience. In addition, IPPOSI coordinates Ireland’s first Patient Education Programme in Health Innovation with a number of 10-week blended learning modules focusing on Understanding Clinical Trials, Medicines & Medical Device Regulation and Health Technology Assessment.

With a strong European focus, IPPOSI engages with the European Commission in relation to the over-arching European environment which Ireland has to adhere to, with respect to clinical research and information governance as well as possessing strong links with BBMRI-ERIC and ECRIN networks, detailed below.

There is a requirement to establish a public-facing national registry of active clinical trials and research that can be utilised to inform patients and the public of research which may benefit them. The registry should build on existing sites developed by IPPOSI and Cancer Trials Ireland and it should link to the unified portal and database planned under the forthcoming EU Clinical Trials Regulation.

**RECOMMENDATION 3.8**
Appropriate measures and processes to encourage greater public and patient involvement in clinical research are required. Both researchers and patients alike need greater support, guidance and resources to implement these initiatives.

**RECOMMENDATION 3.9**
Building on Irish patient experience initiatives (in hospital settings and cross-settings), co-design and co-produce a patient experience survey of patients who have participated in clinical research in Ireland and disseminate findings widely to improve both researcher and patient experience of research and groups involved in clinical research in Ireland.

**RECOMMENDATION 3.10**
Establish a public-facing national registry of active clinical trials and research that can be utilised to inform patients and the public of research which may benefit them.

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\(^2\) See https://www.ipposi.ie/our-work/publications/public-attitudes

\(^3\) See http://www.clinicaltrials.ie
3.1.6 Medical Research Charities Group (MRCG)
The Medical Research Charities Group (MRCG) is the national umbrella organisation for charities
with a focus on health and medical research. Its 38 members range from large research funding
charities to small, voluntary-run patient organisations, all aiming to improve patient care through
research, much of which falls into the area of clinical research. They span many areas of health,
including rare diseases, childhood illnesses, mental health and multiple forms of chronic illness
and disability. They contribute to clinical research through funding projects, patient registries and
research posts and through playing leading roles in PPI and the dissemination of research results.

The MRCG supports and acts on behalf of its members in the following ways:

- By supporting their increased research capacity and impact on behalf of patients, through
  one-to-one support, events, workshops, educational talks and best-practice guides. One recent
  publication with relevance to clinical research provides practical guidance on the development of
  patient registries). Most notably, the MRCG also offers members access to a joint funding scheme
  with the HRB through which they can obtain matched funding for patient-focused research
  projects. This scheme demonstrates impressive outcomes and impacts.

- By providing networking and community-building opportunities through meetings, events and
  a valuable shared learning group for PPI) This shared learning group encourages and supports
  the involvement of patients and their representatives as partners in all stages of the health
  research process e.g. through advising on clinical trial protocols.

- By providing members with a shared voice for positive change and advocating for improvements
  in the Irish health research environment. This is in part achieved through the MRCG’s
  management and funding of the Irish Health Research Forum (IHRF). Many of the topics
  addressed by the IHRF have relevance to clinical research, including PPI, researcher careers
  and more recently, the impact of new data protection legislation on health research).

Clinical research groups, both academic and industry, should engage early with patient
organisations particularly in the planning process for clinical research, in order to facilitate
meaningful PPI and to help ensure the relevance and feasibility of clinical research.

**RECOMMENDATION 3.11**
Medical research charities should be included in all significant committees and groups involved
in clinical research in Ireland.

**RECOMMENDATION 3.12**
Clinical research groups, both academic and industry, should engage early with patient
organisations.
3.2 European and International Coordination/Cooperative Groups
There are many European and international coordination/cooperative groups around the world involved in clinical research.

The European Clinical Research Infrastructure Network (ECRIN) is a not-for-profit intergovernmental organisation that supports the conduct of multinational clinical research in Europe. ECRIN links the resources and capacities of national networks across Europe to access patients and medical expertise. Headquartered in Paris, it works with European Correspondents (EuCos) in member countries, national networks of clinical trial units (CTUs)/CRF/Cs, as well as numerous European and international stakeholders to provide advice, management services and tools to overcome hurdles to multinational trials and enhance collaboration. In November 2018, Ireland became a full member of ECRIN with HRB CRCI acting as the national scientific partner. A EuCo for Ireland has been appointed and is in position in HRB CRCI.

The Biobanking and BioMolecular resources Research Infrastructure European Research Infrastructure Consortium (BBMRI-ERIC) and the European Research Infrastructure for Translational Medicine (EATRIS) are European infrastructure networks focused on biobanking and translational medicine.

BBMRI-ERIC, EATRIS and ECRIN recently signed an agreement to build a long-term sustainable collaboration strategy, enabling greater user access to pan-European medical research infrastructures and supporting the development of tools, joint services and common approaches on quality, standards and advocacy. The agreement brings together the three research infrastructures, working closer with patients within the personalised medicine research continuum in the areas of sample and data collections and biobanking, clinical trials and translational medicine.

A major obstruction to the development of certain aspects of clinical research in Ireland is the fact that Ireland is not a member of critical European Infrastructures such as BBMRI-ERIC and EATRIS. As such, it cannot access the infrastructures' resources nor can it participate in the consortiums’ research programmes.

BBMRI-ERIC brings together researchers, biobankers, industry and patients to enhance biomedical research. Irish membership of BBMRI-ERIC would mean that Ireland could capitalise on its current strong involvement in the development of ISO standards for biotechnology (ISO/TC276), incorporating biobanking.

If Ireland were to become a member of EATRIS, Irish researchers could avail of a variety of clinical expertise and high-end facilities in academic centres across Europe. The Irish research community could benefit substantially from membership of EATRIS as its main objective is to create a European, globally competitive infrastructure for biomedical translational research.

Ireland is an active member of the Clinical Research Infrastructure for Global Health Initiative (CRIGH). CRIGH was officially launched in January 2017 and it aims to serve as a support structure for international collaboration in clinical research for the benefit of patients, healthcare professionals and health systems. The initiative seeks to optimise clinical research programmes in participating countries, to develop global standards on clinical research, and to promote the take-up of innovative methodology and technologies. To date, 14 organisations have joined as Members; the WHO and OECD are Observers. ECRIN shares the secretariat with the National Institutes of Health (NIH).
As well as acting as the national scientific partner to ECRIN, HRB CRCI are active members of the UK CRF Network, with representatives from across the HRB CRCI network participating in different work streams of this network. HRB CRCI also acts as the national HUB for the conect4children (c4c) project. c4c is a large collaborative European network that aims to facilitate the development of new drugs and other therapies for the paediatric population.

Cancer Trials Ireland are affiliated to many international cancer clinical trial networks in Europe, the USA and Australia. These affiliations have enabled Irish patients to gain access to trials and treatments that would not be commercially available in Ireland for a number of years. In many cases, Ireland has been the only European partner for these USA and Australian cancer trial networks, and as such, Irish patients have been the first in Europe to be given access to such clinical trials and treatments (see, eg, the TAILOR X case study in Chapter 1).

Irish investigators are active members in many international therapeutic networks, playing important roles as recognised international key opinion leaders.

An international cooperative group that enables interaction between investigators at a multi-site level is necessary. HRB CRCI currently acts as the national hub organisation within a number of international cooperative groups and organisations, e.g., ECRIN, CRIGH and c4c, and has the capacity to do so for others such as BBMRI-ERIC and EATRIS, subject to Ireland’s membership of these organisations being approved and implemented.

**RECOMMENDATION 3.13**
An international cooperative group that enables interaction between investigators at a multi-site level is necessary.

**RECOMMENDATION 3.14**
Continuation of the HRB Clinical Research Coordination Ireland and the European Clinical Research Infrastructure Network coordinator role based within HRB Clinical Research Coordination Ireland.

**RECOMMENDATION 3.15**
Ireland to become a member of European Research Infrastructure for Translational Medicine and Biobanking and BioMolecular resources Research Infrastructure European Research Infrastructure Consortium.

While the Irish Government has invested significantly in the infrastructure for clinical research primarily under the aegis of the HRB, long-term, core funding is required to further develop the centralised coordination services that are necessary to support a world class integrated national clinical research system.

The next chapter outlines the current infrastructural and resource landscape of the Irish clinical research system.
Ireland’s Involvement in International, Multicentre Stroke Research

Professor David Williams
Associate Professor in Geriatric and Stroke Medicine, Royal College of Surgeons in Ireland (RCSI) and Beaumont Hospital

Stroke is a major cause of death worldwide and the most common form of acquired major physical disability in adulthood. There are approximately 11,000 strokes in Ireland annually and some 2,000 patients die from a stroke while thousands more are left with stroke-related disabilities.

According to the Stroke Alliance for Europe (SAFE), the incidence of stroke in Ireland is due to rise by 50% in the next eight years because the country’s population is ageing. The average age for a person to have a first stroke is 74.

Significant breakthroughs have been made in the acute management of stroke in the past 20 years, which have greatly improved people’s survival and outcomes, including capacity to return home after stroke and resume normal daily activities. Thrombolysis, a treatment to dissolve dangerous clots in blood vessels, was established as an effective acute treatment for strokes caused by blood clots in the late 1990s and today Ireland has one of the highest usage rates of this treatment in the world.

Thrombectomy is a more recent intervention for acute ischemic stroke, involving the endovascular removal of the blood clot by a neuroradiologist. Irish doctors participated in the ESCAPE Study, a major international collaborative study that demonstrated the effectiveness of thrombectomy. This Canadian-led study by Prof Michael D Hill of the University of Calgary was conducted in 22 sites around the world including Beaumont Hospital in Ireland which represented the second largest patient recruiting site with 34 patients taking part over a six-month period. The first thrombectomy was carried out in Beaumont Hospital in 2010 and to date a total of 750 procedures have been performed at the hospital.

The ESCAPE study found that positive outcomes for patients with acute ischemic stroke receiving rapid thrombectomy increased from 30% to 55% and that many patients who would normally have suffered major neurological disability as a result of their stroke were instead able to go home and get on with their lives. In addition, the overall mortality rate among patients receiving this treatment fell by 50%.

Speaking about the study, Irish Co-lead Investigator Prof David Williams said, “The results of this study represent the most significant development in stroke treatment in the past 20 years and will impact stroke care in Ireland and around the world. This treatment has the potential to improve survival rates and quality of life of more than 15 million people worldwide who suffer a stroke each year.”

In line with international best practice, the Health Research Board funded the establishment of a stroke clinical trials network in 2014 that brings together Irish clinical scientists, healthcare teams and patients, linking them with global experts in the field of stroke research. The HRB Stroke Clinical Trials Network aims to improve Ireland’s ability to do high-quality collaborative clinical trials of new treatments to prevent strokes, to treat them in emergency settings and improve recovery. It also aims to provide patients with increased access to cutting-edge treatments.

The HRB Stroke Clinical Trials Network develops and nurtures links with both national and international researchers, enabling the establishment of multicentre and multinational clinical trials in the UK, Europe and North America. The CONVINCE study is an Irish-led, international, randomised clinical trial of low-dose colchicine for secondary prevention after stroke and it is currently being expanded to sites across Europe, facilitated by the European Clinical Research Infrastructure Network. The Lead Investigator for the study is Professor Peter J Kelly, Clinical Professor of Neurology at University College Dublin (UCD) and Co-Director of the Stroke Service at the Mater University Hospital.

A further example of an international, multicentre study also currently facilitated by the HRB Stroke Clinical Trials Network is the follow-up study of a neuroprotective agent (ESCAPE-NAI) in the management of large vessel occlusive stroke patients receiving thrombectomy.

The establishment of collaborative networks such as the HRB Stroke Clinical Trials Network enables Irish researchers to link with international centres of excellence to the benefit of the patient by providing access to innovative treatments and technologies. Collaboration in clinical research also helps to build capacity, making Ireland more competitive internationally and affording more opportunities to leverage much needed funding for international trials.

The results of this study represent the most significant development in stroke treatment in the past 20 years and will impact stroke care in Ireland and around the world.

1 https://www.safestroke.eu/2017/05/10/burden-stroke-report-launched-eu-parliament/
2 Irish Times, Mon 28 August 2017, Stroke treatment a rare Irish health success but progress could be lost
4 https://hrb-sctni.ie/network-trials/
Chapter 4

Ireland’s Clinical Research Infrastructure and Resources
Chapter 4
Ireland’s Clinical Research Infrastructure and Resources

Introduction
An integrated Irish clinical research system must be built to scale, operate to the best international standards and be responsive to the requirements of all stakeholders to facilitate the conduct of exemplary clinical research. In addition to implementation of strategically focused clinical research policies and centralised coordination of clinical research, investment in clinical research infrastructure and resources is required to achieve such a system.

Of the utmost importance is the investment in, and integration of, clinical research as a fundamental component of Irish healthcare delivery. Recognition of clinical research as a core clinical activity is essential and requires the development of a research governance framework for the health service to facilitate clinical research activity. The value of clinical research should be emphasised to patients and the public with a concomitant increase in clinical trial offerings to patients.

The number of interventional clinical trials conducted in Ireland is far lower than would be expected given the large presence of the pharmaceutical and MedTech industry here. Investment in the Irish clinical research infrastructure must ensure that Ireland is the preferred location for the conduct of academically led as well as industry led clinical trials and investigations. The necessary enhancements to the resources, expertise and regulatory environment for clinical research will have to be made before this can be realised.

Underpinning the success of an integrated Irish clinical research system will be the performance of highly trained and specialist clinical research staff. Long term funding for clinical research roles would enable the development of secure career pathways and retention of such staff. Further investment is also required for the use of patient data through integration of IT systems and the establishment and maintenance of biobanks and patient registries which are necessary for efficient and effective conduct of clinical research.

This chapter outlines the recommendations for investment in clinical research infrastructure and resources to realise our vision of an integrated clinical research system.

4.1 Clinical Research in the Health System – Hospitals and the Community
The Irish health service is research active¹. An online census carried out as part of a HSE research activity scoping exercise in 2018 received circa 2000 responses of self-declared research active staff. The majority of research active staff belong to the clinical professions (medical doctors, nurses and midwives, and health and social care professionals) and are based mainly in hospitals and in community services but there are also research active staff among the administration and management categories.
Medical consultants with an academic appointment are particularly research active. The research activity of medical doctors without a formal academic appointment is also significant, despite the fact that they may have less access to university supports and no protected time for research: about one third of Scopus indexed publications between 2012 and 2017 were authored by staff without a formal academic appointment.

In 2017, the total number of projects approved by all the Research Ethics Committees associated with healthcare organisations (31 in total) amounted to circa 2,000 projects nationally; these include all health research projects involving patients, patients’ biological samples or their data. A minority of those (approximately 1.5% of all REC approved studies) were HPRA regulated clinical trials for IMPs, which are most frequently sponsored by pharmaceutical companies, indicating that there is significant room for expansion in clinical trial activity in Ireland.

The role of Irish universities as clinical trial sponsor has increased significantly in the last ten years, fuelled by clinical research funding from the HRB. However, the lack of equivalent investment in clinical research in the health sector has resulted in inadequate research management capability in hospitals and CHOs, thus impeding the ability of the health service to engage appropriately with the universities for clinical research and to ensure appropriate governance and quality assurance for clinical research taking place outside the CRF/Cs. Despite the significant clinical research efforts being made by a variety of healthcare staff, the lack of acknowledgement of clinical research as a core driver of quality improvement within a healthcare system, at a managerial level, acts as a further barrier to the enhancement of clinical research in the health service.

The development of research governance and support structures in the health service to manage and facilitate engagement with both the commercial and university sector is critical to enhance clinical research, to enable alignment of activity with service priorities and to further integrate clinical research into healthcare delivery. Resources must be provided to hospital sites to provide research governance, oversight and support. At a minimum, each Hospital Group should have a resourced research office with capacity to register, monitor and oversee research.

Additional personnel (dedicated individuals and committees) and information management systems are required by the research offices to implement sufficient research governance and oversight procedures. The systems will be required to register research for approval and reporting purposes, to capture consent and to anonymise data so that it can be shared.

For timely hospital corporate sign-off of studies to take place, resources will need to be in place to facilitate a number of specialties including legal, finance, data protection, Intellectual Property, tech transfer, monitoring and quality management. Hospital-based researchers will also require increased access to statistical supports, journal access, data protection training and PPI training.

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It is necessary to build a robust framework to support our nascent research culture within the health service with coordinated educational activities for all managers and identification of local champions of clinical research. The delivery of unit level research targets and metrics should be measured and reviewed at a senior managerial level with research related funding awarded relative to degree of research activity.

RECOMMENDATION 4.1
The development of a research governance framework for the health service to facilitate clinical research activity and to enable further integration of clinical research into healthcare delivery.

RECOMMENDATION 4.2
Each Hospital Group should have a resourced research governance office with capacity to register, monitor and oversee research.

RECOMMENDATION 4.3
To cultivate a clinical research culture within the health service.

In 2006, the HRB commissioned Professor David Mant of the University of Oxford, to write a report entitled ‘Primary Care R&D in Ireland’. The report succinctly outlines the very strong case for supporting primary care R&D including the following:

- Primary care is central to the health system and patient care and is where over 90% of all patient contacts occur
- Most serious disease presents first in primary care and most minor illness is treated entirely in primary care
- Chronic illnesses are treated mainly in primary care
- Most preventive care is provided in primary care, and
- Much of the required evidence for the above activities can therefore only be provided in primary care.

In 2008, the HRB Centre for Primary Care Research at RCSI was established. With its successful second phase of funding, the Centre has continued to lead on work with national and international impact, focusing on patient safety in terms of prescribing, ICT diagnostic and therapeutic approaches and clinical prediction rules. It has successfully supported the career development of a new generation of primary care researchers. The HRB Clinical Trials Network Primary Care Ireland was established in 2015 at NUI Galway. The network aims to improve individual patient health and healthcare by conducting high quality, internationally recognised, randomised trials in Irish primary care, addressing important and common problems. In its first three years, it has supported as many trials as were conducted in Ireland in the previous eighteen.

The importance of primary care R&D is widely recognised and accepted. Research support structures developed in the hospitals must be extended to primary care, community services and to public health and health services research at a Hospital Group level and supported by the CRF/Cs. For effective national and cross-service research to take place, the introduction of community-based research lead roles will be important.

**RECOMMENDATION 4.4**  
Research support structures should be implemented for community and health services research.

**RECOMMENDATION 4.5**  
Establish the role of community-based research lead.

4.1.1 Paediatric Clinical Research  
With the largest proportion of young people among the EU Member States accounting for more than one in five (21.9%, Eurostat 2016) and specialist paediatric healthcare centralised in a small number of hospitals, Ireland is ideally placed to conduct paediatric trials. There is a very positive engagement from families in paediatric clinical research and a very high participation rate in clinical trials and non-interventional research compared to the adult population. Recent years has seen a significant increase in the level of research activity.

Hospitals that are currently active in this paediatric clinical research include the following Children’s Hospitals: Our Lady’s Children Hospital Crumlin, Children’s University Hospital, Temple Street and National Children’s Hospital at Tallaght as well as paediatric departments at regional hospitals. There are many specific paediatric clinical trial networks.

One of the most active clinical research areas within paediatric trials in Ireland is in oncology and haematology. A ‘shared-care model’ operates here in Ireland with Our Lady’s Children’s Hospital Crumlin providing the specialist care for children and young adolescents with cancer. Following initial assessment and treatment, children who can return home will have their care provided locally, per agreed protocols, with input from the specialists at Crumlin hospital. In many cases, where standard of care treatments are not appropriate for these patients, suitable clinical trials are investigated and where possible, the oncology and/or haematology clinical research teams will open these trials in Ireland so as to obtain for their patients (even if it is just 1 child or adolescent) access to new treatments.

4.2 Academic Clinical Research  
4.2.1 Universities – Clinical Research Facilities and Centres (CRF/Cs)  
A significant portion of the investment in clinical research in Ireland over the last 15 years has been in the development of the university based CRF/Cs across the country. There are currently eight - see Appendix IV. The aims of the CRF/Cs are to provide the infrastructure, physical space and facilities, experienced research and specialist support staff and the necessary quality and oversight programs that are critical for the successful conduct of world class clinical research. Research is delivered across numerous clinical specialties in all of the CRF/Cs. With the recent reorganisation of health services into Hospital Groups, each with an affiliated university containing a medical school, a ready structure exists in which to further develop research support services.
The rationale for this is further supported by the discussions with the SCA to recognize the CRF/Cs as designated entities covered by the CIS. The term CRF will be used as a specific designation for the unit fulfilling this purpose, however, different universities may refer to their specific CRF/C by different titles.

As detailed earlier, there are currently eight CRF/Cs located throughout Ireland at different stages of development with a range of funding models in operation. Programmatic funding is provided by the HRB to the facilities in Cork, Galway and Dublin and St James’s Hospital. This funding is generally core funding related to the costs of the physical infrastructure and core staff for a limited timeframe. The centres in UCD (St Vincent’s and Mater Misericordiae University Hospitals), Crumlin (National Children’s Research Centre), RCSI Beaumont and Limerick (HRI Clinical Research Support Unit) are all supported primarily by their own local universities or organisations and do not receive significant core funding from national government. Recognition of research as a core clinical activity underpins the need for permanent core funding of the CRF/Cs along similar lines to any other clinical department.

Core funding for the CRF/Cs would allow for the recruitment of long-term staff, the development of a research career structure and the ability to contractually commit to long term projects with the necessary personnel employed to provide expertise to these studies. Funding from other sources (e.g. grants) could then be directed to other elements of the research studies ensuring that all studies have the necessary resources to carry out the research effectively. The core funding would support and protect the central essential elements of the CRF/Cs and ensure the persistence of an organization with sufficient corporate memory and attributes as to allow for timely upscaling as and when activity levels increase.

**RECOMMENDATION 4.6**

*Each Hospital Group-affiliated university should be funded for a clinical research facility that facilitates the conduct of clinical research within the hospital group as an essential core clinical service.*

Given Ireland’s small size, it is neither necessary nor desirable that all of the CRF/Cs would provide the entire range of potential research supports and services to all customer segments. There is a strong rationale and clear efficiencies of scale in each of the CRF/Cs developing Clinical Trial Coordination Units (CTCU) with specific expertise in specialist services such as data management, regulatory affairs or pharmacovigilance (not all specialist services developed in all CRF/Cs), in addition to the common core competencies shared by all CRF/Cs. This would ensure the adequate development of the service and training of specialist staff, and allow for horizon scanning and business development both nationally and internationally. It is essential that staff with sufficient knowledge and experience in the specialist service area, are embedded within the other individual CRF/Cs to promote engagement, efficient communication and the seamless integration with the specialist service nationally. To avoid the negative impact arising from a monopoly due to a lack of competition and to ensure a minimal degree of redundancy to protect against unexpected failure or collapse of a CTCU for any reason, it is reasonable that most critical specialist services be established in at least two CRF/Cs.
Funding for CTCU providing such specialist services should be provided as core funding. The business model as to how any two such specialist services interact will likely vary with the specific type of service.

Extensive costs are associated with and research supports are required to establish research at other hospital sites including private hospitals. Hospitals with CRF/Cs should link with and share expertise and resources with other hospitals in their respective Hospital Groups. This would allow a larger number of hospital sites to engage in regulated research more easily and efficiently. Research leads for nurses/midwives, doctors and allied health professionals in the other hospitals should be identified to support research projects at local level; this could include an increased volume of staff with dual appointments and increasing the scope of these roles beyond doctors.

**RECOMMENDATION 4.7**
Clinical Trial Coordination Units providing specialist services should be established, with specific expertise in at least two Clinical Research Facilities/Centres and these services should be available to all Clinical Research Facilities/Centres and researchers in all hospitals across the country.

**RECOMMENDATION 4.8**
Clinical Research Facilities/Centres should share expertise and resources with other hospitals in their hospital groups to facilitate the establishment and conduct of research studies.

**4.2.2 Translational Research Laboratories**
Translational research brings scientific discoveries from the laboratory and translates them into treatments for patients, bridging the gap between more basic biomedical research and clinical research. Every university has laboratories, research facilities and research groups focusing on translational research.

The expansion of translational research has been driven both by the researchers who want to develop their research into treatment for patients and by the funding agencies who have increasingly directed funds towards translational research, in response to the National Research Prioritisation Exercise\(^3\). The report of the National Research Prioritisation Exercise, published in 2012, focused on fourteen priority areas positioned within six broad enterprise themes. Major funders, such as Science Foundation Ireland, redirected the majority of their funding towards research in these 14 priority areas. The prioritisation exercise was updated in 2018 and the health theme has been renamed Health and Well-being which includes four priority areas: Connected Health and Independent Living, Medical Devices, Diagnostics, and Therapeutics. As a result of the expansion of translational research, there is a need for Phase I facilities in Ireland to adequately deal with the anticipated volume of such work arising from translational projects nationally.

**RECOMMENDATION 4.9**
Establish two Phase I facilities in Ireland

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4.2.3 Clinical Research Networks
Academic clinical research networks in Ireland are groups of clinicians and scientists from across Ireland who have come together to conduct research around a particular disease/therapeutic area, or clinical interest.

A large number of clinical research networks have been established in Ireland. The HRB provides funding to the Cancer Trials Ireland network and in recent years has funded the establishment of four new clinical trial networks in the areas of stroke, critical care, perinatal care and primary care (Appendix V). There are many more networks in existence in Ireland. Some rare diseases have a high prevalence rate in Ireland and there is much ongoing clinical research into these disease areas. There are major challenges for these networks in terms of sustainability of funding with some networks receiving programmatic funding from the State and others from charities. Long-term funding is required.

Closer working relationships between the networks and CRF/Cs is desirable and would aid in identifying how and where to resource staff or specialized services. A cross-function core group with the necessary integrated skill and expertise could be developed to promote the success of the thematic group. The networks’ specialist staff (data managers, biostatisticians and monitors) would also be members of a larger professional grouping within the CRF/Cs rather than working individually in isolation. To avoid developing multiple redundant parallel structures outside the CRF/Cs, the patient facing activities of the networks could be optimally conducted via the CRF/Cs. There are exceptions to this where specific qualifications, substantial expertise or work experience is required in order to efficiently conduct the research e.g. cancer nursing. In such cases, the necessary staff could either be employed within the thematic network or by the CRF/Cs. There is also a requirement and benefit to separately fund and support the specific scientific leadership groups that oversee and guide the development of each network. Once a network has been awarded funding through a competitive funding process, the funding should be subdivided to fund the leadership of the thematic network to develop and oversee the work and to the CRF/Cs (either directly or indirectly) for the staff conducting the actual research.

__RECOMMENDATION 4.10__
Long-term core funding is required to develop and maintain academic clinical research networks.

__RECOMMENDATION 4.11__
Better integration and collaboration of the academic clinical networks with Clinical Research Facilities/Centres is required to enhance the network’s thematic research.

__RECOMMENDATION 4.12__
Awarded funding for networks should be subdivided to fund the leadership of each network to support the development of the research and to the Clinical Research Facilities/Centres to carry out the research.
4.3 People involved in Clinical research

4.3.1 Patients and Public

The democratisation of research, with the proactive engagement and involvement of patients and the public at all levels of research planning and conduct, is critical to the long-term success of the Irish research environment. Active involvement of patients and the public in the clinical research process enables researchers to better understand patients’ priorities, to co-design processes that are participant friendly and to improve access, understanding and participation, so that Irish patients become an equal partner in the process of discovery. Significant investment and developments in Public and Patient Involvement (PPI) in clinical research commenced in earnest in 2016, as Ireland sought to mirror the achievements of other countries.

Research carried out by the HRB identified clear evidence of gaps that needed to be filled to better support PPI in Ireland and as a result the HRB and the Irish Research Council (IRC) jointly funded the PPI Ignite Awards. The PPI Ignite Awards aim to support and promote capacity building for high quality PPI in health research (across all health research and social care disciplines) and represents an investment of nearly €2 million over three years across five academic research settings. Meanwhile since 2016, IPPOSI has partnered with HRB CRCI on the topic of PPI specifically in clinical research. A working group consisting of IPPOSI board members, the network of CRF/Cs in Ireland, MRCG, as well as, HRB CRCI and IPPOSI representatives was established to work collaboratively on a number of activities under the HRB CRCI and IPPOSI umbrellas, to promote active PPI as part of the infrastructure for clinical research in Ireland.

The mission of the Clinical Research PPI Working Group is to facilitate cooperation and sharing within the member organisations with respect to PPI knowledge, resources, training and innovation. These national developments are now beginning to bear fruit with a host of PPI training courses, and materials (including a repository of PPI information) coming on stream to support clinical investigators as they seek to embed PPI into clinical research in Ireland.

In addition to involving patients and the public in research planning, it is necessary to take steps to encourage and facilitate the recruitment of patients and members of the public to clinical studies. The HSE should consider establishing, within its patient charter, the provision that all patients, regardless of location, age or social circumstance, should have the right to be informed about a clinical trial or research project which may benefit them. This would require a searchable national registry of trials and clinical research which can be assessed by patients, their families or by a research liaison officer. A public information campaign, to explain the value of clinical research and what to expect in the consent process would also be very valuable in preparing patients and the public for an increase in clinical research activity.

RECOMMENDATION 4.13
Clinical Research Facilities/Centres should have a designated Public and Patient Involvement lead, to embed the importance of Public and Patient Involvement in all phases of the planning and undertaking of clinical research.

RECOMMENDATION 4.14
Training in Public and Patient Involvement should be provided to clinical researchers, other clinical research support roles and to patients interested in being involved in research planning and decision-making.
RECOMMENDATION 4.15
Establish a public-facing national registry of active clinical trials and research that can be utilised to inform patients and the public of research which may benefit them.

RECOMMENDATION 4.16
A public information campaign should be undertaken to inform people of the value of clinical research.

4.3.2 Clinical Research Staff
The conduct of high quality clinical research requires a wide variety of highly trained and specialist roles such as clinical research nurse, clinical investigator, study coordinator, data entry technician, clinical trial pharmacist, clinical research associate, clinical trial monitor, clinical project manager, clinical trial manager, data manager, bio-statistician, pharmacovigilance officer, methodologist, quality and regulatory manager.

Clinical research roles are generally funded through programmatic funding or individual study funding, rather than through core long term or permanent funding which limits the career pathways for those involved in clinical research and makes it difficult to retain staff. With the development of the national infrastructure i.e. CRF/Cs and national thematic networks, more secure roles and career paths have developed but the majority of this infrastructure is also funded through programmatic funding (generally three-year terms) rather than long term funding which is problematic in terms of career paths.

RECOMMENDATION 4.17
Core funding to provide career pathways for specialised staff required for clinical research.

4.3.3 Protected Time for Clinical Research
Healthcare staff such as consultants, non-consultant clinicians, advance nurse practitioners, physiotherapist, General Practitioners and pharmacists should have protected time for research e.g. for a day a week over a two-year interval. Currently, clinical teams are overburdened which affects patient recruitment to research studies and negatively impacts the quality of research. There are no mechanisms available to enable the involvement of healthcare staff in research activities.

Protected time for research was historically an accepted element of the consultants’ work and responsibilities under the terms of the consultants’ contract. However, modern work practices and scheduling requirements have rendered this provision meaningless in the absence of formal protected time and adequate backfill. The HSE should re-address this provision by supporting within a university hospital a backfill position that could cover such a buy-out for general medical activities for a number of clinicians. An approach similar to that of the UK where clinicians are able to avail of protected time and this is taken into account by way of their banding (pay scales) could be appropriate. A backfill position could be an attractive early career option for newly qualified specialist registrars providing their first initial experience at a consultant grade or for newly commencing consultants with a strong track record in research. Protected time for research would enhance the attractiveness of healthcare posts.
4.3.4 Clinical Research Nurses/Midwives

The International Association of Clinical Research Nurses (IACRN) describes clinical research nursing as a speciality practice that centres on the care of the research subject whilst at the same time ensuring adherence to the protocol. In addition to the protection of subjects and advocating on their behalf, the role also encompasses project management, protocol development, ethics and regulatory submissions, budget negotiation and grant application, amongst others4.

In the past decade, the number of clinical research nurse/midwife (CRN/M) posts has also increased, although it is not known how many research nurses/midwives work in Ireland due to the different employment structures. Many CRN/Ms work in the established CRF/Cs that are affiliated to academic institutions (and their contract of employment is with a university). The CRN/Ms employed by a CRF/C either work in the CRF/C itself or in a public hospital setting. Other CRN/Ms are based within hospitals working independently of these research units, as well as in primary care, clinical trials networks, research charities and private companies.

The challenges facing the CRN/Ms population in Ireland have been well documented in previous publications. The Report on the Role of the Nurse or Midwife in Medical-Led Clinical Research (2008) made a number of recommendations which included the need to develop a career pathway for CRN/Ms, identification of standardised job titles, roles and responsibilities, identification of CRN/M competencies and appropriate orientation to the CRN/M role5. Unfortunately, there has been little change following this report. Furthermore, many CRN/M posts are associated with grant funded research and are often short-term contracts, which offers limited job security. CRN/M contracts are often temporary roll over contracts and there is currently no national consensus on salaries which has led to a huge variance in salary structures. As many CRN/Ms hold their employment contract with a university; their terms and conditions of contracts to their counterparts employed through hospital/HSE contracts. These factors have a direct impact on nursing and midwifery recruitment and retention which ultimately risks both patient safety and the ability to deliver clinical studies. While there have been advancements in training and development opportunities for CRN/Ms in recent years, there is a lack of coordination of education for CRN/Ms at undergraduate and post-graduate level.

However despite the challenges, CRN/Ms enjoy the autonomy and diversity that the role offers and the knowledge that they play a key role in the delivery of high-quality research6.

There is a pressing need to establish a clear career structure and recognition for the unique role of the research nurse/midwife as well as research specialists. A process needs to be established to allow for temporary secondment of nurses from full time clinical jobs to a full time or shared research position, without loss of salary or pension. To oblige clinical staff to resign from the HSE in order to undertake research training and experience is unwise. Allowing secondments will facilitate further training of staff and a greater exposure to formal research activity which will in turn facilitate a gradual cultural change in the existing perception of research as a clinically irrelevant activity.

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The secondment of clinical healthcare staff is especially vital in research based around clinical services that operate on a 24/7 basis – such as in the emergency department or critical care units - where it is not logistically feasible to deploy independent research nurses/midwives on a 24/7 basis in order to capture episodic events of interest.

The Irish Research Nurses Network (IRNN) is currently completing a scoping and evaluation exercise for CRN/Ms. This project is funded by the Health Research Board (HRB) and the findings and recommendations from the project will be published by the end of 2019.

**RECOMMENDATION 4.19**
Clinical Research Nurses/Midwives should be embedded into HSE supported posts in hospitals in an acknowledged career pathway with appropriate salary scales, reporting lines and clear responsibilities.

**4.4 Commercial Clinical Research**
4.4.1 Pharmaceutical industry
On a globally comparative basis, the biopharmaceutical industry has a very large manufacturing footprint in Ireland that continues to grow. In contrast, the number of interventional clinical trials carried out in Ireland is low.

Ireland’s foreign-owned pharmaceutical companies directly employ 30,000 people, with similar numbers working in spin-off jobs. Ireland hosts 75 pharmaceutical companies, including the top 10 in the world. Ireland manufactures five of the world’s top 12 medicines. Over the past 10 years, the pharmaceutical industry has invested close to €10 billion in manufacturing and research sites around the country. This represents close to the biggest wave of investment in new bio-technology facilities anywhere in the world. Between 2003 and 2018, the number of biotechnology manufacturing sites jumped from two to 207.

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Ireland is the largest net exporter of pharmaceuticals in Europe and the seventh largest in the world. The pharma-chemical sector maintained its position as the largest exporter of goods from Ireland in 2017, with record total exports of €68 billion, an increase of 2% on the previous year.

The chart below shows how Ireland compares with other EU countries by the value of pharmaceutical product exports7.
In the context of global clinical trials, the population of Ireland (and hence the number of potentially eligible clinical trial participants) is small at approximately 4.8 million inhabitants. Furthermore, healthcare in Ireland is delivered through a large number of separate institutions (e.g. GP practices and hospitals), thus increasing the logistical complexity of accessing these patients to potential clinical trials.

The number of interventional clinical trials conducted in Ireland is far lower than would be expected given the footprint of the pharmaceutical industry here. There is a paucity of centralised data sources from which to gather data. A search of ‘industry funded’ and ‘interventional’ studies currently ‘recruiting’ on clinicaltrials.gov (9 April 2019) showed 128 studies for Ireland, 376 for Denmark, 480 for Israel and Belgium 737. In 2007, the HPRA approved 114 interventional clinical trials, 102 in 2013 and it reduced to 96 in 2017. These numbers comprise both ‘company-sponsored’ and ‘investigator-sponsored’ studies. Denmark, with a similar sized population to Ireland, conducts approximately 300 new interventional clinical trials each year.

The research-based pharmaceutical industry in Ireland currently struggles to attract allocation of company-sponsored global clinical trials. The key imperatives for conducting global clinical trials are:

- overall patient enrolment numbers
- reliability in attaining recruitment targets within agreed timelines
- quality of data captured in clinical trials
- costs

Compared to many other countries, clinical research in Ireland is not prioritised as a key component of routine healthcare delivery. As such, it is confined to pockets of activity within a highly fragmented infrastructure. Ultimately, global pharmaceutical companies will allocate clinical trials to countries that reliably and consistently deliver quality data from patients enrolled into clinical trials in a timely and predictable manner.
The CRF/Cs and HRB-CRC should continue to support feasibility assessment, setup and conduct of pharma studies. There are several important reasons for supporting the conduct of industry funded research in Irish hospitals including not only access to new interventions, but critically, as a means of increasing the research readiness of different clinical specialities. It is a cost-effective way of training investigators and staff in the conduct of regulated research, in order to allow for maintenance of staff and activity levels in a setting of variable and unpredictable funding from academic projects. It provides access to new medications but also experience with generic versions of established treatments which may encourage their adoption. The ratio between academic and industry funded studies varies between centres and over time, depending on available volume of academic work, but is likely to fall within the range of 30-60% depending on circumstances. To be competitive, we must focus on quality, reliable efficient setup and approval processes and predictable delivery to target and on time.

**RECOMMENDATION 4.20**

Clinical Research Facilities/Centres to support pharma-sponsored clinical research with a focus on data quality, patient recruitment and efficient site setup.

4.4.2 Medtech industry

Ireland is currently ranked as one of the top five hubs for medtech and has a proven reputation for supplying highly innovative and dynamic technologies, products and services to the global markets. The Irish medtech sector operates across four key areas:

1. medical sub-supply
2. finished medical devices
3. diagnostics, and
4. the rapidly growing digital health.

IDA Ireland data shows that the sector currently employs +37,000 people in Ireland and has annual exports of €11.2 billion.

The medtech sector within Ireland is a diverse ecosystem, with companies of various size and scale operating in what is a dynamic and competitive marketplace. 60% of these medtech companies are indigenous Irish companies, of which 80% are SMEs.

To secure their agility and their longevity, over 60% of these Irish medtech companies have actively invested in dedicated in-house R&D supports. Further investment supports have been introduced via various government initiatives; BioInnovate Ireland, Enterprise Ireland / IDA Technology Centres, Health Innovation Hub, BioExcel etc to sustain a culture of innovation, collaboration and commercialisation in Ireland so that the sector can continue to grow, compete and diversify.

However, innovation within the industry brings significant pressures on the regulatory authorities to provide guidance and support on the requirements and procedures for conducting clinical research on new technologies and products across the sector. In addition, the changing regulatory landscape within the EU for medical devices, digital health offerings and in vitro diagnostics (Medical Device Regulation (MDR) 2017/745 and In Vitro Device Regulation (IVDR) 2017/746) dictates that all companies must comply with stricter regulation and data collection requirements from 2020 onwards.
This current environment presents a significant challenge for all medtech companies but especially for Ireland’s SMEs that are newly formed and with no direct experience in achieving certification marking or regulatory approval. In recent years, SMEs have benefited from the guidance and direction of HRB-CRCI’s Clinical Industry Liaison Officer and Quality and Regulatory Affairs Manager. Further development of these roles and this service is needed in partnership with the universities. There is a substantive gap in the resources available to SMEs with regard to the technical development of the device under the remit of a quality system that meets the requirements of the competent authority and notified body.

Funding and support should be provided to one or more third level institutions to allow them to partner with SMEs in either using a university quality system, or in developing a bespoke system with the assistance of the university, under which to develop the device. Given the broad diversity of medical devices, different universities might plausibly focus their support on different types or classes of devices. This would allow SME and ‘academic spin out’ companies to partner with the universities under the terms of an appropriate IP sharing agreement and allow for the timely and efficient development of the device prototype in a regulatory compliant fashion. Universities should furthermore acquire insurance to indemnify appropriately developed and fabricated prototypes to be used under stringent supervision in proof of concept Investigation (effectively first in human clinical investigations of the medical devices) prior to forwarding the prototype for large scale production by a manufacturing company for use in a definitive clinical investigation.

Despite the largescale presence of medtech companies in Ireland, there is relatively little engagement between these companies and Irish clinicians. This disconnect can have a direct cost burden on companies who must spend additional time and money sourcing clinical partners abroad to conduct their trials. This issue could be addressed in part by a scheme promoting such interactions, facilitated by HRB CRCI and the Clinical Industry Liaison Officer. Establishing such a dialogue would increase visibility of Irish Investigators and may underpin the development of future interactions, such as hosting an advisory board or meeting with Irish clinicians coincident with a visit from company senior management to the plant.

Ultimately, a clinical research network within Ireland which is more strategically aligned to the requirements of industry would benefit the medtech ecosystem, and further elevate Ireland’s ability to compete effectively in global markets.

**RECOMMENDATION 4.21**
Investment required in the clinical expertise within the current Clinical Research Facilities/ Centres to conduct clinical investigations, specifically Phase I clinical trials.

**RECOMMENDATION 4.22**
Further development of Clinical Industry Liaison services provided by HRB Clinical Research Coordination Ireland to Small and Medium-sized Enterprises (SMEs), including linking SMEs with appropriate clinicians.

**RECOMMENDATION 4.23**
Provision of funding to third level Institutions to partner with SMEs in the development of devices under the remit of a certified quality system.
4.4.3 Notified bodies

The NSAI is the only notified body designated by the HPRA under the medical device directives in Ireland. While the HPRA is responsible for reviewing applications to conduct clinical investigations of medical devices in Ireland, the notified body reviews the output of those investigations as part of the technical file review. Notified bodies may issue a CE certificate if the device meets all of the necessary requirements of the relevant legislation allowing commercialisation of the device in the EU. Manufacturers in Ireland are free to use any notified body designated by a European competent authority.

The Medical Device Regulation (MDR)\(^8\) will replace the existing Medical Devices Directive (93/42/EEC) (MDD) and the Active Implantable Medical Devices Directive (90/385/EEC) (AIMDD). The MDR was published in May 2017, marking the start of a three-year period of transition from the MDD and the AIMDD. During the transition phase, products certified under the directives and products certified under the regulation will coexist on the market. Both will have equal status under the law, and no discrimination on eligibility criteria in public tenders may take place.

The new regulation reinforces the requirements for clinical evaluation, introducing some of the biggest changes compared to the previous regime. As under the directives, it includes the collection of clinical data already available in the literature as well as the setting up of any necessary clinical investigations. The concept of equivalence with other devices for which clinical data already exists can still be used, but only in a limited number of situations, and the new rules are tighter. The regulations set out the new and more precise requirements for clinical investigations. With only certain exceptions, implantable and Class III medical devices must now go through clinical investigations. For all Class III devices, and for Class IIb devices intended to administer a medicinal product (or remove it from the body), the manufacturer has the option to consult a group of European experts to obtain an upstream review of its intended clinical development strategy.

These changes in medical device regulation are impacting on resources with both notified bodies and medical device manufacturers seeking suitable experienced personnel. Adequate staffing and expertise is required across the European notified bodies’ network to fully support the needs of all Irish based medical device companies. Additionally, increasing the capacity of the Innovation Office in the HPRA to provide support to both clinical trials and clinical investigations is necessary. Assistance with protocol review has been identified as of particular interest.

**RECOMMENDATION 4.24**

The Health Products Regulatory Authority should be resourced to respond to increased activity in clinical trials and clinical investigations in Ireland and the rest of the EU.

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4.4.4 Contract Research Organisations

There is an active Contract Research Organisation (CRO) industry in Ireland with a number of CROs providing support to the pharmaceutical, biotechnology and medical device industries in the form of research services outsourced on a contract basis. While CROs can provide a large range of services, many specifically provide clinical-study and clinical-trial support for drugs and/or medical devices. In Ireland, there is a significant presence of CROs ranging from larger, international full-service organisations to small niche specialty groups. However, while many CROs are headquartered here, their clinical trial work is predominantly carried out abroad.

An opportunity exists to increase the amount of CRO clinical trial work carried out in Ireland but not until the necessary enhancements to the resources, expertise and regulatory environment for clinical research have been made. Many CROs based both within and outside of Ireland have engaged with HRB CRCI for its feasibility service. When CROs carry out a study feasibility assessment in Ireland they may be at the bidding stage with the sponsor company and may not necessarily be successful in the bid. This can result in a number of studies not progressing beyond the feasibility stage. If CROs and industry sponsors are operating from outside of Ireland, their local site, investigator and systems knowledge can be limited and sometimes out of date. Support services such as those provided by HRB CRCI can improve the situation and add significant value to the system.

4.5 Training and Education

A number of the universities in Ireland offer postgraduate courses in clinical research. Many of the CRF/Cs also provide training courses in ICH GCP for IMP and medical devices and sponsorship responsibilities among others.

The HRB-TMRN has a strong remit in education and provides a range of courses, conferences, webinars etc. primarily in trial methodology as well as providing some PhD scholarship programmes across the partner universities.

The CRDI Education and Development Team coordinate key cross-institutional training programmes and online resources to support clinical research. The Wellcome-HRB ICAT Programme is an all-Ireland integrated academic and clinical training track with a multi-partner investment of over €16m to support five annual intakes of ICAT Fellows identified through a rigorous selection process. The ICAT partnership comprises six academic institutions (QUB, TCD, UCD, NUI Galway, RCSI, UCC), two health services (HSE NDTP, HSC R&D) and postgraduate medical training bodies in RoI and NI. CRDI short courses provide skills to researchers from PhD to clinical investigator level; these include ‘Techniques & Strategies in Molecular Medicine’ (running annually since 2003) and the online module ‘Case Studies in Drug Discovery and Development’. CRDI also coordinates the HRB Neonatal Encephalopathy PhD Training Network, which is developing clinical researchers in this neglected area. CRDI is a partner in the European Erasmus+ training network ‘Curriculum Development of Human Clinical Trials for the Next Generation Biomedical Students’.

E-Learning is a focus of CRDI’s partnership with CÚRAM working closely with the HPRA, NSAI and industry. In addition, CRDI is developing a ‘MedTechTranslate’ online interactive portal that will support medical device developers with stage-of-development focused regulatory information together with clinical support for device development and trials. However, while many CROs are headquartered here, their clinical trial work is predominantly carried out abroad.
The Irish Medtech Skillnet, a training network for the medtech and engineering sectors, have developed a comprehensive training offering for the medtech sector in the area of quality and regulatory affairs. Key programmes include a Masters in Medical Technology Regulatory Affairs, a BSc in Quality & Regulatory Affairs for Medical Technology and a Fundamentals in Regulatory Affairs for Medical Technology which run annually and nationally. To date, over 500 medtech professionals have been upskilled through these programmes.

Cancer Trials Ireland also offer specialised training to clinical research staff and investigators and hospital research staff such as ICH GCP at introductory and refresher level, relevant legislation such as clinical trials regulations, data protection related to health research, and diseasespecific/therapeutic area training among others. Principal Investigators are trained to ensure that the responsibilities associated with the role are understood and agreed. Continual and standardised training and education in these areas is vitally important for all stakeholders due to frequent updates in regulatory requirements and guidelines and the need to develop procedures in order to be compliant with the requirements. Other opportunities such as research team development events are offered through workshop settings where relevant topics may be chosen by the research teams for training or information sharing with discussion and consensus-building on approaches to take. Such events are also important for generating partnerships between research organisations and hospital research staff in the conduct and management of research studies and clinical trials.

To provide training for healthcare staff in the healthcare system, dedicated modules on the fundamentals of clinical research should be provided in nursing/midwifery, doctors and allied health professionals training programmes.

Despite the career opportunities in the academic sector and increasingly in the private setting, the educational and training pathway for clinical research specialist staff is disjointed and not responsive to these career opportunities. For example, despite a marked absence of biostatisticians to meet the needs of either academic or commercial research, there is no formal training programme for biostatisticians in Ireland. Formal engagement between the Department of Education, universities, enterprise sectors and commercial partners should examine and respond to these deficits in a coherent fashion and ensure adequate supply of appropriately trained specialist staff. A suite of tailored training programmes and courses should be developed for those engaged in all aspects of clinical research. A number of key areas have been identified for the development of new or enhanced training courses such as biobanking, data protection, ICH GCP, regulatory and ethical requirements for the medtech industry and SMEs.

**RECOMMENDATION 4.25**
All stakeholders should examine and respond to the deficits in training in specialist areas of clinical research to ensure an adequate supply of appropriately trained specialist staff.

**RECOMMENDATION 4.26**
National coordination is required to ensure a comprehensive suite of training is available.
4.6 Information Management & Technology Infrastructure

4.6.1 Challenges of IMT infrastructure for Clinical Research

The clinical research Information Management & Technology (IMT) infrastructure in Ireland is site or study specific, with little use of common or central systems and services.

In the healthcare system, there are a disparate range of patient and associated information systems in use and an almost total lack of integration or sharing of data between these hospital systems. There does exist some national, shared systems that can be accessed across different sites. These are, however, in certain disease specific areas, such as epilepsy or maternity care and are not specifically designed or permitted to be used in the research sector. Access to patient systems (paper or electronic) is obviously heavily restricted for research staff.

Within the CRF/Cs, each has different levels of expertise and resources in the area of IMT and little use of shared systems across sites. Some of the CRF/Cs are starting to provide clinical data management services to investigators and studies that are sponsored by the host institution or where the study PI is located at the site. Most commercially sponsored clinical trials will come with a dedicated Clinical Data Management System (CDMS), however, academic and investigator led studies for the most part need to source and develop a CDMS solution for their study data. The task of finding and developing a suitable CDMS solution is dependent on the funding available to the study and the level of such funding is normally neither planned nor allocated with sufficient level of understanding of the requirements.

One exception to the shared system issue is the CRF Manager system, which is in use at all of the CRF/Cs. CRF Manager is a centrally supported cloud-based system which allows CRF/Cs to manage their clinical research studies, resources and recruitment. However, the capabilities of CRF Manager are underutilised in most cases, for various reasons. This system is designed to manage the running of studies at the CRF/Cs and does not address the need for patient clinical data collection and management.

The challenges faced by CRF/Cs and investigators relating to IMT stem from the lack of available resources that can be utilised to aid the effective and accurate management of data collected during a research study. There is a lack of available expertise to advise and work with study teams during the life cycle of a study. No centralised facility for data management means no common, reusable tools can be developed and made available for future studies.

A database of study type and patient participation in studies is also required to ensure that patients do not ‘over subscribe’ to studies and to allow for future analysis and comparison of study findings where the patient cohorts are similar or overlap.

Issues related to the use of patient data in research are addressed elsewhere in this report.

RECOMMENDATION 4.27
Electronic Health Records are required throughout the entire healthcare system.

RECOMMENDATION 4.28
Individuals resident in Ireland should be assigned an Individual Health Identifier.
RECOMMENDATION 4.29
In advance of implementation of the above, any existing Information Management and Technology systems should be reviewed and leveraged where possible.

RECOMMENDATION 4.30
Electronic Health Records should be designed with input from clinical research experts to ensure they can be utilised for clinical research.

RECOMMENDATION 4.31
Implement a centrally funded, resourced and supported Clinical Data Management System available to investigators and sponsors to utilise for study data collection and management.

4.6.2 Virtual Trials in Ireland
A significant opportunity exists for the adoption of virtual trials in Ireland. Such trials exploit IT solutions to address some of the traditional accessibility obstacles for patients with chronic diseases and which can useful for less complex interventional and observational studies. For patients, improved trial accessibility can expand clinical care options, and boost retention. For clinical investigators, the ability to interact virtually with larger numbers of participants provides deeper insights from richer data, and data from remote monitoring devices could be accessed in real time, opening possible efficiencies in data cleaning. Remote monitoring capabilities could thus facilitate an adaptive clinical trial approach, allowing improvements in trial design based on the accumulating data. Decisions to terminate a drug’s development could also be made faster, improving patient safety and reducing expenditure on failed trials.

Finally, the virtual trial design may provide stakeholders with more opportunities to play an active role in the study, potentially leading to better data quality and shorter timelines. However, patient privacy, data protection and the interaction with patients with low computer literacy are considerations.

Adoption of emerging technologies can increase the chances of trial success through adaptive clinical trials, provide patient-centric trials, improve value-based care and facilitate remote trials for faster and more cost-effective outcomes. There is an opportunity for medtech, CROs and pharma companies to collaborate in Ireland.

4.7 Regulatory & Ethics Infrastructure
Before any patient is recruited to a clinical research study in Ireland, a number of approvals is required such as Research Ethics Committee (REC) approval, regulatory approval and hospital/organisational approval.

The RECs for clinical trials in Ireland are overseen by the Department of Health. There are 12 approved research ethics committees which can grant one central ethical approval for clinical trials of medicinal products which applies to all sites in Ireland approved by the committee. Regulatory approval for clinical trials is granted by the HPRA. Hospital/organisational approval for clinical trials is granted at each hospital site where the trial is being conducted.
For clinical investigations of medical devices, REC approval and hospital/organisational approval is required for every site where the study is being conducted. Regulatory approval is required for clinical investigations from the HPRA who issue a “letter of authorisation” for the study to proceed.

Non-interventional/observational studies require REC approval and possibly hospital/organisational approval dependent on the site. However, regulatory approval is not required for these studies. REC approval is required at every site where the study is being conducted. This can result in a requirement for multiple REC approvals for such studies which is resource-heavy and time consuming. At present, there is no central coordination of RECs in Ireland. However, it was announced in February 2019 that the Minister for Health is to prepare a General Scheme of a Bill to provide for a national research ethics committee.

Ahead of the implementation of a single national research ethics committee, for non-interventional/observational studies research, cross-recognition of the different ethics committees within a Hospital Group should be established. Therefore, only one committee within the group would need to conduct an ethics review of the study, although each participating hospital would still be required to approve the study for conduct within the hospital. This would avoid unnecessary duplication of work and speed up approval processes. Ultimately, this may develop into a single, appropriately resourced, professional ethics committee to cover all research within the Hospital Group and a national cross-recognition of ethics approval across Hospital Groups, at least for low risk research.

Developing a single national ethics review for medical device research would be especially valuable given the limited expertise in reviewing medical device applications which may delay the approval process. A legislative solution supporting a national ethics review of regulated medical device research would facilitate such research and increase the appeal of establishing such research in Ireland, while allowing for the development of appropriate expertise within the single coordination national REC.

**RECOMMENDATION 4.32**
A single coordinated national research ethics committee for clinical research providing approvals for clinical trials, non-interventional studies and with specialist expertise for review of medical device trials.

**4.8 Biobanks**
The biobanking landscape contains individual unconnected biobanks with no central searchable directory, no strategy for collections in the national interest, differing approaches of quality and governance across the biobanks with each biobank approaching the issues of consent and data protection differently based on their local ethics committees’ and Institutions’ legal advice. Multi-site studies involving sample collection must seek ethical approval from each local ethics committee in a cumbersome, resource-heavy manner.

Almost all biobanks struggle with sustainability once the initial funding has ended. There is a lack of understanding and infrastructure within academic institutions to allow for continuous core financing of established biobanks. Furthermore, there is a clear need to protect the researchers who establish these biobanks by providing access to an advisory system to counsel on sharing biological resources.
Biobanks often work together internationally to allow researchers to access large cohort information for specific diseases, with particular effect in the rare disease area, e.g. www.birthcohorts.net. This strategy of open sharing of data and collaboration has the potential to unlock molecular expressions and patterns of disease and to fast-track medical discoveries. Despite the huge amount of time, energy and funds that go into setting up a biobank, many biobanks are not fulfilling their true potential. The underuse of voluntarily donated and consented biological samples and data for research is a genuine ethical issue.

**RECOMMENDATION 4.33**

Dedicated funding should be provided to support the core running costs of biobanks, to support scientifically valuable repositories in long term storage after conclusion of the originating study, and to provide for central coordination across all biobanks.

Between 2006 and 2010, a number of reports, guidelines and initiatives for biobanking were published9 10 11 12 13 14 15 16 which have placed Ireland in a key position to move towards the creation of a national biobank. However to date, there is still no single national body in place to offer a clear direction regarding best practices, regulations and standards to existing and emerging biobanks. Furthermore, there is no national legislation or authority that governs biobanking in Ireland, such as the Human Tissue Act 2004 in the UK.

There is a strong desire within the biobanking community to see a formalised Irish approach to biobanking, capitalising on experiences and cooperative relationships gained by Irish national experts within ISO and the National Biotechnology Standards Committee. This committee was established in 2014 by the NSAI to provide expert and stakeholder input to the development of new international standards for biotechnology (ISO/TC 276) which include the recently published ISO 20387:2018 Biotechnology - Biobanking - General requirements for biobanking.

A national biobanking policy or strategy to act as a primary source for informing all biobanking stakeholders is urgently required. A policy to coordinate, network and promote successful management of biobanking in Ireland would offer support for biobanks and the end users; and foster a world-class translational research environment that will allow Ireland to be competitive in the era of multi-omic analysis, systems biology and personalised medicine. A national strategy would give clarity to Irish researchers and to funders to ensure they are compliant with the relevant regulations and adhering to standards and adopting an appropriate approach to governance.

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10 HEA and Forfás report ‘Research Infrastructure in Ireland – Building for Tomorrow 2007”
11 CIRCA group report to Enterprise Ireland, 2007.
12 Forfas: “Health Life Sciences in Ireland – An Enterprise Outlook 2009”.
15 Action Plan for Health Research 2009-2013 appointed a sub-group for biobanking to develop & implement a ‘National BioBanking Initiative’. As part of this work, the survey of biobanks in Ireland was carried out by Jan Guerin.
A significant opportunity exists for Ireland to become a full member of the Biobanking and Biomolecular Resources Research Infrastructure - European Research Infrastructure Consortium (BBMRI-ERIC) which is a European research infrastructure for biobanking bringing together researchers, biobankers, industry and patients to enhance biomedical research. Ireland can capitalise on the current strong Irish involvement in the development of ISO standards for biotechnology which incorporates biobanking. Ireland’s membership of ECRIN is coordinated by HRB CRCI through a European Correspondent. HRB CRCI could provide similar coordinating support to Ireland’s membership of BBMRI-ERIC.

**RECOMMENDATION 4.34**
A national biobanking policy should be developed to coordinate, network and promote successful management of biobanking in Ireland.

**RECOMMENDATION 4.35**
Ireland should join BBMRI-ERIC and develop a central agency or office to oversee the development of biobanking services in Ireland and other international biobanks.

### 4.9 Patient Registries
Health information in Ireland is fragmented and isolated impeding the advancement of clinical research. To compound the issue, patient registries, which can offer quality patient information to clinical research, are under-resourced in terms of funding, time and expertise. There are currently no funding streams in Ireland to support the development or maintenance of registries and expertise is limited. Rare diseases, some of which are more common in Ireland than other parts of the world, particularly suffer from a lack of registries resulting in an inability to capture information on prevalence or to identify patients for clinical trials.

HIQA hosts a catalogue of 122 national health and social care data collections. Some of these registries have been established as research projects while others are set up by the HSE to monitor and evaluate the health service. MRCG conducted a survey of patient registries in 2012 and found most registries operate on a national or regional basis and just over half register more than 100 new patients each year. Just under half of all registries follow patients from registration through to death and the majority (90%) record at least one outcome measure.

For the most part, registries have the same ethical, legal and societal issues as biobanks and registries established with programmatic research funding have similar sustainability issues.

**RECOMMENDATION 4.36**
The development of registries should be supported through a competitive, dedicated funding stream.

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17 See https://www.hiqa.ie/areas-we-work/health-information/data-collections
RECOMMENDATION 4.37
New registries should be developed in a way that they are interoperable with Electronic Health Records and other data sources. They should also have the capacity to be built upon over time to fulfil additional functions, including supporting the running of clinical trials and post marketing studies.

The MRCG have also published a guide to developing patient registries in 2018 and proposed that the future of registries in Ireland is increased collaboration and the sharing of resources between registries achieved through an independent national federation of registries acting as a trusted third party for patient health information. The collaboration of patient registries under one national infrastructure could offer enormous benefits, while at the same time allowing for individual registries to maintain their own independence and drive their own agenda.

An appropriately funded and supported federation of registries could support:

1) Registries being operated in a cost-efficient manner, through the sharing of common resources (research nurses/coordinators, statisticians) and expertise;

2) A coordinated and informed approach to tackling pertinent registry issues, from research ethics committee approval challenges to a lack of registry funding;

3) The development of guidelines for new and emerging registries, focused on topics such as ethics and privacy, data standards and quality, evaluation, governance structures and processes, etc;

4) Steps to bring Ireland into line with established European and US standards for patient registries;

5) An overall improvement in standards within registries, so as to enhance their role within health services; and

6) Steps towards the adequate resourcing of registries.

RECOMMENDATION 4.38
Development of an independent national federation of registries for increased collaboration, sharing of resources and establishment of registry standards.
4.10 Bioresources Facilities
There is a lack of validated bioresource facilities in Ireland which impedes innovation and early stage research for medicines and medical devices. A centralised testing facility is required to generate the clinical evidence for new medical devices to bridge the translation of medical device trials to human trials. Additionally, there is a requirement for agreed standards or processes for such research to allow for comparison of studies and results.

CÚRAM, the SFI centre for medical devices, has conducted a feasibility study into the development of a national bioresource testing lab for medical devices in early 2019 and a white paper on how the facility would operate is expected by June 2019. One of the Universities has also developed an early proposal to provide a facility.

RECOMMENDATION 4.39
Enhance the bioresource infrastructure for the benefit of clinical research in Ireland.

4.11 Funding and Development Agencies
The principal health research funder in Ireland is the national government. For many aspects of R&D in Ireland, funding comes through government agencies such as the HRB, EI, SFI or the IDA Ireland, in addition to funds leveraged from businesses and from relevant funders internationally, especially the EU’s R&D programmes (FP7, Horizon 2020 and IMI funding calls in recent times). Health research benefited from an increase in public funding through the Government’s Strategy for Science, Technology and Innovation (SSTI)20, but it nevertheless remains below the Organisation for Economic Co-operation and Development (OECD) average. Ireland lags behind in terms of expenditure on health research by the health system as a percentage of the overall health services budget. In 2013, health research, funded through the HRB, accounted for 0.33% (€45m) of the overall health services budget (€13.6bn). In contrast, in England, health research funding though the NIHR accounted for 0.87% (£958.9m) of the overall health services budget (£110bn).

In 2017, the HRB’s budget remained the same as in 2013 while the overall health services budget increased to €14.6bn21. Thus, the percentage of the health services budget actually spent on health research in 2017 dropped to 0.31%. In comparison, the NHS UK budget was £144.3bn in 2017 with a total spend on the NIHR coming to £1,035m, 0.72% of the overall health services budget that year 22. For the implementation of health research as a driver of quality improvement in the health system and the integration of health research into healthcare delivery to be realised, greater investment by government is required.

RECOMMENDATION 4.40
Existing Government funding to the funding and development agencies to be maintained and enhanced in line with recommendations of this report.

Investment in the clinical research infrastructure and resources, as outlined in this chapter, will address the challenges for enhancing clinical research activity in Ireland and will lead to an integrated clinical research system that drives excellence and innovation and improves the nation’s health. The next chapter outlines the investment required to achieve this vision.

21 HRB website and DOH press release 11.10.2016
22 House of Commons Library, Briefing Paper CBP0724 13 April 2018, NHS funding and Expenditure and NIHR Annual Report 2016/2017
Focus on Paediatric Clinical Research in Ireland
Professor Colm O’Donnell
Consultant Neonatologist, National Maternity Hospital & Our Lady’s Children’s Hospital; Professor, UCD; Director of Clinical Research, National Children’s Research Centre

Paediatric medical care presents unique challenges to doctors and researchers - patients vary in size and stage of development, from 500g extremely premature newborn babies to young adults, and present with a variety of conditions, many of which are specific to children. Conditions that develop in childhood and their treatment often have life-long and far-reaching consequences for the patients, their families and society, but researching paediatric care can be difficult because the patients are a dependent and vulnerable population who cannot provide consent for themselves.

Despite the well-documented challenges that exist in doing research in children, Paediatrics is an example of the value of performing collaborative research. There is a proud tradition of performing collaborative multicentre trials comparing chemotherapy treatments for children’s cancer and for many years most children receiving treatment for cancer in Ireland have done so within the context of an international collaborative clinical trial.

This has seen a step-wise improvement in the rate of survival from acute lymphoblastic leukaemia 10 years after diagnosis from 10% to 90% over 35 years (see figure right1). Indeed, paediatric oncology has become the standard bearer across medicine in terms of collaborative research.

The survival of premature babies provides another example of the value of collaborative trials. Advances in prenatal and postnatal care through trials, have seen remarkable increases in survival, such that a baby born at 28 weeks who would have been classified as a stillbirth in the 1980s now has an 80% or greater chance of survival. A recently funded randomised trial named POPART (Prophylactic Oropharyngeal Surfactant for Preterm infant), researching the effectiveness of a drug (prophylactic oropharyngeal surfactant) in improving outcomes of extremely premature babies is currently recruiting infants in seven European countries. The study is Irish-led by Professor Colm O’Donnell.

The EU has highlighted the importance of paediatric research and has funded the Paediatric Clinical Research Infrastructure Network (PedCRIN) to link clinicians and researchers across Europe and to fund paediatric research, such as the aforementioned POPART2 trial.

More recently, children with Cystic Fibrosis (CF) have participated in industry trials of innovative therapies that have yielded impressive results. The Irish Network for Clinical Trials in Kids with Cystic Fibrosis known as C:INK, links the paediatric CF sites and specialists across Ireland, with the aim that every child in Ireland with CF can be involved in clinical research studies and potentially access cutting edge treatments before they are widely available3.

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There are widely published benefits to patients who have access to clinical trials and thus have earlier access to newer and more innovative treatments. There are also tangible benefits to the health system, such as attracting more experienced clinicians. There are very real benefits to the industry and economy; clinical trials are a valuable source of revenue and investment from abroad and support the considerable indigenous pharmaceutical industry in Ireland.

Paediatric clinical research in Ireland is thriving and can be further enhanced by supporting researchers, such as protecting time for doctors to undertake research, increasing public awareness of the value of clinical research, and investing in the infrastructure supporting clinical trials, such as, providing dedicated paediatric research nurses and administrative staff.

2 See: https://www.ecrin.org/sites/default/files/PedCRIN/PedCRIN%20POPART%20Trial%20updated.pdf
3 See: https://www.nationalchildrensresearchcentre.ie/childrens-clinical-research-unit/respiratory-medicine/
Chapter 5

Future Investment in Clinical Research
Chapter 5
Future Investment in Clinical Research

The figures below outline the cost projection for Future Investment in Clinical Research in Ireland. These figures are costed in €millions at 2019 inflation levels, with an inflation factor needed for each year hereafter.

It is widely accepted that:

1. We have a level of activity in clinical research with highly experienced and highly regarded researchers engaged in active research work
2. We have some excellent facilities developed over a number of years
3. Strategic and focused investment has been made by a range of entities
4. We have however a level of investment and activity that is far below that required
5. The health and economic value of investing in research infrastructure and research activity as clearly set out in this report is recognised
6. Additional investment leads to significant advances in health
7. Additional investment leads to significant economic advances, including increased employment
8. Additional investment provides for further leveraged investment from various sources including European and International funding programmes
9. Industry have indicated their intention to coinvest with the Exchequer
10. The report sets out detailed recommendations, and planning how to meet these recommendations is now required across all stakeholders, and
11. Our recommendations for future investment are made on the premise that the quantum of all existing funding streams is maintained, recognising that some of this existing funding may be re-directed.
The investment requirements set out in the table below are recommended under the following headings:

**Strategy**
This allocation responds to the recommendations for a national over-arching strategy lead at central Government level.

This lead role should comprise a named senior full-time appointee with appropriate support staff and infrastructure.

**Coordination**
This allocation responds to the recommendations for a robust system of coordination of clinical research at National level. In making this recommendation, the excellent work that is already being delivered by a range of bodies is acknowledged. In particular, in the Department of Health arena, the HRB provides very substantial support, coordination, and indeed funding. In the Department of Business, Enterprise and Innovation (DBEI) arena, Science Foundation Ireland and Enterprise Ireland provide excellent supports and funding. IDA Ireland are also heavily involved in life sciences supports but to date less so in direct supports to clinical research. The universities and the Clinical Research Facilities/Centres are also heavily involved.

In calculating this additional allocation, it is assumed that all existing funding of clinical research coordination, from whatever source, is maintained. Existing funding is provided to Clinical Research Development Ireland (CRDI), HRB Clinical Trials Methodology Network (HRB-TMRN), Cancer Trials Ireland (CTI) and HRB – Clinical Research Coordination Ireland (HRB CRCI), along with a range of other funding streams to local and national coordination efforts.

While the detailed arrangements are to be agreed, it is foreseen that this allocation would be shared between:

1. **An overarching national coordinating entity**, which would have oversight of all clinical research and would provide the vehicle for coordination of the additional Exchequer and Industry co-funding as well as providing the agreed centrally funded and supported IT-based registration, approval and management system for clinical research recommended (this element estimated at €12million per year recurring). (The multi stakeholder Steering Committee which has overseen the development of this report could serve as a readymade part of the governance arrangements for this national coordinating entity) and;

2. **An agreed entity at the HSE/Service Delivery Level** which would be responsible for coordinating all activities at HSE/Service Delivery level (public and private) and be the entity which manages the additional Exchequer and Industry co-funding that would be channelled to HSE/Service Delivery managed centres.

**Resources**
This allocation responds to the recommendations regarding increased core funding required for physical infrastructure and for the employment of core research staff.

In response to the recommendations, it is foreseen that an additional capital spend of up to €10 million would be available for each of the eight CRF/Cs to expand their physical infrastructure during the first four years, plus an additional 2 x €10 million allocation for the development of 2 Phase I units, plus an additional allocation of €30 million for medical device specific facilities.
Responding to the recommendations on core staffing, the allocation, starting at €10 million in year one, rising to €25 million in year two, €65 million in year three, and €100 million in year four and subsequent years, foresees that by the end of the first four year period an additional 400 core full-time dedicated clinical research staff, comprising research nurses and all other support staff, will be in place, and that an equivalent number of clinical investigators will have 20% or more of their time ring-fenced and fully allocated to clinical research.

The Equipment/Capital allocation of €20 million recurring, responds to the need for ongoing investments that will be required across the system.

<table>
<thead>
<tr>
<th></th>
<th>Y1 (2020)</th>
<th>Y2</th>
<th>Y3</th>
<th>Y4</th>
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<td><strong>Strategy</strong></td>
<td>Each year</td>
<td>2</td>
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<td>2 (recurring)</td>
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<td><strong>Coordination</strong></td>
<td>Each year</td>
<td>10</td>
<td>22</td>
<td>22</td>
<td>22 (recurring)</td>
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<td><strong>Resources</strong></td>
<td>CRF/Cs x 8 existing 10m each Plus 2 x Phase I units 10m each; one in Year 2 and one in Year 3; Plus 2 x 15m medical devices specific investments</td>
<td>0</td>
<td>50</td>
<td>40</td>
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<td></td>
<td>Equipment/Capital</td>
<td>0</td>
<td>20</td>
<td>20</td>
<td>20 (recurring)</td>
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<tr>
<td></td>
<td>Core staffing (incremental increase to €100m per year ongoing)</td>
<td>10</td>
<td>25</td>
<td>65</td>
<td>100 (recurring)</td>
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<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td>22</td>
<td>119</td>
<td>149</td>
<td>184</td>
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</tbody>
</table>

Exchequer and Industry to share investment in an agreed model

*All amounts are in €millions*

Strategy, Coordination and some core staff are foreseen in Year 1 (2020).

The Strategy function and the Coordination activity will enable investments from Year 2 onwards to be properly planned and implemented.

Of very great significance is the commitment from industry to part fund any additional investment. The detailed implementation of this commitment would be agreed and enabled in Year 1.
Conclusion
Conclusion

The members of the Steering Committee on the *Future Investment in Clinical Research* initiative have been pleased to work together on this extensive report.

Acknowledging the considerable investments made in clinical research over recent years, the Committee have presented the case for the significant opportunity that exists, and the additional investment required to realise that opportunity.

The commitment from industry stakeholders to co-fund with the Exchequer is very welcome and is in itself a major opportunity.

The Steering Committee commends this report and its recommendations to policy makers and to all stakeholders and stands ready to assist in delivering its implementation.
Appendices
Appendix I

Future Investment in Clinical Research Steering Committee
Mandate and Terms of Reference

Background
A well-resourced and functioning clinical research capability is an essential part of any National infrastructure. It benefits patients, the healthcare delivery system and academia, and is a unique selling point for the very large life-sciences sector operating in Ireland.

With a view to exploring the mid and long-term needs for clinical research infrastructure in Ireland, following a series of bilateral meetings, Clinical Research Development Ireland (CRDI) convened a discussion with a number of key stakeholders in March 2018. These stakeholders included patient representatives, funding and enterprise agencies (HRB, EI, SFI and IDA Ireland), industry representative bodies (IPHA, IMSTA, BioPharmachem Ireland and Irish MedTech Association), the Directors of the Clinical Research Facilities/Centres, and Board and staff colleagues from CRDI.

Following an interesting and wide-ranging discussion, and with due regard to the valuable efforts and funding investments already made by stakeholders, it was agreed by all present that significant opportunity exists to enhance the level of clinical research in Ireland and that the issue of resourcing to enable this opportunity to be realised needs to be reviewed. A range of key issues were highlighted including, but not limited to: investment in core infrastructures, both facilities and staff; need for career structure for research staff; protected time for investigators; electronic health records; and the approach to biobanking and patient registries.

It was agreed to establish a **Future Resourcing of Clinical Research Steering Committee (FRCR SC)** with a mandate to strategically examine and define the optimal future clinical research infrastructure, support, capacity and capability. The report developed will inform a plan that clearly outlines the evidence to support the need identified and will provide a draft high-level coordination road-map on how best to achieve the desired outcome.

All stakeholders identified above have agreed to participate in and support the work of the FRCR SC. It is foreseen that additional stakeholders will be invited to join the initiative and to participate in the Steering Committee as appropriate.

**Mandate and Terms of Reference**
The Steering Committee’s mandate comes from its constituent stakeholders, all of whom agree that there is a need for the plan to be developed. The Steering Committee is responsible for:

1. Establishing the baseline of Ireland’s current clinical research infrastructure and performance.

2. Formulating a plan for clinical research in Ireland that examines and defines in broad terms:
   - The required physical and human capital infrastructure to sustain all forms of clinical research in Ireland.
   - The estimated capital and revenue costs of providing and maintaining this infrastructure for clinical research based in both hospital and CRF settings.
   - Any legislative or policy change that enables the development of clinical research in Ireland.

3. Ensuring that the development of the plan is resourced with the personnel who have the relevant knowledge and expertise, along with appropriate contributions from the individual Committee members and the stakeholders they represent.

4. Ensuring the scope of the plan addresses the needs of all stakeholder groups, including; patients, industry, academia, healthcare service, government, development agencies, research charities and clinicians.
5. Ensuring that the plan outlines a system for economic sustainability of the proposed infrastructure over the long term.

6. Endorsing the plan and promoting it internally to the stakeholder each member represents and externally to representatives of the Government and the general public.

7. Making themselves available for the work of the Committee and the various meetings that may be scheduled.

**Steering Committee Membership**
The Steering Committee shall comprise senior representatives from the following:

- Patient Representative Organisations
- IPHA
- IMSTA
- BioPharmaChem Ireland
- Irish MedTech Association
- Cancer Trials Ireland
- Health Research Board
- Health Services Executive
- Enterprise Ireland
- Science Foundation Ireland
- IDA Ireland
- Directors, Irish Clinical Research Facilities and Centres (RCSI, UL, UCD, HRB-CRF-G, HRB CRF-C, Wellcome HRB CRF at St. James’s Hospital)
- HRB – CRCI
- CEO, Clinical Research Development Ireland
- Hospital Groups, CEOs and Chief Academic Officers
- Other stakeholder representatives as required.

The Steering Committee will be chaired by the CEO of CRDI. In addition, the Steering Committee will be supported by a Working Group consisting of:

- Dr. Pat O’Mahony, CEO, CRDI
- Dr. Fionnuala Keane, COO, HRB-CRCI
- Dr. Áine Murphy, Translational Research Manager, CRDI
- Dr. Fiona Killard, Head of Strategic Research Development, TCD
- Mr. Jeremy Towns, Programme Manager, Wellcome - HRB Clinical Research Facility
- Ms. Ciara Peters, CRDI
- Other members as may be required.
Meetings
The Steering Committee shall meet to review the progress and development of the plan on the following dates:
• 26 June 2018
• 15 January 2019
• 16 April 2019
• 14 November 2018
• 12 March 2019
• 14 May 2019

Further meetings may be scheduled by general agreement, or at the call of the Chair. Meetings will be held at in the Dublin area and longer meetings may be held at an offsite location. All agenda packages will be issued at least five working days in advance of meetings.

Decision Making
Steering Committee decisions and approvals of the clinical research plan will be made by consensus of those present at the meetings, facilitated by the Chair of the Steering Committee.

Members are expected to be in physical attendance at meetings. In circumstances where a member cannot attend in person, members will nominate an alternate representative to attend on their behalf. Alternates are invited to participate in the discussion and decision-making process.

In a circumstance where a Steering Committee member is not a party to the final consensus, he/she may opt not to be represented in the final report.
## Appendix II
External Contributors to the Future Investment in Clinical Research Report

<table>
<thead>
<tr>
<th>Name</th>
<th>Job Title</th>
<th>Organisation</th>
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<tbody>
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<td>Professor Paddy Gillespie</td>
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<td>International Consortium for Health Outcomes Measurement</td>
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<tr>
<td>Rose Kidd</td>
<td>Senior Vice-President, Global Clinical Operations</td>
<td>ICON plc</td>
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<tr>
<td>Name</td>
<td>Job Title</td>
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<td>Weber Shandwick</td>
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<tr>
<td>Gaël Parent</td>
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<td>Clinical Research Development Ireland</td>
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<td>Ian Smith</td>
<td>Director</td>
<td>Big Top Multimedia</td>
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<td>Dr Mark Watson</td>
<td>Head of Education and Development</td>
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<td>Professor David Williams</td>
<td>Associate Professor in Geriatric and Stroke Medicine</td>
<td>Royal College of Surgeons in Ireland and Beaumont Hospital</td>
</tr>
</tbody>
</table>
Appendix III
Future Investment in Clinical Research Steering Committee Members

1. **Appointment of a senior strategy lead at cross-departmental level**

   **Recommendation 2.1 and 3.2:**
   A Strategy Lead for clinical research should be appointed at a senior cross-departmental level. This appointee should have a well-funded support office.

2. **Provision of funding and establishment of a national coordinating entity and an office at HSE/Service Delivery Level to coordinate all aspects of clinical research and the application of the additional Exchequer and Industry co-funding proposed in this report.**

   **Recommendation 2.2 and 3.3:**
   A National Coordinating Entity and an Office at HSE/Service Delivery Level should be established to coordinate all aspects of clinical research and to coordinate the additional Exchequer and industry co-funding proposed in this report.

   **Recommendation 2.12:**
   Implement a national IT-based registration, approval and management system for clinical research.

   **Recommendation 2.16:**
   The additional funding supported by the recommendations in this report is additional, incremental long-term funding to enable clinical research to develop at the pace and to the scale identified. It does not replace any existing supports and funding provided from all sources.

   **Recommendation 3.1:**
   Long-term, core funding is required to further develop the centralised coordination services that are already in place and necessary to support a world class national clinical research system in Ireland.

   **Recommendation 3.4:**
   A central coordinating hub is required to facilitate the conduct of multicentre research in the form of HRB Clinical Research Coordination Ireland.

   **Recommendation 4.31:**
   Implement a centrally funded, resourced and supported Clinical Data Management System available to investigators and sponsors to utilise for study data collection and management.

3. **Additional investment in clinical research infrastructure and staffing, co-funded by Exchequer and industry, while maintaining all existing funding.**

   **Recommendation 2.4 and 4.6:**
   Each Hospital Group-affiliated university should be funded to deploy a Clinical Research Facility/Centre that facilitates the conduct of clinical research within the Hospital Group and Community Health Organisations as an essential core clinical service. This should also be seen as a significant step towards the establishment of academic health sciences centres/systems.

   **Recommendation 2.9:**
   The Health Products Regulatory Authority, which is tasked with approval and monitoring regulated clinical trials and clinical investigations, should be adequately resourced so it can continue to monitor and support clinical research.

   **Recommendation 2.13:**
   Adequate support to be provided to endure appropriate Quality Management Systems are implemented across all clinical research.
Recommendation 2.16: The additional funding supported by the recommendations in this report is additional, incremental long-term funding to enable clinical research to develop at the pace and to the scale identified. It does not replace any existing supports and funding provided from all sources.

Recommendation 3.1: Long-term, core funding is required to further develop the centralised coordination services that are already in place and necessary to support a world class national clinical research system in Ireland.

Recommendation 3.6: The target (KPI 20) set in the National Cancer Strategy 2017 – 2026 to double the number of people with cancer on Investigational Medicinal Product trials from the 3% to 6% by 2020 will not presently be met. Commitment is needed to funding core teams at hospital cancer units and Cancer Trials Ireland’s general central office.

Recommendation 3.7: Implement an integrated system between Cancer Trials Ireland and HRB Clinical Research Coordination Ireland with specialist staff sharing experience and learnings in a combined working group with their Clinical Research Facility/Centre counterparts, e.g., in pharmacovigilance and biostatistics.

Recommendation 3.10: Establish a public-facing national registry of active clinical trials and research that can be utilised to inform patients and the public of research which may benefit them.

Recommendation 3.13: An international cooperative group that enables interaction between investigators at a multi-site level is necessary.

Recommendation 3.14: Continuation of the HRB Clinical Research Coordination Ireland and the European Clinical Research Infrastructure Network coordinator role based within HRB Clinical Research Coordination Ireland.

Recommendation 3.15: Ireland to become a member of European Research Infrastructure for Translational Medicine and Biobanking and BioMolecular resources Research Infrastructure European Research Infrastructure Consortium.

Recommendation 4.6: Each hospital group affiliated university should be funded for a clinical research facility that facilitates the conduct of clinical research within the hospital group as an essential core clinical service.

Recommendation 4.9: Establish two Phase I facilities in Ireland.

Recommendation 4.10: Long-term core funding is required to develop and maintain academic clinical research networks.

Recommendation 4.11: Better integration and collaboration of the academic clinical networks with Clinical Research Facilities/Centres is required to enhance the network’s thematic research.

Recommendation 4.12: Awarded funding for networks should be subdivided to fund the leadership of each network to support the development of the research and to the Clinical Research Facilities/Centres to carry out the research.

Recommendation 4.17: Core funding to provide career pathways for specialised staff required for clinical research.

Recommendation 4.18: Funding to provide for protected time for healthcare staff including backfill of the position.
Recommendation 4.21:
Investment required in the clinical expertise within the current Clinical Research Facilities/Centres to conduct clinical investigations, specifically Phase I clinical trials.

Recommendation 4.22:
Further development of Clinical Industry Liaison services provided by HRB Clinical Research Coordination Ireland to Small and Medium-sized Enterprises, including linking SMEs with appropriate clinicians.

Recommendation 4.23:
Provision of funding to third level Institutions to partner with SMEs in the development of devices under the remit of a certified quality system.

Recommendation 4.24:
The Health Products Regulatory Authority should be resourced to respond to increased activity in clinical trials and clinical investigations in Ireland and the rest of the EU.

Recommendation 4.32:
A single coordinated national research ethics committee for clinical research providing approvals for clinical trials, non-interventional studies and with specialist expertise for review of medical device trials.

Recommendation 4.33:
Dedicated funding should be provided to support the core running costs of biobanks, to support scientifically valuable repositories in long term storage after conclusion of the originating study, and to provide for central coordination across all biobanks.

Recommendation 4.36:
The development of registries should be supported through a competitive, dedicated funding stream.

Recommendation 4.37:
New registries should be developed in a way that they are interoperable with electronic health records and other data sources. They should also have the capacity to be built upon over time to fulfil additional functions, including supporting the running of clinical trials and post marketing studies.

Recommendation 4.38:
Development of an independent national federation of registries for increased collaboration, sharing of resources and establishment of registry standards.

Recommendation 4.39:
Enhance the bioresource infrastructure for the benefit of clinical research in Ireland.

Recommendation 4.40:
Existing Government funding to the funding and development agencies to be maintained and enhanced in line with recommendations of this report.

4. Enhancing patient involvement and patient centredness in clinical research

Recommendation 2.8:
A combined and coordinated information campaign should be in place to inform patients, their families and carers of the benefits involved in participating in clinical research. This should also extend to healthcare staff.

Recommendation 3.8:
Appropriate measures and processes to encourage greater public and patient involvement in clinical research are required. Both researchers and patients alike need greater support, guidance and resources to implement these initiatives.
Recommendation 3.11:
Medical research charities should be included in all significant committees and groups involved in clinical research in Ireland.

Recommendation 3.9:
Building on Irish patient experience initiatives (in hospital settings and cross-settings), co-design and co-produce a patient experience survey of patients who have participated in clinical research in Ireland and disseminate findings widely to improve both researcher and patient experience of research and groups involved in clinical research in Ireland.

Recommendation 3.12:
Clinical research groups, both academic and industry, should engage early with patient organisations.

Recommendation 4.13:
Clinical Research Facilities/Centres should have a designated Public and Patient Involvement lead, to embed the importance of Public and Patient Involvement in all phases of the planning and undertaking of clinical research.

Recommendation 4.14:
Training in Public and Patient Involvement should be provided to clinical researchers, other clinical research support roles and to patients interested in being involved in research planning and decision-making.

Recommendation 4.15:
Establish a public-facing national registry of active clinical trials and research that can be utilised to inform patients and the public of research which may benefit them.

Recommendation 4.16:
A public information campaign should be undertaken to inform people of the value of clinical research.

5. Delivering the required changes and enhancements to the clinical research system and healthcare delivery system

Recommendation 2.5:
The Clinical Research Facilities/Centres should operate under a combined governance of both the university and Hospital Group/Community Health Organisations with appropriate comprehensive legal agreements in place between the parties.

Recommendation 2.6:
Clinical Research Facility/Centre staff should be joint staff of both the university and affiliated hospital/Community Health Organisation.

Recommendation 2.7:
 Universities should engage with and educate healthcare staff as to the importance of their role in clinical research.

Recommendation 2.13:
Adequate support to be provided to endure appropriate Quality Management Systems are implemented across all clinical research.

Recommendation 2.14:
Outcome-based measures should be applied to all clinical research and to funding and reimbursement programmes.

Recommendation 2.15:
Clinical research within the healthcare delivery system should have a well-defined research translation plan. This should be linked to the clinical programmes.
Recommendation 3.5:
Post-graduate training and exposure to clinical trials for all clinical staff should be a basic component of continuing professional development.

Recommendation 3.7:
Implement an integrated system between Cancer Trials Ireland and HRB Clinical Research Coordination Ireland with specialist staff sharing experience and learnings in a combined working group with their Clinical Research Facility/Centre counterparts, e.g., in pharmacovigilance and biostatistics.

Recommendation 4.1:
The development of a research governance framework for the health service to facilitate clinical research activity and to enable further integration of clinical research into healthcare delivery.

Recommendation 4.2:
Each Hospital Group should have a resourced research governance office with capacity to register, monitor and oversee research.

Recommendation 4.3:
To cultivate a clinical research culture within the health service.

Recommendation 4.4:
Research support structures should be implemented for community and health services research.

Recommendation 4.5:
Establish the role of community-based research lead.

Recommendation 4.7:
Clinical Trial Coordination Units providing specialist services should be established, with specific expertise in at least two Clinical Research Facilities/Centres and these services should be available to all Clinical Research Facilities/Centres and researchers in all hospitals across the country.

Recommendation 4.8:
Clinical Research Facilities/Centres should share expertise and resources with other hospitals in their hospital groups to facilitate the establishment and conduct of research studies.

Recommendation 4.19:
Clinical Research Nurse/Midwives should be embedded into HSE supported posts in hospitals in an acknowledged career pathway with appropriate salary scales, reporting lines and clear responsibilities.

Recommendation 4.20:
Clinical Research Facilities/Centres to support pharma-sponsored clinical research with a focus on data quality, patient recruitment and efficient site setup.

Recommendation 4.25:
All stakeholders should examine and respond to the deficits in training in specialist areas of clinical research to ensure an adequate supply of appropriately trained specialist staff.

Recommendation 4.26:
National coordination is required to ensure a comprehensive suite of training is available.

Recommendation 4.27:
Electronic Health Records are required throughout the entire healthcare system.
Recommendation 4.28:
Individuals resident in Ireland should be assigned an Individual Health Identifier.

Recommendation 4.29:
In advance of implementation of the above, any existing Information Management and Technology systems should be reviewed and leveraged where possible.

Recommendation 4.30:
Electronic Health Records should be designed with input from clinical research experts to ensure they can be utilised for clinical research.

Recommendation 4.32:
A single coordinated national research ethics committee for clinical research providing approvals for clinical trials, non-interventional studies and with specialist expertise for review of medical device trials.

Recommendation 4.34:
A national biobanking policy should be developed to coordinate, network and promote successful management of biobanking in Ireland.

Recommendation 4.35:
Ireland should join Biobanking and BioMolecular resources Research Infrastructure European Research Infrastructure Consortium and develop a central agency or office to oversee the development of biobanking services in Ireland and other international biobanks.

6. Legislative changes recommended to develop clinical research in Ireland

Recommendation 2.3:
A legislative mandate for health research should be created in law, which places a positive obligation on the State to carry out evidence-based health research.

Recommendation 2.10:
The academic institutions to be supported in providing academic-led clinical research to participants where commercial insurance is unavailable.

Recommendation 2.11:
All academic-led research conducted under the auspices of the Clinical Research Facilities/Centres should be covered under the provisions of the State Claims Agency Clinical Indemnity Scheme and all Clinical Research Facilities/Centres and subordinate sites should be designated as “authorities” for the purposes of the state indemnity.

Recommendation 4.32:
A single coordinated national research ethics committee for clinical research providing approvals for clinical trials, non-interventional studies and with specialist expertise for review of medical device trials.

Recommendation 4.34:
A national biobanking policy should be developed to coordinate, network and promote successful management of biobanking in Ireland.
## Appendix IV

The 8 Clinical Research Facilities/Centres in Ireland are:

1. **HRB CRF-C:** Health Research Board Clinical Research Facility Cork at University College Cork and Mercy University Hospital, Co Cork

2. **HRB CRFG:** Health Research Board Clinical Research Facility Galway at University Hospital Galway, Co Galway

3. **Wellcome Trust HRB CRF SJH:** Wellcome Trust Health Research Board Clinical Research Facility at St. James’s Hospital, Dublin 8

4. **RCSI CRC:** Royal College of Surgeons Ireland Clinical Research Centre at Beaumont Hospital, Dublin 9

5. **UCD CRC:** University College Dublin Clinical Research Centre at Mater Misericordiae University Hospital, Dublin 7

6. **UCD CRC:** St. Vincent’s University Hospital, Dublin 4

7. **UL HRI-CRSU:** Health Research Institute Clinical Research Support Unit at University Hospital Limerick, Co Limerick

8. **NCRC:** National Children’s Research Centre at Our Lady’s Children’s Hospital, Crumlin, Dublin 12
Appendix V
List of HRB-Funded Networks

1. Cancer Trials Ireland
Cancer Trials Ireland has been acting as a central coordinating point for oncology research for many years. Established in 1996, Cancer Trials Ireland, formally the All-Ireland Cooperative Oncology Research Group (ICORG), enables patients in Ireland to gain early access to novel cancer treatments and therapies. Cancer Trials Ireland operates cancer clinical trials across a number of disease areas – Breast, Gastrointestinal, Genitourinary, Gynaecology, Haematology/Lymphoma, Lung, etc. They work closely with international collaborative groups such as ECOG, NSABP, ANZUP and also have developed strong links with pharmaceutical partners.

Through Cancer Trials Ireland Irish patients participating in cancer trials can have access to:

- Innovative treatments paid for by the industry, considered better than current standard of care options, and reduce their dependence (e.g. diagnostics) on the public health system. Estimated in 2016 to be €6.5M annually.
- New targeted radiotherapy techniques which can reduce the side effects of radiotherapy and reduce the complexity and cost of their follow up cancer care.
- Surgical techniques which can provide better outcomes

2. HRB Stroke Clinical Trial Network Ireland
The HRB Stroke Clinical Trial Network Ireland is led by Professor Peter J Kelly, Mater University Hospital and University College Dublin. The Network involves eight Irish hospitals, six leading universities, and all seven Hospital Groups. It has strong links with international researchers in the UK, Europe, and North America. In addition to the HRB, other Network partners are the Irish Heart Foundation and industry.

3. HRB Critical Care Clinical Trials Network Ireland
The HRB Critical Care Clinical Trials Network Ireland (HRB CCTNI) is led by Professor Alistair Nichol, St Vincent’s University Hospital and UCD. The HRB CCTNI will bring together doctors, nurses and researchers to test new treatments that can improve outcomes for critically ill patients. The network offers ICU patients the highest quality care, give them access to the latest innovations in intensive care and ensure future patients benefit from the lessons learned in national and international research. The group includes the academic leadership in our speciality and encompasses more than 75% of all the ICU capacity in Ireland.

4. HRB Primary Care Clinical Trial Network Ireland
The HRB Primary Care Clinical Trials Network Ireland is a collaborative partnership that brings together key people in Ireland to run clinical trials in primary care. Working closely with the public, with patients and with GPs and other healthcare professionals, the Network aims to improve individual patient health and health care by conducting high quality, internationally recognised, randomised trials in Irish primary care, addressing important and common problems.

Led by Professor Andrew Murphy, NUI Galway, the network includes a multidisciplinary team of colleagues from NUI Galway, Royal College of Surgeons in Ireland, Queen’s University Belfast and the Irish College of General Practitioners.

5. HRB Mother & Baby Clinical Trials Network Ireland
The HRB Mother & Baby Clinical Trials Network Ireland (HRB M&B CTNI) is a partnership between the perinatal research entities currently operational in Ireland, INFANT and Perinatal Ireland.

The primary aim of the HRB M&B CTNI is to unite the combined experience of both the medical teams and resources in all centres. This combination provides a world class research infrastructure which is at the forefront of translation research regarding the transition of fundamental research into the clinical environment. HRB M&B CTNI has a balanced and extensive portfolio of both “home-grown” and international clinical trials of novel interventions and diagnostics in pregnancy and neonates.
## Glossary

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>AIMDD</td>
<td>Active Implantable Medical Devices Directive</td>
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<tr>
<td>BBMRI-ERIC</td>
<td>Biobanking and BioMolecular resources Research Infrastructure European Research Infrastructure Consortium</td>
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<tr>
<td>c4c</td>
<td>conect4children</td>
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<tr>
<td>CDMS</td>
<td>Clinical Data Management System</td>
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<tr>
<td>CE</td>
<td>European Conformity</td>
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<tr>
<td>CECR</td>
<td>Corporate Enabling of Clinical Research</td>
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<tr>
<td>CHO</td>
<td>Community Healthcare Organisation</td>
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<tr>
<td>CILO</td>
<td>Clinical Industry Liaison Officer</td>
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<tr>
<td>CIS</td>
<td>Clinical Indemnity Scheme</td>
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<tr>
<td>CRDI</td>
<td>Clinical Research Development Ireland</td>
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<tr>
<td>CRF/C</td>
<td>Clinical Research Facility/Centre</td>
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<tr>
<td>CRN/M</td>
<td>Clinical Research Nurse/Midwife</td>
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<tr>
<td>CRO</td>
<td>Contract Research Organisation</td>
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<tr>
<td>CTU</td>
<td>Clinical Trial Unit</td>
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<tr>
<td>CURAM</td>
<td>SFI Centre for Research in Medical Devices</td>
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<tr>
<td>DoH</td>
<td>Department of Health</td>
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<tr>
<td>EC</td>
<td>European Community</td>
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<tr>
<td>ECRIN</td>
<td>European Clinical Research Infrastructures Network</td>
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<tr>
<td>EHR</td>
<td>Electronic Healthcare Record</td>
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<tr>
<td>EuCo</td>
<td>European Correspondent</td>
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<tr>
<td>EI</td>
<td>Enterprise Ireland</td>
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<tr>
<td>EU</td>
<td>European Union</td>
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<tr>
<td>FDI</td>
<td>Foreign Direct Investment</td>
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<tr>
<td>GCP</td>
<td>Good Clinical Practice</td>
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<tr>
<td>GDP</td>
<td>Gross Domestic Product</td>
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<tr>
<td>GDPR</td>
<td>General Data Protection Regulation</td>
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<tr>
<td>GVA</td>
<td>Gross Value Added</td>
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<td>HEA</td>
<td>Higher Education Authority</td>
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<tr>
<td>HRB</td>
<td>Health Research Board</td>
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<tr>
<td>HRB CRCI</td>
<td>Health Research Board Clinical Research Coordination Ireland</td>
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<tr>
<td>HRI-CRSU</td>
<td>Health Research Institute Clinical Research Support Unit</td>
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<tr>
<td>HRB-TMRN</td>
<td>Health Research Board Trials Methodology Research Network</td>
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<tr>
<td>HSE</td>
<td>Health Service Executive</td>
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<tr>
<td>ICAT</td>
<td>Irish Clinical Academic Training</td>
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<tr>
<td>ICH</td>
<td>International Conference on Harmonisation</td>
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<tr>
<td>ICT</td>
<td>Information and Communications Technology</td>
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<tr>
<td>IHI</td>
<td>Individual Health Identifier</td>
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<tr>
<td>IMDA</td>
<td>Irish Medical Devices Association</td>
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<tr>
<td>IMI</td>
<td>Innovative Medicines Initiative</td>
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<tr>
<td>IMP</td>
<td>Investigational Medicinal Product</td>
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<tr>
<td>IP</td>
<td>Intellectual Property</td>
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<tr>
<td>IVDR</td>
<td>In-Vitro Device Regulation</td>
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<tr>
<td>IMT</td>
<td>Information Management and Technology</td>
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<td>IPHA</td>
<td>Irish Pharmaceutical Healthcare Association</td>
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<tr>
<td>IPPOSI</td>
<td>Irish Platform for Patient Organisations, Science and Industry</td>
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<tr>
<td>IHRF</td>
<td>Irish Health Research Forum</td>
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<tr>
<td>KPI</td>
<td>Key Performance Indicator</td>
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<td>Medtech</td>
<td>Medical Technology</td>
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<td>MDD</td>
<td>Medical Devices Directive</td>
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<td>MDR</td>
<td>Medical Device Regulation</td>
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<td>MRCG</td>
<td>Medical Research Charities Group</td>
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<td>NCRC</td>
<td>National Children’s Research Centre</td>
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<td>NIH</td>
<td>National Institutes of Health</td>
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<tr>
<td>NIHR</td>
<td>National Institute for Health Research</td>
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<tr>
<td>NIHR CRN</td>
<td>National Institutes for Health Research Clinical Research Network</td>
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<tr>
<td>NSAI</td>
<td>National Standards Authority of Ireland</td>
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<tr>
<td>NUIG</td>
<td>National University of Ireland, Galway</td>
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<tr>
<td>OECD</td>
<td>Organisation for Economic Co-operation and Development</td>
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<tr>
<td>Pharma</td>
<td>Pharmaceutical</td>
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<tr>
<td>PhD</td>
<td>Doctor of Philosophy</td>
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<tr>
<td>PI</td>
<td>Principal Investigator</td>
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<tr>
<td>PPI</td>
<td>Public Patient Involvement</td>
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<tr>
<td>PRTLI</td>
<td>Programme for Research for Third Level Institutions</td>
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<tr>
<td>QMS</td>
<td>Quality Management System</td>
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<tr>
<td>R&amp;D</td>
<td>Research and Development</td>
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<tr>
<td>RCSi</td>
<td>Royal College of Surgeons in Ireland</td>
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<td>REC</td>
<td>Research Ethics Committee</td>
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<td>SCA</td>
<td>States Claims Agency</td>
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<td>Science Foundation Ireland</td>
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<td>SME</td>
<td>Small to Medium Sized Enterprises</td>
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<td>SWATs</td>
<td>Studies Within A Trial</td>
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<td>TCD</td>
<td>Trinity College Dublin</td>
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<tr>
<td>UCC</td>
<td>University College Cork</td>
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<td>University College Dublin</td>
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<td>UKCRN</td>
<td>United Kingdom Clinical Research Network</td>
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<td>WHO</td>
<td>World Health Organisation</td>
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<tr>
<td>WT HRB CRF- SJH</td>
<td>Wellcome Trust Health Research Board Clinical Research Facility St James’s Hospital</td>
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