Regulatory Impact Analysis
on the General Scheme of the National Research Ethics Committee Bill
2019

July 2019

1. Summary

1.1 Having regard to the importance of health research and the need to support it, the intention is develop a fit for purpose National Research Ethics Committee (REC) mixed model framework (encompassing new national RECs and retaining existing institutional RECs) that would encompass all human health research with clear lines on what would be considered by the National RECs and the institutional RECs. Such a model for all health research in Ireland, whether publicly or privately funded, would particularly support the undertaking of important national health research projects and attract international ones, particularly in clinical trials of medicinal products in the post-Brexit era.

1.2 Its successful implementation would necessitate an accompanying National Office that would develop and support a workable and robust mixed REC model and help maximise synergies and value-for-money outcomes.

2. Description of Policy Context and Objectives

2.1 Policy Context

2.1.1 Human health research means innovation and enhanced care for patients. It also promotes the recruitment and retention of outstanding clinicians, ensures better returns on healthcare expenditure and supports broader Government goals of employment and economic gain. For all of those reasons, Ireland, as a country, must work to be the best when it comes to supporting such research.

2.1.2 The Government has committed to the continued development of a research-active health system in Ireland. That commitment has already seen significant public investment in
physical infrastructure, personnel, new skills and technology. At the same time, the Government is equally determined to ensure good research governance as well as appropriate and streamlined regulatory processes. A fit for purpose research ethics committee (REC) structure is an essential element of the necessary regulatory framework. The current structure is problematic for carrying out health research in Ireland, particularly in terms of being competitive in attracting international research projects or supporting major national ones.

2.1.3 Over many years, the Irish Government has invested significantly in clinical research through a variety of Government Departments and agencies. The Health Research Board (HRB) alone has invested more than €150 million in clinical research infrastructure over the last decade. To capitalise on such investment, and to help achieve other strategic objectives, it is essential that Ireland should be seen internationally to have a high standard of, and an efficient system for, research ethics approval.

2.1.4 Despite significant improvement in Ireland’s clinical research infrastructure in recent years, Ireland still punches below its weight in international terms when it comes to conducting clinical trials, especially considering the size of the pharmaceutical industry’s footprint here. In 2016, there were approximately 200 clinical trials either open or recruiting in Ireland, compared with almost 450 in Finland and around 1,000 in Denmark.

2.1.5 To help address this situation, in October 2018, the Minister for Health secured Cabinet approval for Ireland to become a member of the European Research Infrastructure Consortium, namely the European Clinical Research Infrastructure Network (ECRIN). In December 2018, Ireland officially joined as a member country. ECRIN supports the conduct of clinical research across countries in Europe and provides its members with a range of supports and services, including facilitating the preparation and implementation of international trials. This is a positive development for the health research community and should enhance Ireland’s reputation as a place to conduct industry trials. However, this opportunity further impresses the need for REC reform.

2.1.6 This reform process is particularly pressing given that Ireland is likely to hold a unique place in the European clinical trial arena as the lead English-speaking country in Europe post-Brexit. As a member of ECRIN, Ireland is perfectly positioned to take on the country sponsor role for more pan-European clinical trials. After Brexit, it is also likely that
opportunity will significantly increase for Ireland to expand its role as the Reporting Member State (RMS) which leads on the EU-wide assessment of a clinical trial application. This BREXIT opportunity presents itself at a time when Ireland must also be ready by mid-2020 to be fully compliant with the new EU Regulation on Clinical Trials of Medicinal Products which provides a very tight timeframe for ethics approval.

2.1.7 Further, if Ireland is to be a major player internationally in new directions in clinical research (such as genomics), there simply must be a REC structure that not only serves the needs of researchers but is constituted in such a way that it builds essential public confidence in such research through transparency in what it does, expertise in the decisions it makes and oversight in ensuring that it is not a rubber stamping process. In that regard, as a first step, the Minister made Health Research Regulations, in August 2018, under the Data Protection Act 2018 designed to promote health research and public confidence in health research through greater transparency in the use of patient personal data in health research. REC reform is an essential follow up to this legislation.

2.1.8 In addition, and to complement these policy actions taken by the Department of Health, the appointment of Head of Research and Development in the HSE was made during 2017, and a key priority in the HSE National Service Plan for 2019 is to progress the development of a research governance framework in the HSE to support the expansion of high quality research conducted in health and social care settings while safeguarding public and patient confidence in the research conducted. Reform of the national REC system is critical for, and complementary to, the development of this research governance framework.

2.1.9 It is also important to note that while there is some limited statutory regulation of RECs reviewing clinical trials of medicinal products (under the EU Clinical Trials on Medicinal Products Directive as transposed into national law by the Clinical Trials on Medicinal Products for Human Use Regulations 2004 (SI 190 of 2004)), there is no legislative framework whatsoever for RECs dealing with health research other than such clinical trials.

2.2 Historical development of Research Ethics Committees in Ireland

2.2.1 Research ethics committees (RECs) have an important role to play in ensuring the ethical standards and scientific merit of research involving human subjects meets the high standards expected by society. The membership composition of a REC should always be
diverse enough in terms of knowledge, experience and backgrounds to ensure that a range of relevant societal perspectives are brought to bear on research applications.

2.2.2 In Ireland, RECs have historically been established as a consequence of a local institutional initiative (for example, in a hospital or university) rather than a result of any national policy. As a result, there are several kinds of RECs with different jurisdictions and scopes of operation. A survey conducted by HIQA in 2012 identified 72 RECs and anecdotal evidence suggests there are currently 80 plus RECs in existence across the country. They include RECs established in universities, in Institutes of Technology, in hospitals, in voluntary community organisations (e.g. Saint John of Gods, Stewarts Hospital), in government agencies (e.g., TUSLA) and in professional organisations (e.g. RCPI and ICGP), and they vary greatly in the scope of what they will review and the volume of applications they review. Importantly, institutional RECs can only give ethical approval applicable to research in their institution. Therefore, national health projects can become tied up in seeking ethical approval from a significant number of individual institutional RECs leading to delays and significant costs.

2.2.3 Currently, 12 of those 80 plus RECs are what are called “recognised RECs” for the purposes of considering applications for clinical trials of medicinal products. They are institutional RECs that applied to be so recognised under the Clinical Trials on Medicinal Products for Human Use Regulations 2004 (SI 190 of 2004). While “recognised RECs” can give multi-site approval for clinical trials of medicinal products, the reality is that this model of ethical review is not working for stakeholders. The main problems are set out below in 2.3.

2.2.4 Further, despite the large number of RECs in Ireland, there are many studies (especially those which fall outside of biomedical or hospital-based research) that can prove difficult to find an appropriate REC to review them because of a lack of substantive expertise on committees. Some research is not done within an institution (e.g. epidemiological studies, vaccine field trials, studies on health and the environment), and such research would benefit from a centralised REC review system. Many studies are carried out across multiple institutions and actors, and would benefit from a single, national approval process. As stated previously, only those RECs approved for the purposes of the Clinical Trials of Medicinal Products Directive can give a multi-site opinion, and that is only in the case of such trials.
2.2.5 Many countries have evolved to have a mixed model of RECs, with institutional or local RECs and centralised RECs (often called National RECs or Multicentre RECs). In many instances, National RECs are established to guarantee high-quality and timely reviews, typically in areas such as clinical trials or human genome research.

2.3 RECs and Clinical Trials of Medicinal Products

2.3.1 RECs that deal with clinical trials of medicinal products are regulated under a transposed EU Directive by the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, as amended. A new EU Clinical Trials Regulation 536/2014 was adopted in May 2014 and is now scheduled to be fully implemented in 2021. The delay has arisen from ongoing problems with the planned EU-wide, web-based portal known as the Clinical Trials Information System (CTIS), which will allow sponsors to submit a single application dossier to all Member State participants at the same time, while also serving as a publicly accessible database where all relevant information pertaining to a clinical trial is stored. That implementation delay has provided an opportunity for Ireland to better prepare for the implementation of the Regulation. It will be a wasted opportunity not to be fully ready and operational in advance of the implementation deadline.

2.3.2 Ireland’s existing research ethics committee system for clinical trials of medicinal products has been identified by several prominent stakeholders as a significant obstacle to attracting more clinical trials to Ireland. The current structure has 12 recognised (by the Minister for Health) institutional RECs, but in practice most of the RECs do not operate efficiently or effectively. At this time, up to one third of applications that receive regulatory approval (by the HPRA) do not receive the parallel ethics approval within the prescribed timeline, if at all. A recent survey (May 2019) conducted by the Irish Pharmaceutical Healthcare Association (IPHA) found that it takes an average of 86 days for sponsors of clinical trials to receive REC approval compared to an average of 52 days for regulatory approval (there is also significant variation in timelines across disease areas). The new Clinical Trials Regulation requires that a single decision (for ethics and regulatory approval) be granted within 60 days or it will result in tacit approval. This has significant implications for Ireland’s current system. Furthermore, some trial sponsors are still being asked to submit multi-centre studies for multiple reviews, even though the intention of establishing a system to deliver a single national opinion was that this would no longer occur.
2.3.3. The vast majority of EU Member States are reforming their ethics committee structures in preparation for the 2020 implementation of the new Clinical Trials Regulation, with many opting for a centralised system of ethical review to address concerns about accountability, common standards and quality assurance. Some are adapting their system for clinical trials of medicinal products only, whereas others have taken, or are taking, a broader look at research in health and social care. This is, therefore, an ideal time for Ireland to effect reform across the spectrum of health-related RECs so that our RECs are efficient and effective in the increasingly competitive international research environment. The Health Products Regulatory Authority (HPRA), as a key stakeholder, has pressed for action to have an efficient national system in place and operational as quickly as possible.

2.3.4 Based on recent levels of clinical trial activity in Ireland, it is estimated that Ireland will have approximately 120 clinical trials of medicinal products applications per year that require ethical review, with approximately 300 substantial amendment applications. A national structure is the logical way to proceed and would also allow for an appeals process, as required under the Clinical Trials Regulation.

2.4 RECs and the Health Information and Patient Safety Bill

2.4.1 The revised General Scheme of the then envisaged Health Information and Patient Safety (HIPS) Bill proposed a long overdue reform of the REC structure for health research other than clinical trials of medicinal products. In fact, the HIPS Bill approach was essentially modelled on the “recognised RECs” framework for clinical trials in that it provided for “approved RECs” – that is RECs to be approved by HIQA. The experience gained from the time that decision was made in 2010 together with the related views of those involved in health research indicates that that choice can no longer be regarded as feasible. It is also fair to say that the 2010 decision owed much to the very difficult economic situation at the time over the freedom to pursue a better strategic approach.

2.4.2 Pre-Legislative Scrutiny on the HIPS Bill (December 2016-May 2017) identified concerns among researchers and RECs on the proposed model including “potential impracticalities and workload issues” – see also 5 Consultations.
2.5 RECs –other considerations

2.5.1 It is also important to note that the transposition of the Basic Safety Standards Directive requires a national system of ethical approval for research studies involving ionising radiation. Furthermore, approval of the Medical Device Regulation (EU) 2017/745 (MDR) and the In Vitro Diagnostic Regulation (EU) 2017/746 (IVDR) by the EU Commission in April 2017 (with mandatory conformity dates of May 2020 and May 2022, respectively) are likely to have implications for research ethics review also.

2.6 Objectives

2.6.1 Given the policy context and background set out above, the objective must be the development of a fit for purpose, quality assured research ethics committee framework that encompasses all human health research (including clinical trials of medicinal products) that can deliver efficiently and effectively in terms of predictable, consistent and timely decisions at a national level and maximise synergies and value-for-money outcomes.

2.6.2 The Health Information and Quality Authority (HIQA) has conducted a useful review of the REC framework in other countries that shows different models are in use (available on the HIQA website, www.hiqa.ie). However, while having regard to such international evidence the most important thing is to deliver the model that will work best for Ireland and then act accordingly to implement it quickly.

3. Identification of Policy Options

Option 1- Do Nothing

On the basis of what is set out above, leaving the current model in place is to simply accept a far from satisfactory REC framework that acts as an impediment to health research in Ireland. This will result in continuing the status quo where large amounts of time and effort is required by researchers and sponsors, there is duplication of resources, lack of common processes and forms, inconsistency, potential conflicts of interest, lack of oversight, quality assurance and monitoring, delays in decisions (especially for multisite studies) and an overall decline in Ireland’s reputation as a place to conduct high quality research. In particular, the current situation for review of clinical trials of medicinal products will mean that Ireland will simply not comply with the 60 day
timeline set out in the Clinical Trials Regulation. That is especially unacceptable when the situation can be improved significantly by taking appropriate action.

**Option 2- No National RECs but provide supports to institutional RECs**

With such a model a supervisory authority would then be needed to be staffed and resourced to monitor and oversee the RECs, and as that body would exercise regulatory functions it would likely mean that a separate national development office to support institutional RECs would also be required.

With over 80 institutional RECs, the level of financial and other supports would be very significant and would not ensure consistency of decision-making or that timelines would be met. Most importantly of all, it would not guarantee that the decision of one institutional REC would always be fully respected by all other RECs (even if an approved REC system was in place).

This option would mean fragmentation of scare resources and lack of a coherent and consistent approach. The current system of institutional RECs approved for the review of clinical trials is not working and this would disimprove further due to the necessity to ensure a single decision within 60 days (which, in essence, requires a meeting of the committee once a week).

**Option 3- National RECs only**

Under this option, all institutional RECs would cease to exist and the contribution they make to the ethical consideration of health research projects would be lost for no good reason. In their absence, there would be a need for a large number of National RECs to deal with all health research projects (including the very many low risk research studies including by trainees etc). That would be costly and, very probably, time consuming in terms of time taken for applications to be decided on. The most likely outcome of this approach would be that the National REC system would quickly be overwhelmed by applications to such an extent that it would collapse under the burden of what it was being asked to do.
**Option 4- A mixed model with new National RECs and the continuation of institutional RECs**

This is a model that will see the introduction of National RECs for clinical trials and other specified health research while retaining and harnessing the valuable contribution that existing institutional RECs make to health research in Ireland. Essential for its success will be a centralised National Office that that will develop, support and oversee the National RECs.

4. **Analysis of Cost, Benefits and Impacts of Options**

**Option 1 - Do Nothing**

There are no direct costs associated with this approach, but the problems with the existing system are already causing reputational damage to Ireland as a potential location for health research. Furthermore, when the EU Clinical Trials Regulation becomes fully effective in 2020, trial sponsors will avoid Ireland with a consequent loss of research activity and the economic and health benefits that flow from that activity. In relation to health research other than clinical trials of medicinal products, national projects will take longer and be more costly to complete because of the need to secure ethics approval from a number of single opinion institutional RECs. International research, as with clinical trials, will likely avoid Ireland completely.

**Option 2- No National RECs but provide supports to institutional RECs**

With over 80 institutional RECs in play and each with its own particular characteristics and operational issues, it is difficult to quantify the level of support needed and the accompanying related cost but since this approach cannot deliver on the objectives of a fit for purpose REC model for Ireland quantification of supports and costs would be purely academic at any rate.

**Option 3- National REC only**

A National REC only model is possible if the significant level of public funding required to sustain it efficiently and effectively is made available but that begs a simple question: namely, given that public funding is always scarce and needs to be targeted where it can have the most impact and benefit what rationale could be employed to justify every health research project (including all student projects) going through a national REC process. The answer to
that question is none especially since institutional RECs already perform that function very well.

**Option 4- A mixed model with new National RECs and the continuation of institutional RECs**

This is the only feasible model and with proper resourcing (estimated to be less than €1.5 million annually) for the National RECs and the National Office it will be fit for purpose. This is a small figure relative to the overall annual public and private spend on health research and will be well justified in terms of the benefits it can bring with proper implementation. In 2017, DBEI reported that the Government budget allocation for R&D in the health sector was €48.7 million (6.6% of the overall GBARD, €739.3 million). An annual spend of €1.4 million on a fit for purpose National REC model set against this (public only) investment in health R&D represents a small investment (2.8%) to ensure that the overall spend is spent more efficiently, effectively and increases Ireland’s brand and attractiveness to all R&D stakeholders, nationally and internationally.

Furthermore, the CSO indicated that €14.6 billion was spent by Government on healthcare in 2016. In a resource constrained environment, R&D has a key role to play in supporting better decisions in healthcare, and in yielding direct and indirect savings. A recent report produced by Clinical Research Development Ireland (CRDI) entitled *Future Investment in Clinical Research* (May 2019) noted that each patient participating in a clinical trial will generate a benefit of €13,500 to the economy. They estimated that clinical trials involving Irish patients has saved the health services €13 million over two years.

In addition to the societal and economic benefits deriving from investing in a vibrant, research active health research system, the REC model proposed will also facilitate greater public transparency about the work of (national) research ethics committees, and the consistency of decision-making will ensure greater predictability for health researchers when making applications. Further, while it is important that the National Office and National RECs are independent in carrying out their functions, it is considered that establishing the National Office as a distinct and separate statutory office located within the Health Research Board (HRB) will guarantee operational independence and also help ensure that the new structure can benefit from the quality brand associated with the HRB.
Options- Conclusions

The reality is that the present REC system for clinical trial of medicinal products does not work for trial sponsors or other stakeholders. The fault does not lie with individual recognised institutional RECs but with the system that sought to address national challenges through local endeavours. With shorter timelines and tacit approval coming into play under the new EU Clinical Trials Regulation, the current framework needs a radical overhaul to make it fit for purpose. A consideration of all the relevant factors – including background issues, experience gained, costs, benefits and impacts - points clearly to the need for a model of National RECs supported by a National Office.

When it comes to other health research, the existence of over 80 institutional RECs quickly reveals a fragmented system that works reasonably well where a research project relating solely to the institution concerned is being considered by the REC established by the institution. It does not work at all where national projects are involved and separate applications have to be made to numerous institutional RECs with no guarantee of consistency in decision-making and at considerable cost for the researcher. Such a time-consuming model does little to encourage national research projects and nothing to attract international ones.

The optimal solution, therefore, is that-

(a) all clinical trials of medical products go to a National REC to ensure that applications can be made and considered not only consistently with the requirements (including timelines and single national decisions) of the new EU Regulation, but also with positioning Ireland as an excellent location for attracting such trials, and

(b) the same National REC model also apply for other specified types of health research (mainly national projects) to ensure consistent, timely and single point decision-making with the institutional RECs continuing to operate at an institutional level.

As it is envisaged that the same National Office will develop, service and oversee (a) and (b), rather than having a separate National Office for each, there will be savings and economies of scale in shared staff and infrastructural facilities (e.g., website, centralised online application and review system, training/CPD).
Option 4 is therefore recommended as not only the sole workable model, but as one that can deliver major benefits across all health research for a low level of public expenditure.

**Impacts -National Competitiveness**

Attracting international health research to Ireland, particularly in the area of clinical trials of medicinal products, is a highly competitive business. The model proposed will significantly enhance Ireland’s competitive position in that regard.

Investment in clinical research alone provides returns in several different ways. In the short-term, there is pay off as an economic driver. In the long-term, there can be pay off in terms of new and better standards of care, increased productivity or readiness due to a healthier population, and improved quality of life for individuals. The Irish Government has invested significantly in clinical research infrastructure to ensure that we attract trials and that these trials benefit the patient, the healthcare system and the wider economy.

HRB-CRCI reported recently that there are 8 clinical research facilities/centres in Ireland, with 232 directly employed staff and over 400 investigators, resulting in 219 actively recruiting trial sites across 32 hospitals. Failure to deliver a streamlined, efficient, single national opinion for clinical trials will put this existing investment in jeopardy.

Furthermore, the Minister for Health recently launched Ireland’s membership of ECRIN. Ireland is likely to hold a unique place in the European clinical trial arena as the lead English-speaking country in Europe post-Brexit. As a member of ECRIN, Ireland is perfectly positioned to take on the country sponsor role for more pan-European clinical trials. After Brexit, it is also likely that opportunity will significantly increase for Ireland to expand its role as the Reporting Member State (RMS) which leads on the EU-wide assessment of a clinical trial application.

**Impacts -Compliance Burden**

While approval of a research ethics committee is currently only legally required in certain areas –mainly clinical trials of medicinal products- the de facto reality is that all health research in Ireland undergoes ethical examination by a REC. Accordingly, the model proposed does not give rise to a compliance burden but will, in fact, reduce it for many research projects.
5. **Consultations**

The indisputable need for reform in the research ethics area has been articulated by many bodies and persons over the past decade including the Health Research Board, HIQA, the Health Products Regulatory Authority, researchers, research ethics committees, research performing organisations, funders, industry and others. All have articulated the value of a national framework involving National RECs.

In the context of the research ethics provisions in the Health Information and Patient Safety Bill, the Department of Health met with numerous groups and delivered presentations in many institutions. Nationally, the Department in association with HIQA organised a national event in Dublin Castle on 30 June 2014 on research ethics issues relating to all health research, including clinical trials. Almost 200 persons attended—they included researchers, ethics committee representatives, hospitals and universities, patient advocates, funding bodies and industry.

The Oireachtas Committee on Health, as part of its Pre-Legislative Scrutiny on the Health Information and Patient Safety Bill, publicly invited submissions (December 2016) on the Bill and the submissions received dealing with the research ethics part of the Bill were featured in the published Report of the Committee on the Bill (May 2017). The preparation of the General Scheme of the National Research Ethics Committee Bill was fully informed by that Report and the submissions made to the Committee.

As the Oireachtas Committee on Health had undertaken a public consultation process (see above), the Department did not carry out an additional formal consultation exercise, but it has engaged with stakeholders. For example, it met recently with representatives from the current recognised RECs for Clinical Trials on Medicinal Products, and will continue to engage with them and others as the Bill is progressed.

More generally, in terms of public involvement, the implementation of the planned National REC model will see a public call for Expressions of Interests to be a member of a National REC and the composition of the National RECs will see strong representation from lay members to ensure that a broad and balanced societal perspective underpins the ethical consideration process.
6. **Enforcement and Compliance**

6.1 The nature of what is being proposed – namely, National Research Ethics Committees backed by a centralised National Office that will develop and support them – will also see the National Office monitor how the Committees are performing and take such actions (as will be specified in the Bill) to ensure that the Committees operate in line with both the legislation and any guidelines issued by the National Office. In some cases, performance issues may emerge that can be best addressed informally by a discussion between the National Office and the Chairperson. On some occasions, that discussion may need to be of a more formal nature and it may even be necessary to remove the chairperson, other members or even the entire membership of the National REC concerned.

7. **Review**

7.1 It is important to bear in mind that the structures proposed are new and may take a little time to bed down fully. This is where the development and support role of the National Office will be crucial. However, it is also the case that another of the express functions of the National Office is to monitor and review and to take appropriate action, where necessary, to better steer the model towards achieving its objectives. Should problems emerge that are more fundamental or systemic, it may be necessary for the National Office to bring this to the attention of the Minister. That would especially be the case where a change in legislation might be required.

7.2 The Bill will also provide that the Minister must, not later than 5 years after the passing of this Act, commence a review of the operation of this Act and when the review is completed make a report to each House of the Oireachtas on the findings and conclusions resulting from the review.

7.3 Separate from 7.2, there is also a formal process of post-enactment scrutiny for almost all primary legislation in Ireland by Oireachtas Committees. The 2016 Programme for Government commits to continuing the requirement that, 12 months following the enactment of a Bill, the member of Government or Minister of State who is officially responsible for implementation of the Act must provide a report which will review the functioning of the Act.