National System of Research Ethics Review –
Transition to National RECs for Regulated Health Research
FAQs

This is a working document, intended as indicative information. Content is subject to change.

1. How are NRECs established?

It is the intention of the Minister for Health to appoint National Research Ethics Committees (NRECs) in the initial priority areas of clinical trials of medicinal products and clinical investigations of medical devices, in line with the imminent EU Regulations in these areas, EU CTR No. 536/2014 and EU MDR No. 207/745, respectively. A public call for Expressions of Interest for NREC membership was launched by the National Office in December 2020 to ensure the diverse membership base required to consider applications likely to be made to the NRECs, including varied expertise and experiential knowledge. Individuals with and without prior REC experience were welcome to apply. The EoI assessment process is in the advanced stages, with a view to making a selection for recommended consideration by the Minister for appointment. Recommendations are made on individuals' merits and not necessarily in a representative capacity, mindful of the balance of expertise and perspectives required.

2. Who decides the membership of the NRECs?

The Minister for Health decides on the formal appointments to the NRECs. The National Office is managing an assessment process following a public call for Expressions of Interest for NREC membership with a view to making a selection for recommended consideration to the Minister for Health for appointment; this process is in the advanced stages. Recommendations will be made on individuals' merits and not necessarily in a representative capacity, mindful of the balance of expertise and perspectives required. Member recommendations are also informed by appropriate representation of both 'expert' and 'lay' members in line with best practice. Where in the view of the National Office there is likely to be a particular gap in expertise or representation, prospective Members may be approached to invite an Expression of Interest.

3. Will NREC members receive training?

Yes; the National Office plans to facilitate training for NREC members on the fundamentals of research ethics review and other components of the health research environment in Ireland.

While some NREC members will have prior REC experience, many may not, so it is important to begin on a common solid grounding of training, particularly given the regulated remits of clinical trials and medical devices.

4. Will CPD points be possible for NREC participation?

Training for and participation in NREC meetings may be eligible for recognition for Continuing Professional Development (CPD) points. The National Office team can provide confirmation of attendance and other evidence to support CPD applications.

The Royal College of Physicians of Ireland (RCPI) have confirmed that NREC training and participation may be eligible for recognition as 'Committee Meetings' for the Internal CPD Category (Practice Evaluation & Development) subject to satisfactory evidence of participation (1 CPD credit for each hour spent on eligible activities). Interested NREC Members should consult the RCPI website, which currently states:

Committee Meetings: *Credits for activities related to Committee Meetings can be claimed under the Internal category. However a doctor's PCS activity must be balanced and mirror his/her clinical practice and activity and reflect his/her scope of practice across all domains of practice. Participation on committees is eligible for Internal CPD credits to a maximum of 5 credits each year. There must be a patient safety element to the remit of the committee.*

https://www.rcpi.ie/professional-competence/information-for-enrolled-doctors/cpd-explained/

5. Will the posts in the NREC be remunerated?

NREC Membership is a voluntary role in public service. Given the extent of the commitment required for the roles of Chairperson and Deputy Chairperson, annual fees will be paid of €10K and €5K to these appointees respectively. Acknowledging that Committee work may not be professionally recognised or may clearly fall outside of typical responsibilities for some, PPI Members will be offered an annual fee of €2.5K. Other NREC Members will not be paid. All Members will be eligible to be reimbursed for reasonable out-of-pocket expenses.

6. **Can recognised local RECs continue to review Clinical Trials of Investigational Medicinal Products (CTIMPs) in addition to the NREC-CT?**

   Yes; to enable a smooth transition, the majority of 'recognised RECs' have agreed to continue to provide research ethics review for CTIMPs during a defined period. Accordingly, both the NREC-CT and 'recognised RECs' will have authority to review CTIMPs, and therefore will collectively support this important research area, from May to December 2021. When the NRECs are formally established, it is expected that the research community lean on the NREC system in the first instance before exploring the option of a 'recognised REC' for the duration of the transition.

   The concurrent operation of NREC-CT and 'recognised RECs' over the transition period will maintain momentum in clinical trial research while maximising opportunity for preparedness at a national level for the EU Clinical Trials Regulation (CTR) (EU No 536/2014). In line with the anticipated application of the EU CTR in January 2022, it is essential that Ireland has a fully operational national system for CTIMP regulation and review, including returning nationally applicable ethics opinions, following processes in line with international best practice. Importantly, the NREC review process will run in coordination where necessary with the HPRA to ensure Ireland meets its Member State obligations to return a 'single national opinion' in relation to the EU CTR, in addition to the EU Medical Device Regulation (EU No 2017/745). This will be best achieved by a cohesive system of independent NRECs supported operationally by the National Office; correspondingly, existing 'recognised RECs' will not have authority to review CTIMPs after the transition period. This will not affect the local REC jurisdiction in relation to health research that falls beyond the scope of the defined remit of the NRECs.

   We recognise that this transition represents a major change to the research environment and our goal is to make it as seamless as possible; this will require coordination, communication and a degree of patience from the parties involved, in particular the National Office, local RECs and the research community.

7. **What if an ongoing study originally approved by a local REC requires a substantial amendment?**

   The responsibility for review of substantial amendments to ongoing studies, previously approved by local RECs (including 'recognised REC'), which now fall within the remit of the NREC-CT or NREC-MD, lies with the respective NREC. In this case, the applicant will be requested to provide all original documentation that supported the original local REC approval, to the National Office. The National Office and the local REC may share information in relation

to the study in question to support informed ethics review and oversight of the study. Such amended studies will report to the NREC thereafter including annual, final, and safety reporting.

The transition to the NREC system triggered by a substantial amendment will begin in May once the NRECs are fully established. Once a study transitions to the NREC system through the submission of a substantial amendment, the National Office will take on the role of monitoring and reporting for that study.

8. What about annual reporting for ongoing studies previously approved by a local REC?

In the spirit of pragmatism, studies previously approved by local RECs (including those 'recognised') and ongoing in May 2021, should continue to report operationally (e.g. annual reporting, safety reporting) to the approving REC. The requirement for a substantial amendment to an ongoing study that now falls within the remit of the NREC-CT or NREC-MD will be the trigger for review by the NREC. Such amended studies will report to the NREC thereafter including annual and safety reporting (see Q7).

9. Can applications be made to local RECs for clinical investigations of medical devices in addition to the NREC-MD?

No; a pivotal component of the NREC system will be the return of a single nationally applicable ethics opinion following robust processes in line with international best practice. There is no mechanism currently for a multisite medical device study ('clinical investigation') to secure ethics approval that is nationally applicable. Importantly, the NREC review process will run in coordination where necessary with the HPRA to ensure Ireland meets its Member State obligations to return a 'single national opinion' in relation to pending EU Regulations, including for CTIMPs (EU No 536/2014) and clinical investigations of medical devices (EU No 2017/745). This will be best achieved by a cohesive system of independent NRECs supported operationally by the National Office.

The NREC-MD will be established in May 2021 and will provide ethics review for clinical investigations of medical devices in line with the MDR. This will not affect the local REC jurisdiction in relation to health research that falls beyond the scope of the defined remit of the NREC-MD. To minimise disruption to the research community, local RECs will continue to facilitate ethics review for as long as practically possible up to the transition.

The MDR will be applicable in Ireland from 26th May 2021. Clinical investigations that are due to be commenced after the 26th May 2021 will need to be authorised under the MDR, and therefore will need to be issued with a single nationally applicable ethics opinion. Any

application ‘in hand’ by local RECs for which the date of commencement of the clinical investigation is indicated after 26th May 2021 should be forwarded to the National Office (copying the applicant) for NREC-MD review.

We recognise that this transition represents a major change to the research environment and our goal is to make it as seamless as possible; this will require coordination, communication and a degree of patience from the parties involved, in particular the National Office, local RECs and the research community.

10. Should single-site studies be directed to NRECs for ethics review?

Yes; if the study falls within the remits of health research defined for the NRECs, it should be submitted to the National Office for review.

11. In what areas will future NRECs be established?

The Minister for Health will establish NRECs in select health research areas of national strategic importance. In this regard, the Head of the National Office for Research Ethics Committees will make recommendations. In the first instance, NREC remits will pertain to those areas for which Ireland has a legislative obligation, including CTIMPs and clinical investigations of medical devices. Future NRECs may be established in such areas as assisted human reproduction and genomics.

12. Are NREC-approved studies recognised for insurance purposes under the Clinical Indemnity Scheme (CIS)?

For those studies that fall under the Clinical Indemnity Scheme (CIS), the State Claims Agency has confirmed that an NREC approval is recognised for their purposes. It is the responsibility of the Principal Investigator (PI) to notify the State Claims Agency of their study. This is an important requirement of research governance and for good research practice.

13. What is the expected turnaround time for an NREC decision?

The timelines for NREC decisions will be consistent with those required by pending EU Regulations for clinical trials (EU No 536/2014) and medical devices (EU No 2017/745). In the first instance, the National Office is planning for an NREC meeting schedule that facilitates CTIMPs to be considered twice per month and clinical investigations of medical devices to be considered monthly.

The National Office will collaborate with the HPRA in 2021 to run the CTR National Collaboration Project with select volunteer applicants to prepare for a 'single national opinion' by testing the processes and timelines required for the EU CTR; in this regard, the timing of an NREC decision will be coordinated with the regulatory decision of the HPRA. When the EU CTR is applicable (anticipated January 2022), the NREC-CT will work to the timelines set out in the EU CTR. From the initial launch of the NRECs in May 2021, applicants submitting to the NREC-CT may expect a decision on a valid application within 60 days.

For clinical investigations of medical devices, applicants wishing to avail of parallel regulatory & ethics review, should submit by the monthly NREC-MD cut-off date to ensure optimal review time. Applicants submitting to the NREC-MD may expect a decision on a valid application within 55 days.

14. Do researchers need to seek approval from their local REC in addition to the NREC?

No; NRECs will be legislatively mandated to return decisions that are applicable nationally, and as such, the research community including local RECs, will be expected to respect the outcomes from the NREC process. Conversely, an NREC will not revisit a decision made by a local REC within its local remit. In line with good research practice and research governance, researchers should secure the necessary local approvals required to conduct the research at each site and notify their local REC and Research Office or equivalent body in their institution of NREC decisions.

15. Will the NRECs (and their decisions) have a legal basis?

Yes, the NREC-CT and NREC-MD will operate on a statutory basis from the outset under new and / or amended regulations (secondary legislation) to be made by the Minister for Health early in 2021. The National Research Ethics Committees Bill represents the second "track" of a twin-track legislative approach to reforming the ethics review system across all types of human health research. Work on the NREC Bill will continue throughout 2021.

16. What if an applicant is unsure of the route to take for ethics approval of their study?

Applicants should determine if their study meets the scope of NREC review. The scope of review of the NRECs will be determined by imminent EU Regulations in the areas of clinical trials of investigational medicinal products (EU No 536/2014) and clinical investigations of medical devices (EU No 2017/745) respectively. It is the applicant's responsibility to determine

the nature and definition of their study; however where an applicant is in any doubt as to whether their study falls under the EU CTR or EU MDR, both the HPRA and the National Office can assist.

If a study meets the definition of a CTIMP, it may be considered by the NREC-CT or a 'recognised REC from May 2021.The majority of 'recognised RECs' will continue to review CTIMPs from May throughout the defined transition period until December 2021. When the NRECs are formally established, it is expected that the research community lean on the NREC system in the first instance before exploring the option of a 'recognised REC'. The National Office team will be pleased to assist with identifying the most efficient route for ethics review, mindful of the meeting schedule and agenda of the NREC-CT.

If a study meets the definition of a medical device and its commencement date falls after 26th May 2021, it will need to be authorised under the MDR, and as such, must be considered by the NREC-MD. Applicants wishing to avail of parallel regulatory & ethics review should submit by the monthly cut-off date to ensure optimal review time.

17. What if a research institution or local REC has a query on an NREC-approved study?

The National Office seeks to work in partnership with research institutions and local RECs and is pleased to answer any queries on the NREC process including sharing summary information on applications receiving approval. Queries should be directed to nationaloffice@nrec.ie

18. What's the mixed-model REC system?

Health research infrastructure will be strengthened in Ireland by a mixed-model system of research ethics review as provided for by the NREC Bill. This means that NRECs will work alongside local RECs, each with clearly defined remits, to ensure that Irish health research is underpinned by the highest ethics standards. The mixed-model system will be supported by parallel reforms in research governance led by the R&D Team at the HSE.

19. The National Office will have a monitoring role for NRECs; will this extend to local RECs?

No; the legislation will provide for a monitoring and oversight role for the National Office over NRECs only. This is to ensure that NREC performance and standards align with the guidelines adopted by the National Office, in addition to prevailing national and international law.

However, an important aspect of the National Office remit pertains to education and outreach; in this regard, the National Office will engage with the local REC community for educational

outreach and training purposes, with a view to further improving the overall operational and decision-making quality of all RECs in Ireland.

20. What about studies involving ionising radiation?

Studies involving ionising radiation represent a regulated remit for health research and as such, will be encompassed in the national system of research ethics review. The National Office is working with the Department of Health and local REC stakeholders to find an appropriate mechanism for review of studies involving ionising radiation, recognising the niche expertise required. It is expected that a national route for ethics review of studies involving ionising radiation for medical purposes will be developed by Q3 2021. In the meantime, such applications should continue to be directed to existing 'recognised RECs' under this remit.

21. Will the currently used local forms be used for NREC review?

For practicality and to assist with a seamless transition of ethics review, in the immediate term the National Office will accept applications for NREC-CT review on application documentation currently used in the local REC system. The NREC-CT will also require a Data Protection Impact Assessment (DPIA) or statement why this is not required, and site-specific assessment form(s). Additional supporting information or documentation may be requested of applicants to inform the NREC review process. The format for application documentation will likely be revised in in January 2022 to meet EU CTR requirements; the research community will be informed of this in a timely manner.

The National Office will initially accept applications for NREC-MD review on the Standard Application Form for Non-clinical Trials, currently used for medical device studies in the local REC system. A DPIA, or statement why a DPIA is not required, and a site-specific assessment form (or site suitability form) will also be required.

22. When will the EU Clinical Trial Regulation be applicable in Ireland?

The EU Clinical Trial Regulation (EU CTR) No 536/2014 was adopted and entered into force in 2014. The timing of its application depends on confirmation of the full functionality of the Clinical Trial Information System (CTIS), the centralised EU portal and database for clinical trials. The EU CTR becomes applicable six months after the European Commission publishes notice of this confirmation. The European Medicines Agency (EMA) and Member State representatives

are developing a ‘go-live’ plan for the CTIS with a working assumption of a ‘go-live’ date of January 2022. The National Office and HPRA are represented on a number of the Member State working groups and are committed to staying abreast of developments with the EU CTR and CTIS.

23. Will there be fees associated with NREC reviews?

Yes; applications for NREC review should be submitted to the National Office accompanied by a prescribed fee. In the first instance from the time of NREC launch, the fees for ethics review will align with those currently in place for the local REC system.

It is anticipated that a new fee structure will be required for the NREC-CT with application of the EU CTR, anticipated in January 2022. These fees will be determined in consultation with the relevant Government departments including the Department of Health and Department of Business, Enterprise & Innovation. Fees due under the EU CTR will represent a combined fee for both ethics and regulatory approval.

24. Will decisions taken by the NRECs be made public?

The National Office is committed to transparency and will make publicly available on our website the minutes of NREC meetings and details of decisions taken.

25. Will NREC review pre-clinical studies or pilot studies for medical devices?

The NREC-MD will review clinical investigations of medical devices as defined in the Medical Devices Regulation (MDR; EU No 2017/745). Pre-clinical studies do not come under the MDR and therefore should be reviewed by the relevant local RECs. Early-stage clinical investigations can be regulated studies per the MDR so they may fall within the NREC-MD remit. Applicants should discuss the appropriate route for ethics review of their study with the National Office in advance.

26. Could you clarify what happens with non-trial clinical multicentre studies - LREC or NREC?

Non-trial clinical multicentre studies do not come under the imminent EU Regulations, therefore remain within the remit of the local RECs. Parallel reforms in research governance and the local

REC system led by the R&D Team at the HSE will assist in streamlining REC approvals for multisite clinical studies in the future.

27. What about external organisations such as charities, services that do not come under HSE or Hospital RECs - where do they go the get ethical review?

Both the NREC-CT and NREC-MD will have defined health research remits in line with the respective relevant EU Regulations in clinical trials and medical devices. Any research study that falls within the remits of the NREC-MD or NREC-CT must be reviewed through the NREC system. The NRECs will not review studies that do not come under these Regulations.

The National Office is aware of the limited options for researchers who do not have access to an institutional / local REC. We are contributing to discussions with key stakeholders, led by the HSE R&D Team, to find a solution in the context of wider reform of the ethics review system in Ireland.

28. What role will the NRECs take on in relation to safety reporting?

In line with current practice, from the time of NREC launch, applicants must notify the NREC-CT about urgent safety measures, suspected serious unexpected adverse reactions, and submit annual safety reports for notification, related to studies approved by the NREC-CT. For studies ongoing prior to May 2021, the safety reporting relationship is established to the NREC-CT from the time it considers a substantial amendment (see Q7). Assessment of safety reports and notifications will be undertaken by the HPRA.

The process for the assessment of safety reporting will necessarily change under the EU CTR. In this regard, the specific role of the NREC-CT in safety reports will be further be clarified.

29. Will the NREC-CT have access to the Clinical Trials Information System under the requirements of the Clinical Trials Regulation?

The National Office will have access to the CTIS, in addition to the HPRA, once launched. As Member State representatives at EU level, both organisations are currently receiving CTIS training and orientation by the EMA.

30. Will the NREC-CT have any specific application / Part II template requirements?

The National Office will trial the recommended European Medicine Agency templates for the CTR Part II documentation dossier under the CTR National Collaboration Project (see Question 13 for more information). These templates may be adapted later in the year based on insights and feedback from the Collaboration Project, with a view to continued use once the EU CTR is applied.

The submission of a completed DPIA, or a statement outlining why a DPIA is not required, will be a requirement for all submissions to the NREC-CT in future.

31. Why is a DPIA required as part of the submission process?

As part of the ethics review process, the NREC-CTs and the NREC-MD need to be assured that the research study will be carried out in accordance to national and European data protection legislation. For this reason, a Data Protection Impact Assessment will be required as part of the submission process. If a DPIA is not relevant to your project, then a statement outlining why a DPIA is not necessary will be required. The expectation will be that the DPIA is reviewed by the institutional DPO ahead of submission to the NRECs.

The National Office will not be issuing an NREC-specific DPIA template. Instead we will accept submissions using institutional DPIA templates.

32. What is the remit of studies reviewed by the NREC-CT?

The NREC-CT will review applications that meet the requirements under the EU Clinical Trial Regulation. This encompasses interventional trials, including low-interventional trials, with medicinal products for human use.

Under this remit, the NREC-CT will review applications that include a combination of investigational medicinal products and ionising radiation such as chemo-radiotherapy trials.

Non-interventional studies and trials that do not include medicinal products will continue to be assessed through the local REC system.