

MMI Position Paper

Ireland's Continued Participation in European Research Infrastructures for Biobanking and Clinical Research

1. Background

In 2000, at the Council of Ministers meeting in Lisbon, the EU member states committed themselves to the creation of the European Research Area (ERA). One of the objectives of the ERA is to create infrastructures for world class research in the EU. In 2006, the representatives of the member states in the European Strategy Forum for Research Infrastructure (ESFRI) recommended the development of over 30 research infrastructures at European level, across all disciplines from the humanities to astronomy¹. They recommended six infrastructures for biomedical research. In 2007, the Health Research Board led Irish participation in two of these research infrastructures – the European Clinical Research Infrastructure Network (ECRIN) and the Biobanking and Biomolecular Research Infrastructure (BBMRI) and nominated the Dublin Molecular Medicine Centre (now Molecular Medicine Ireland (MMI)) as the scientific partner of BBMRI and ICRIN (a business unit of MMI) as the scientific partner of ECRIN. Both ECRIN and BBMRI were successful in a call to support the development of the new research infrastructures under FP7. The preparatory phase of these programmes will be completed in February 2011. The ECRIN correspondent for Ireland is employed by MMI.

Both ECRIN and BBMRI have made substantial progress in developing a networked, distributed infrastructure to facilitate biomedical researchers undertake studies and research activities on a scale and of a complexity not previously possible at European level. ECRIN and BBMRI are linking biological collections and clinical expertise and resources in the member states to create a capacity for biomedical research that will be unique in the world.

Ireland has received an estimated €325,000 (through FP6 and FP7) for participation in ECRIN which funds the European correspondent in Ireland and participation in the work programme. Ireland has received €28,000 (through FP7) for participation in BBMRI which funds Irish participation in the work programme. IPPOSI² is a participant in BBMRI and €188,000 has been allocated under FP7 for its responsibilities to support the BBMRI Stakeholder Forum.

In 2009, following a review of progress towards the ERA, the Council of Ministers agreed a new legal instrument to provide a governance framework for the next phase of the development of the European research infrastructures. The legal instrument is known as the European Research Infrastructure Consortium or ERIC. Because research infrastructures are within the competence of the member states, the establishment of an ERIC requires the active support of the participating member states. BBMRI and ECRIN are at an advanced stage in preparing proposals for the adoption of the ERIC as the governance structure for the next phase of their development. The coordinator of the BBMRI, Professor Kurt Zatloukal (Austria), has written to the Tánaiste and Minister for Enterprise, Trade and Employment

¹ ftp://ftp.cordis.europa.eu/pub/esfri/docs/esfri-roadmap-report-26092006_en.pdf

² Irish Platform for Patients' Organisations, Science and Industry

enquiring as to Ireland's intentions with respect to joining the ERIC for BBMRI. A similar enquiry is expected from the ECRIN coordinator, Professor Jacques Demotes (France).

While the European Commission has played a significant role in 'kick-starting' these and other research infrastructures at European level, the responsibility for their on-going funding lies with the member states as the competent authorities in this field. Future funding for RIs is likely to come from a combination of support from member and associated states for core costs and funding from the EU for access, integrating activities and use of the research infrastructures. Industry may also contribute towards the cost of the infrastructures through payments for access.

2. National Strategic Priorities and European Research Infrastructures

Science and Innovation

In the Strategy for Science, Technology and Innovation 2006-2013 (SSTI), the Government declared its ambition that:

"Ireland by 2013 will be internationally renowned for the excellence of its research, and will be to the forefront in generating and using new knowledge for economic and social progress, within an innovation driven culture."

The SSTI noted that one of the difficulties which had to be overcome to achieve this vision was Ireland's lack of participation in international research, collaborative agreements and networks. The Government noted that success in overcoming this challenge would be marked by:

- increased transnational research activity;
- an international profile for Ireland;
- greater coherence and exploitation of synergies nationally and internationally.

Although the Government's vision for Ireland in 2013 is strong, Ireland is playing catch-up in terms of its national research infrastructure with many other EU member states as it lacks the institutional elements found in those countries such as specialist/sector-specific research institutes and dedicated technology agencies which often play a crucial intermediary role between knowledge producers and knowledge users. The SSTI recognised the need to *'upgrade existing infrastructure and develop new facilities to support research'*.

In 2008, the Advisory Science Council examined Ireland's international engagement in science, technology and innovation. Their report emphasised the need for Ireland to use its international networks in a strategic way to help achieve the targets set out in the SSTI.

Health Research

The Higher Education Authority and Forfás commissioned report *'Research Infrastructure in Ireland – Building for Tomorrow 2007'* recognised that *'genebanks and biobanks'* and clinical research facilities are research infrastructure requirements for the instrument and medical devices industry in Ireland. In 2007, in a report commissioned by Enterprise Ireland, the CIRCA group recommended *'clinical trial facilities'* and *'biobanks'* as infrastructural initiatives needed to improve the environment for generating economic activity from the expertise and research activities in the Irish healthcare system. The Renewed Programme for Government in October 2009 commits to making Ireland *'a leading country for the timing, access and relevance of clinical trials'*. The Health Research Action Plan in November 2009 identifies the

development of clinical research capacity as a strategic objective and noted that *'priority biobank and other infrastructural requirements'* were a requirement *'to underpin clinical research'*. The recent Report of the Taskforce on Innovation points out that *'the development of a clinical trials research system is critical for the future growth and development of (the lifesciences) sector in Ireland (both indigenous and MNCs) and to ensure that we leverage investments in research and development – translating from bench to bedside'* (pg 59). These strategic statements are being matched by significant investment in the establishment of a research infrastructure for Ireland through the creation of clinical research centres and networks, funding bio resources and attracting high quality clinical researchers. Both clinical research and biobanking have an increasing European dimension that complements the Government's strategic commitment and investment.

European Engagement

The SSTI commits to developing Ireland as an internationally renowned centre for excellence in research through *'continued engagement with the EU institutions and appropriate international organisations in a co-ordinated and strategic manner with Irish input being promoted in all areas to ensure the optimum return for our research sector'*. The Report of the Advisory Council for Science, Technology and Innovation, *Towards Better Health: Achieving a Step Change in Health Research in Ireland* noted the need to *'fully exploit the potential for international networking and leveraging funding for health research under the EU's Seventh Framework programme for Research, 2007-2013'*. The Report of the Taoiseach's Department on Ireland's progress towards the Lisbon agenda - *Irish National Reform Programme 2008-2010* - states that Ireland *'is working with the national funders of research and research infrastructure to ensure continued engagement with the ESFRI process and to ensure that Irish research infrastructures continue to be planned within the context of wider European and global strategies'* (pg 85). The Health Research Action Plan highlighted the importance of participation *'in the development and implementation phase of relevant large-scale international research infrastructure which includes Irish hubs under programmes such as ESFRI'*. As a small member state, Ireland has an interest in ensuring that national infrastructures are part of emerging European RIs, especially those endorsed in the ESFRI Roadmap. This will ensure that Irish researchers have access as a right to top class RIs in Europe, Irish RIs will benefit from being part of world class RIs and Ireland's reputation internationally for R&D will be enhanced.

3. Delivering Ireland's strategic priorities by membership of European RIs – BBMRI and ECRIN

Biobanking and Biomolecular Resources Infrastructure (BBMRI)

A biobank is a collection of blood and/or tissue donated by healthy volunteers and/or patients with linked medical information which is made available for medical research and commercialisation of the products of medical research. Biomedical researchers need to study information and samples from large numbers of people, particularly in the understanding of complex disease processes and in investigating the role that different genes play in health and disease. A number of European countries has established population-based and/or disease orientated biobanks including the HUNT in Norway, the UK Biobank, the Estonian Population Biobank and Generation Scotland. If Europe is to realise the full research potential from human biobanks, there is a need for convergence, coordination and harmonisation of the biobanking and biomolecular resources infrastructure across Europe. The consortium that is BBMRI was formed to address this challenge and is being funded in its preparatory phase under Framework Programme 7 (FP7). BBMRI is

funded to establish a European biobanking research infrastructure through the networking, coordination and harmonisation of the biomolecular resources, including population-based cohorts, disease orientated cohorts, twin registries and clinical case/control studies in the participating member states. Networking and harmonisation of biobanking across Europe will increase the success of coordinated, large-scale biomarker discovery and validation; facilitate the identification of susceptibility genes and their association with environment and lifestyle factors; elucidate aetiological pathways for multi-factoral diseases and facilitate discovery of new drugs and therapies.

Seventeen member states and associated countries are members of BBMRI.³ BBMRI has so far identified over 10 million biological samples in its associated 250 biobanks in the participating countries.

As the Scientific Member coordinating Ireland's participating in BBMRI, MMI is also playing an important role in BBMRI, a particular example being the contribution of MMI's Guidelines for Standardised Biobanking which will be adopted by BBMRI to ensure harmonisation of biological materials in Europe across jurisdictions. The use of standardised protocols for sample collection, processing and storage will provide proper safeguards and assurances required for sample quality, consistency and integrity among bio-collections at different sites. This harmonisation will facilitate the global movement of biological materials across research sites and the aggregation of samples for research studies. This will expedite high quality research and reduce its costs. The benefits to Ireland from participation in BBMRI have already been significant as evidenced by the direct contribution of the leaders of BBMRI, Professors Kurt Zatloukal, Eero Vurio and Martin Yuille in sharing their expertise and international best practice as part of the Scientific Advisory Board for the design phase of GeneLibrary Ireland, an all-island control biobank (funded by HRB and the R&D Office, Belfast). The framework developed in this report is applicable to any bio-resource infrastructure developed for Ireland.

In addition to MMI's contribution as a scientific partner, Ireland is playing a leading role in BBMRI's Stakeholder Forum. In recognition of his reputation throughout Europe as an advocate for patient focussed research, Michael Griffith of Fighting Blindness and IPPOSI was invited to be Chair of the Stakeholder Forum. Derick Mitchell, who is employed by IPPOSI, is the Executive Manager of the Forum. The Stakeholder Forum is actively collating the input and requirements of its broad stakeholder community of biobanking in Europe, comprising patients, clinicians, funding organisations, associated project partners, industry, and researchers.

ECRIN

Clinical research refers to biomedical research performed in humans. Such research covers a wide range of activities from randomised clinical trials on medicines, devices and other therapeutic procedures (surgery, radiotherapy), studies evaluating biomarkers and diagnostic procedures, studies on the mechanisms of disease including genetic studies, and epidemiological studies. Multinational clinical research in Europe is currently hampered by the fragmentation of health and legislative systems, making it very difficult to run investigator-driven, clinical research across borders. Industry, and particularly biotechnology and medical device SMEs, faces similar obstacles. The objective of ECRIN is to facilitate clinical research in Europe by offering services to investigators and sponsors to undertake

³ Italy, Germany, Austria, Iceland, the Netherlands, France, Germany, Spain, Estonia, Norway, Sweden, Belgium, Finland, United Kingdom, Malta, Greece and Ireland.

high quality studies simultaneously in a number of member states. ECRIN is unlocking latent scientific potential and access to patients, thus strengthening the competitiveness of Europe in clinical science and its attractiveness to industry for the development of preventive, diagnostic and therapeutic procedures. This is of particular importance for rare diseases, paediatrics and personalized treatments, for the development of biotherapy, for genome-wide studies requiring thousands of subjects, as well as for large clinical trials that are pivotal instruments for evidence-based medicine.

The ECRIN consortium is designed to provide a European not-for-profit platform to support pan-European clinical research projects. ECRIN connects national hubs - coordinating networks of clinical research centres (CRCs) and clinical trial units (CTU) in any medical field. These national partners, closely associated with disease networks and investigators, have the capacity to enrol patients in a wide range of clinical studies, including in rare diseases, orphan drugs, paediatrics, and biotherapy. ECRIN support is not directed towards a specific specialty or disease category, but fosters transfer of best research practice from specialty to specialty all over Europe – a resource that is equally available to Irish investigators.

There are currently 13 national networks participating in ECRIN representing more than 350 million citizens⁴. They provide a critical mass of patients and expertise both at member state and EU level. There is no other equivalent infrastructure in Europe. ECRIN is progressively expanding to include a greater number of EU and associated countries.

Ireland is playing an active role in the development of ECRIN. The ICRIN Coordinator represents Ireland on the Network Committee and the ECRIN Correspondent, whose salary is covered from FP7 support, provides input to the Working Groups and informs ECRIN policies from an Irish perspective. ICRIN faces a similar challenge in setting up a national coordinating network for clinical research in Ireland to that of ECRIN at a European level and involvement in ECRIN has provided a most useful learning environment. The ICRIN/MMI Roadmap on Clinical Research (to be launched in the near future) has, for example, been strongly influenced by engagement with ECRIN.

To date Ireland has benefited significantly from participation in ECRIN not only financially as indicated above, but also in the following ways;

- ICRIN has contributed to the development of policy documents on procedures adopted for European trials, which in turn are being used to ensure that Irish clinical research centres are operating to international best practice.
- ICRIN is working with European partners to influence legislation and policy on European clinical research, for example the revision of European Clinical Trials legislation, giving Ireland a much stronger influence than if we were not members of ECRIN.
- A number of Irish authors are named on peer-reviewed publications about the conduct of clinical trials across Europe.
- ICRIN has identified opportunities for Irish investigators to participate in ECRIN clinical research pilot projects.
- Participation in ECRIN offers opportunities for training and provides access for all national clinical research professionals to education programmes in multinational clinical research.

⁴ The current participants are Austria, Belgium, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Spain, Sweden, Switzerland, and the United Kingdom.

- ICRIN offers Ireland the opportunity to participate in the Innovative Medicines Initiative training platform, (EMTrain), coordinated by ECRIN partners.

For each country participating, ECRIN facilitates the initiation of, and the participation in, multinational clinical research projects, taking advantage of the population size of the European Union. Irish innovators and SMEs who are developing novel therapies will be able to access this European expertise and population through ECRIN and will thus have experience of working in Europe prior to launching their therapies on the commercial markets.

4. Key Features of the ERIC

The European Council Regulation 723/2009 made under Art 171 of the Treaty establishing the European Community enables member states to join together and apply to the Commission to establish an ERIC as a not-for-profit international organisation responsible for a European RI. Prior to this Regulation, member states wishing to establish governing bodies for multinational RIs had to do so by way of international treaties. To secure ERIC status for an RI, at least three member states must apply to the Commission setting out the purpose of the ERIC, submitting its statutes and naming the seat of the ERIC. The statutes amongst other things must provide for an assembly, a director or board of directors and the financial contributions to be made by the participating member states. There is scope for some variation in the manner in which each ERIC will be constituted

It is likely that BBMRI and ECRIN will be the first research infrastructures to submit an application to the Commission for the approval of ERIC status. Both RIs are at an advanced stage in drafting the Statutes and memorandums of understanding required for an ERIC for the consideration of member states.

Membership of BBMRI-ERIC

It is proposed that membership of the BBMRI-ERIC is either as a full member with voting rights, or as an observer, with no voting rights. It is proposed that the cost of full membership will be based on a flat rate contribution and a contribution based on a proportion of GDP, the amount of which is not finally yet agreed. The total annual cost for Ireland is estimated to be in the region of €100,000/ per annum based on a GDP<€200bn. Five of the member states (Italy, Austria, the Netherlands, France, Sweden) have already committed to be members of BBMRI. It is likely that only full members will benefit from any funding from the EU for access to and use of the infrastructure.

Membership of ECRIN-ERIC

As currently proposed, membership of the ECRIN-ERIC is either as a full member, with voting rights, or as a temporary member with no voting rights. Countries that are full members must make a full financial contribution to the ECRIN-ERIC budget for a minimum duration of five years. They are expected to appoint delegates to represent them and to attend and vote at the meeting of the Assembly of Members. Members can participate in training and similar activities relating to the ECRIN-ERIC and are represented in the Board of Directors by a Scientific Partner with voting rights.

The total annual cost of full membership for Ireland of ECRIN-ERIC is estimated to be in the region of €100,000 per annum, based on a GDP<€200bn. Each member will also be

expected to fund the salary of a European Coordinator, estimated at circa €100,000 per annum.

Temporary Members, must, at a minimum, contribute the salary of a European Coordinator. A written justification explaining the reasons for not applying to a full membership must be provided to the Assembly and must be reviewed at the end of two years. Temporary members can attend the meeting of the Assembly of Members without voting rights. They can participate in training and similar activities relating to the ECRIN-ERIC and are represented in the Board of Directors by a Scientific Partner without voting rights

5. Process for Irish Membership of ERIC

At a meeting of Irish representatives involved in the European Research Infrastructures on January 14th 2010 hosted by the Irish ESFRI members (Dr Eucharia Meehan, HEA and Marcus Breathnach, Forfás), the process for Ireland's commitment to membership of the ERIC was discussed and the following points were noted;

- Irish representatives involved in RIs should work closely with their sponsoring agency/agencies who, in turn, must ensure that their parent Government Departments are fully aware of developments and fully involved in any discussions about on-going commitments associated with full membership of or observer/temporary status on the European RIs.
- For BBMRI and ECRIN and the other BMS RIs, the relevant Department is the Department of Health and Children with the responsible Assistant Secretary is Jim Breslin.
- The lead Department will make the decision as to whether Ireland will sign the ERIC legal instrument and the level of membership of the ERIC to which Ireland will commit. The Interdepartmental Committee under the SSTI has no formal role in the process but will be kept informed by HEA/Forfás.
- BBMRI and ECRIN will be the first RIs to go through the process and will test the system.
- The Department of Enterprise Trade and Employment has already received a letter from Professor Kurt Zatloukal, Coordinator of BBMRI with regard to Ireland's commitment to the BBMRI-ERIC. The Department of Health and Children would issue the formal response.

6. Reasons why Ireland should be a Member of BBMRI-ERIC and ECRIN-ERIC

- I. Membership of the BBMRI-ERIC and the ECRIN-ERIC is consistent with SSTI objectives of greater internationalisation of Irish research and national priorities for RIs and health research.
- II. Membership will leverage European funding opportunities for Irish researchers through European Framework Programme and Innovative Medicines Initiative (IMI) calls. At a recent meeting of the FP7 Research Infrastructures Programme Committee, indicative topic areas for FP7 Research Infrastructures autumn call were discussed. The Committee was advised that FP7 financial support in the region of €30m will be available to RI projects that have sufficiently progressed during the preparatory phase. ECRIN and BBMRI are examples of eligible projects. BBMRI and ECRIN have already been successful in achieving a significant funding award through the Innovative Medicines Initiative call, to establish a *'European Medicines Research Training Network (EMTRAIN)*.

It is proposed that EMTRAIN will establish a pan-European platform for education and training covering the whole life-cycle of medicines from basic research through clinical development to pharmaco-vigilance. In addition, BBMRI has submitted a proposal for both FP7 Health and Infrastructural calls in 2009. IMI call topics also include indicative expectations from the “Applicant Consortium” that they leverage the know-how and expertise from, and connect with, existing networks and projects including but not limited to those linked to ESFRI.

ECRIN and BBMRI are strongly influencing future EU Framework Programme calls. Membership of the ERICs for ECRIN and BBMRI will enable Ireland to leverage potential funding opportunities through future funding calls. This is of particular relevance considering that SFI is now requiring Irish researchers to have ‘*success in international research funding competitions*’ as part of the evaluation criterion for Irish funding awards.

From a broader perspective ECRIN is being engaged at Commission level in approaches for collaboration with the US as the instrument for multinational clinical research in the EU.

Full membership of the ERICs for BBMRI and ECRIN, with a combined expected investment of €350k per year, will afford Ireland access to funding opportunities which Irish researchers and SMEs would not otherwise have access to. Membership would be expected to have a significant return on investment.

- III. Membership will ensure that clinical and translational research infrastructures in Ireland are established and operate according to international best practice and are integrated in the creation of infrastructures for world class research infrastructure in the EU. This will enhance Ireland’s capacity for clinical research to the benefit of patients and the country’s reputation in R&D of interest to the healthcare industry.

Membership of the ECRIN-ERIC will allow Ireland to partner in multinational clinical research studies, taking advantage of the population size of the EU, clinical studies which are not viable within Ireland alone. In addition, members will be able to benefit from the development of common standards, tools and procedures, which will strengthen the attractiveness and competitiveness of Ireland’s clinical research infrastructure and its ability to support high quality clinical research in line with European standards.

Membership of the BBRMI-ERIC will allow Irish researchers to perform large international, statistically-powered, collaborative studies by accessing bio-materials through BBMRI which could not possibly be achieved within Ireland alone and would allow Irish researchers to achieve economies of scale not possible at national level. This would also facilitate Ireland’s involvement in the study of rare diseases for which we do not have sufficient bio-specimens at present. In addition, the strategic development of a national biobanking infrastructure in Ireland, which is in its infancy, will benefit significantly from direct access to expertise and international best practice.

- IV. Membership of the ERICs for ECRIN and BBMRI will demonstrate Ireland’s commitment to the development of the European Research Area. Ireland’s current and future participation in ECRIN and BBMRI maps well with the Government’s strategy for deeper engagement with European research policy and programmes. This commitment and strategy has a particular significance with the appointment of Ms Maire Geoghegan Quinn as European Commissioner for Research and Innovation. The Commissioner has

repeatedly referred to her objective to complete the European Research Area, of which the creation of European Research Infrastructure is an important component.

7. Conclusion

For the strategic and financial reasons outlined above, MMI strongly recommends that Ireland commits to full membership of the ERICs for ECRIN and BBMRI.

April 2010