NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

Public Consultation on proposal for NREC Fees

Financial Year 2023

10 October 2022

Table of Contents

Introduction

1.1 National Office

The remit of the National Office for Research Ethics Committees (hereafter the 'National Office')[1], is to enable and embed a robust, transparent and cohesive research ethics review system that strengthens the national health research infrastructure.

In 2021, under the auspices of the Department of Health, the National Office established National Research Ethics Committees (NRECs) to review the submission of ethics applications and deliver a 'single national ethics opinion' in the following regulated areas of health research:

- clinical investigations of medical devices; assessed by the National Research Ethics Committee for Clinical Investigations of Medical Devices (NREC-MD)
- performance studies of *in vitro* diagnostic medical devices; assessed by the 'NREC-MD'
- clinical trials for investigative medicinal products; assessed by the National Research Ethics Committee for Clinical Trials for Medicinal Products (NREC-CT)

To ensure the National Office manages the business of the NRECs with efficiency and rigor, and in accordance with legislative obligations, it committed to review its ethics application fee structure on an annual basis. This commitment was set out in the initial '*Public Consultation on Proposal for HPRA and NREC Clinical Trial Fees – Financial Year 2022*'[2].

In line with that commitment, a review of fees has been carried out by the National Office. In the spirit of transparency, this consultation document provides details of the fees intended to be charged for all ethics applications submitted to the respective NRECs for consideration, in 2023.

Proposed changes to the fees for ethics applications submitted to the NREC-MD and NREC CT, are summarised out in Appendix I.

1.2 Public consultation process

The public consultation on fees for 2022 was a jointly coordinated initiative between the Health Products Regulatory Authority and the National Office and focused solely on the fees for applications submitted under the Clinical Trials Regulation.

The current consultation for 2023 is aimed to gather feedback on all areas of regulated research currently under the auspice of the National Office.

Proposed changes to the fees for applications to the Health Products Regulatory Authority (HPRA) for 2023, can be viewed on the **HPRA website.**

The National Office invites stakeholders to share their views with us on these proposals.

Contributions to the consultation on these proposals may be provided to the National Office by 28th October 2022. Contributions should be sent by email to nationaloffice@nrec.ie with subject "Fees consultation".

[1] https://www.nrecoffice.ie/

[2] https://www.hpra.ie/docs/default-source/default-document-library/public-consultation-on-clinical-trial-fees-2022.pdf?sfvrsn=4

1.3 Current legislative framework in Ireland

Since the establishment of the National Office in 2020, there have been significant and far-reaching legislative reforms to create a robust, transparent, and sustainable regulatory framework for health research. These regulated areas of research drive a harmonised and coordinated approach to the conduct of research studies, for the benefit of participants' safety, dignity, and well-being.

- As of 26 May 2021, all *clinical investigations of medical devices* are regulated by the Medical Device Regulations (MDR, EU No. 2017/745), which is transposed into national law by S.I. 260/261 of 2021[3][4].
- As of 26 May 2022, all new *performance studies of in vitro diagnostic medical devices* are regulated by the In Vitro Diagnostic Medical Devices Regulation (IVDR, EU No. 2017/476), which is transposed into national law by S.I. No 256/257 of2022.
- As of 31 January 2022, all *clinical trials for investigative medicinal products* are regulated by the Clinical Trial Regulation (CTR, EU No. 536/2014), which is transposed into national law by S.I. 99/41[5][6] of 2022.
- As of 31 January 2023, the EU Clinical Trial Directive (CTD: EU No. 2001/20/EC)[7] will be repealed by the CTR), which is transposed into national law by S.I. 190 of 2004[8].

Notwithstanding the above legislative changes since 2021 and 2022, there is a three-year transitional arrangement whereby applicants can continue to

i) submit new ethics application for clinical trials for medicinal products under the CTD, during the first-year post-implementation of the CTR, until January 2023, and

ii) submit substantial modifications during the three-year transition period, until January 2025. During this transition period separate applications to the HPRA and the National Office will continue to be required for clinical trials submitted under the CTD.

The CTR, MDR and IVDR aim to create a robust, transparent, and sustainable regulatory framework, recognised internationally. These regulated areas of research drive a harmonised and coordinated approach to the conduct of research studies, for the benefit of participants' safety, dignity, and well-being.

To this end the National Office is committed to delivering a single national opinion for Ireland on the ethical aspects of a study in regulated area of research, within EU-mandated timelines. This is a positive development for Sponsors conducting research in Ireland, and participants in such studies.

1.4 Application & Fee process In Ireland

Applications under the MDR and IVDR

To enable Ireland in meeting its regulatory requirements, in May 2021 the National Research Ethics Committee for Clinical Investigations of Medical Devices (NREC-MD) was established

[3] https://www.irishstatutebook.ie/eli/2021/si/260/made/en/print

[4] https://www.irishstatutebook.ie/eli/2021/si/261/made/en/print

[5] https://www.irishstatutebook.ie/eli/2022/si/99/made/en/print

[6] https://www.irishstatutebook.ie/eli/2022/si/41/made/en/print

[7] https://health.ec.europa.eu/system/files/2016-11/dir_2001_20_en_0.pdf

[8] https://www.irishstatutebook.ie/eli/2004/si/190/made/en/print

to review the submission of ethics applications regulated by the MDR. As of May 2022, the remit of the Committee broadened to also include the review of ethics applications for Performance Studies of In Vitro Diagnostic Medical Devices, regulated by the IVDR.

Applications that fall under the MDR and IVDR require a separate review by the HPRA and by the NREC-MD.

To apply, applicants must pay the relevant fee in advance of submission to the NREC-MD. The process of payment is facilitated through advanced invoice and is outlined in detail on our website: https://www.nrecoffice.ie/apply-2/fees/

Applications under the CTD

To enable Ireland in meeting its regulatory requirements, in May 2021 the National Research Ethics Committee for Clinical Trials for Medicinal Products (NREC-CT) was established to review the submission of ethics applications regulated by the CTD, during the transition phase and implementation of the CTR.

Applications that fall under the CTD, require a separate review from the HPRA and from the NREC-CT.

To apply, applicants must pay the relevant fee in advance of submission to the NREC-CT. The process of payment is facilitated through advanced invoice and is outlined in detail on our website: https://www.nrecoffice.ie/apply-2/fees/

Applications under the CTR

To enable Ireland in meeting its regulatory requirements, in May 2021 the National Research Ethics Committee for Clinical Trials for Medicinal Products (NREC-CT) was established to prepare for the submission and subsequent review of ethics applications regulated by the CTR.

Applicants intending to conduct a clinical trial in Ireland under the CTR must apply for approvals via the single EU portal, Clinical Trials Information System (CTIS)[9].

There are two parts to the assessment: Part I (protocol and investigator's brochure, investigational medical product dossier etc.), and Part II (informed consent documents, suitability of the investigator/facilities etc.). The clinical assessment will be conducted by the HPRA and ethical assessment by the NRECs as per their respective remits. Part I can be submitted alone, and Part II submitted up to two years later. The following principles will apply:

- The full fee will be charged on submission of Part I documents. No refund will be permitted once the clinical trial is validated.
- If an applicant decides subsequently that a trial will not commence in Ireland, and no Part II is submitted, no refund will be permitted.

A single fee is charged by Ireland, managed by the HPRA and on behalf of the National Office. The Applicant will pay the fee to the HPRA at the time of submitting a clinical trial application to the CTIS and following validation the HPRA will transfer the corresponding portion to the National Office.

[9] https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system

For substantial modifications to Part I, Part I and II, or Part II documents, the fee will be paid to HPRA, and a portion transferred to the National Office in the usual way. No refund will be permitted once the application is validated.

The process of payment outlined in detail on the HPRA website:
http://www.hpra.ie/homepage/medicines/regulatory-information/medicines-fees

1.5 Impact of regulations on the business of the National Office and NRECs

When the NRECs were launched in 2021, the National Office fee structure was set at modest rates intended to facilitate and attract health research trials to Ireland. This was particularly important given the changing landscape of ethics review system in Ireland and emerging legislative changes, coupled with the National Office being in its infancy.

Since then, the National Office and NRECs have processed and considered an overwhelming volume of ethics applications of varying complexity and gained learned experience of navigating the regulatory requirements, meeting timelines and deliverables. Furthermore, in this period the National Office developed and embedded key processes to enable Ireland, through its NRECs to deliver robust, consistent and transparent ethical assessments in regulated areas of research, safeguarding the health well-being and safety of research participants.

Since the launch of the NRECs in 2021 the staffing of National office members has more than doubled to a team of 13. Additional staff were recruited to manage the increased volume of workload due to the complex implementation of the CTR, MDR and IVDR, including the management of the studies under the CTD.

Furthermore, in 2022, new NREC members were recruited to all Committees. These members complement and bring additional expertise to ensure preparedness for the IVDR, and to assist with the influx of applications for new studies and substantial modifications under all regulated areas of research.

The National Office will continue to assess the impact of the legislative changes and enhance where possible, associated operational and business needs. To reflect the new structures, increased workload, recruitment of NREC members, upskilling of staff and essential requirement for capacity building for the National Office and NRECs, it is thus necessary to increase the fees for 2023.

MDR and IVDR

Both MDR and IVDR have made a profound change to the regulatory system and significant work is ongoing in this area at national and international level. The first year of MDR has seen a steady rise in the volume of applications for new clinical investigations and substantial modifications submitted to NREC-MD for review. With the implementation of MDR, the reporting relationship of all studies approved under the previous Medical Devices Directive moved under the NREC-MD. Finally, as performance studies of *in vitro* diagnostic devices were not previously regulated, the transition to IVDR poses uncertainty in terms of the volume and complexity of applications submitted to NREC-MD for review in 2023.

CTD

While Ireland fully transitions to the CTR, new clinical trial applications may still be submitted under the current rules and legislation (CTD, S.I. 190 of 2004[10]). Since establishment of the NRECs in May 2021 almost 600 ethics application submissions have been made under the CTD and reviewed by the NREC-CTs (over 80 new applications and over 500 substantial amendments).

Notwithstanding the CTRs entry into force on 31 January 2022, the volume of applications submitted under the CTD remains extremely high, with over 250 substantial modifications and over 40 new study applications considered by the NREC-CTs, to date. Substantial modifications to studies that commenced under the CTD will continue to be received, processed and consider by the NREC-CTs until 31 January 2025.

Furthermore, substantial modifications submitted under the CTD will be reviewed in parallel with those under the submitted under the CTR. These substantial modifications and will continue to involve a high volume of dense and complex clinical trial documentation and require detailed administrative support from the National Office and robust NREC review. It is anticipated that the submission rate and review of substantial modifications under the CTD is likely to remain at a similar rate for at least the next 18-24 months until the transition to the CTR will be complete.

CTR

The CTR has led to profound change in the regulatory system and significant work is ongoing in managing the transitions to CTR at national and international level.

The introduction of the CTR has also seen the introduction of the new Clinical Trial Information System (CTIS) which acts as a single-entry point for submitting clinical trial information in the EU. CTIS will also support the daily business processes of Member States and sponsors throughout the life cycle of a trial.

During the transition to CTR, the National Office and NREC-CT continue to provide additional guidance and support to applicants in navigating the new system. Furthermore, the CTR brings strict timelines imposed by the regulations and CTIS system.

Whilst it was initially anticipated that the NREC-CTs would be required to assess only Part II documentation, it has transpired that Part I documentation shall likely require assessment by the NREC-CTs when Ireland is a Reporting Member State, or as required on a case-by-case basis. This step change is accommodated by the National Office and NREC-CTs, but has resulted in significantly increased workload and additional draw on subject matter expertise from both the National Office and NREC-CTs.

[10] https://www.irishstatutebook.ie/eli/2004/si/190/made/en/print

1.6 Proposed fees for Clinical Investigations & Performance Studies - MDR and IVDR (APPENDIX I, Table 1)

New Clinical Investigations and Performance Studies

Commercial studies[11]**:** It is proposed to increase the current fee of €500 to €1,500. This fee reflects the workload and service provided and brings the NREC-MD fee on par with fees charged by local RECs and NREC-CT for commercial studies. It is also proposed that the fee for each site related to new application is removed and instead the single fee is charged irrespective of the number of sites.

Non-commercial studies[12]**:** It is proposed to increase the current fee of €75 to €150 in line with fees charged by local RECs and NREC-CT and reflect workload and service provided.

Substantial Modifications of Clinical Investigations and Performance Studies

Commercial studies: It is proposed to increase the current fee of €125 to €300. This fee reflects the workload and service provided and bring the NREC-MD fee on par with fees charged by local RECs for commercial studies.

Non-commercial studies: It is proposed to increase the current fee of €25 to €50 in line with fees charged by local RECs.

Appeal of NREC-MD Decision

Commercial studies: In line with the proposed increased fee for new applications, it is proposed to increase the current fee of €400 to €1,200 to reflect the work attributable to facilitating an appeal for an applicant.

Non-commercial studies: It is proposed to increase the current fee of €60 to €100 in line with NREC-CT fees.

[11] Where the study is industry funded or sponsored, commercial fees apply

[12] Where the sponsor is academic/ not-for-profit funded, non-commercial fees apply

1.7 Proposed fees under the CTD (APPENDIX I, Table 2)

New Clinical Trials of Investigational Medicinal Products

Commercial studies[13]**:** It is proposed to increase the current fee of €1000 to €1500. This will bring the NREC-CT fee on par with fees charged by local RECs and with applications for mono trials under the CTR for commercial studies. It is also proposed that the fee for each site related to new application is removed and instead the single fee is charged irrespective of the number of sites.

Non-commercial studies[14]**:** It is proposed to keep the current fee of €150.

Substantial Modifications of Clinical Trials of Investigational Medicinal Products

Commercial studies: It is proposed to increase the current fee of €200 to €400. This is in recognition of the volume and complexity of substantial modification applications received to date and the associated workload involved in processing and reviewing each of these applications.

Non-commercial studies: It is proposed to keep the current fee of €50.

Appeal of NREC-CT Decision

There is no mechanism to appeal a NREC-CT decision under the CTD.

[13] Where the study is industry funded or sponsored, commercial fees apply

[14] Where the sponsor is academic/ not-for-profit funded, non-commercial fees apply

1.8 Proposed fees under the CTR (APPENDIX I, Table 3 & Table 4)

New Clinical Trials of Investigational Medicinal Products

Commercial studies[15]**:** It is proposed to increase the current fee of €1,000 to €1,500 to reflect the added workload of contributing to all aspects of the review process at the strict timelines set out by the regulations. When Ireland is designated as the Reporting Member State (RMS), this fee will be €2,000.

Non-commercial studies[16]**:** It is proposed to keep the current fee of €150.

Substantial Modifications of Clinical Trials of Investigational Medicinal Products

Commercial studies: It is proposed to increase the current fee of €200 to €400. This is in recognition of the volume of substantial modification applications received to date and the associated workload with processing and reviewing these applications.

Non-commercial studies: It is proposed to keep the current fee of €50.

Appeal of NREC-CT Decision

Commercial studies: In line with the proposed increased fee for new applications, it is proposed to implement an appeal fee of €1,200 to reflect the work attributable to facilitating an appeal for an applicant.

Non-commercial studies: It is proposed to implement an appeal fee of €100.

[15] Where the study is industry funded or sponsored, commercial fees apply

[16] Where the sponsor is academic/ not-for-profit funded, non-commercial fees apply

1.9 Contact details

The National Office welcomes comments on these proposals and invites respondents to comment.

Contributions to the consultation on these proposals may be provided to the National Office by 28th October 2022. Contributions should be sent by email to nationaloffice@nrec.ie with subject “Fees consultation”.

Appendix I. PROPOSED NREC FEES

Table 1. Proposed NREC-MD fees

New Clinical Investigations and Performance Studies	Current fees	Proposed fees	Percentage Increase	Justification
Commercial	€500	€1,500	200%	It is proposed to increase the current fee of €500 to €1,500. This will bring the NREC-MD fee on par with fees charged by local RECs and NREC-CT for commercial studies.
Non-Commercial	€75	€150	100%	It is proposed to increase the current fee of €75 to €150.
Fee for Each Site Related to a New Application				
Commercial	€80	-	Withdrawn	It is proposed that the fee for each site related to new application is withdrawn and instead the single fee is charged irrespective of a number of sites.
Non-Commercial	€0	€0		
Substantial Modifications of Clinical Investigations and Performance Studies				
Commercial	€125	€300	140%	It is proposed to increase the current fee of €125 to €300. This will bring the NREC-MD fee on par with fees charged by local RECs and NREC-CT for commercial studies.
Non-Commercial	€25	€50	100%	It is proposed to increase the current fee of €25 to €50.
Appeal of NREC-MD Decision				
Commercial	€400	€1,200	200%	In line with the proposed increased fee for new applications, it is proposed to increase the current fee of €400 to €1,200.
Non-Commercial	€60	€100	67%	It is proposed to increase the current fee of €60 to €100.

Table 2. Proposed NREC-CT fees under CTD

New Clinical Trials of Investigational Medicinal Products	Current fees	Proposed fees	Percentage Increase	Justification
Commercial	€1,000	€1,500	50%	It is proposed to increase the current fee of €1,000 to €1,500. This will bring the NREC-CT fee on par with fees charged by local RECs and with applications for mono trials under the CTR for sponsor funded studies. It is also proposed that the fee for each site related to new application is removed and instead the single fee is charged irrespective of a number of sites.
Non-Commercial	€150	€150	-	It is proposed to keep the current fee of €150.
Fee for Each Site Related to a New Application				
Commercial	€150	-	Withdrawn	It is proposed that the fee for each site related to new application is withdrawn and instead the single fee is charged irrespective of a number of sites.
Non-Commercial	-	-		
Substantial Modifications of Clinical Trials of Investigational Medicinal Products				
Commercial	€200	€400	100%	It is proposed to increase the current fee of €200 to €400. This is in recognition of the volume and complexity of substantial modification applications received to date and the associated workload with processing and reviewing these applications.
Non-Commercial	€50	€50	-	It is proposed to keep the current fee of €50.

Table 3. Proposed NREC-CT fees under CTR

New Clinical Trials of Investigational Medicinal Products	Current fees	Proposed fees	Percentage increase	Justification
Mono national/ Member state concerned (MSC)	€1,250	€1,500	20%	It is proposed to increase the current fee of €1,250 to €1,500 to reflect the added workload of contributing to all aspects of the review process at the strict timelines set out by the regulations.
Reporting member state (RMS)	€1,250	€2,000	60%	It is proposed to increase the current fee of €1,250 to €2,000 to reflect the added workload of contributing to all aspects of the review process at the strict timelines set out by the regulations.
Supplement – where Ireland subsequently becomes the Reporting member state for Mono national trial	-	€500	New	In line with the HPRA fees, it is proposed to introduce a supplement fee of €500 for studies where Ireland subsequently becomes the RMS for Mono National trial.
Reporting member state – 2nd & subsequent waves	-	€500	New	In line with the HPRA fees, it is proposed to introduce a supplement fee of €500 for studies where Ireland subsequently becomes the RMS for second and subsequent waves.
Non-commercial	€150	€150	-	It is proposed to keep the current fee of €150
Substantial Modifications of Clinical Trials of Investigational Medicinal Products				
Mono national/ Reporting member state/ Member state concerned	€250	€400	60%	It is proposed to increase the current fee of €250 to €400. This is in recognition of the volume and complexity of substantial modification applications received to date and the associated workload with processing and reviewing these applications.
Non-commercial	€50	€50	-	It is proposed to keep the current fee of €50.
Appeal of NREC-CT Decision				
Commercial	-	€1,200	New	It is proposed to set the fee for appeals of NREC-CT decisions at €1,200 to reflect the complexity of the process and associated workload.
Non-commercial	-	€100	New	It is proposed to set the fee for appeals of NREC-CT decisions at €100 to reflect the complexity of the process and associated workload.

Table 4. Proposed NREC-CT fees under CTR combined with the HPRA fees

New clinical trial (CT) applications	Proposed HPRA Fees		Proposed NREC Fees		Total Fees	
	CT with IMPD	CT with no IMPD or with simplified IMPD or a low intervention trial	CT with IMPD	CT with no IMPD or with simplified IMPD or a low intervention trial	CT with IMPD	CT with no IMPD or with simplified IMPD or a low intervention trial
Mono national	€1,920	€905	**€1,500**	**€1,500**	€3,420	€2,405
Reporting member state (RMS)	€6,700	€5,500	**€2,000**	**€2,000**	€8,700	€7,500
Member state concerned (MSC)	€1,700	€635	**€1,500**	**€1,500**	€3,200	€2,135
Supplement – where Ireland subsequently becomes the reporting member state for mono national trial	€4,780	€4,595	**€500**	**€500**	€5,280	€5,095
Reporting member state – 2nd & subsequent waves	€500	€500	**€500**	**€500**	€1,000	€1,000
Non-commercial	€150	€150	**€150**	**€150**	€300	€300

Clinical trial substantial modifications (SM)	Proposed HPRA Fees		Proposed NREC Fees		Total Fees	
	SM with the addition of new IMPD	SM other	SM with the addition of a new IMPD	SM other	SM with the addition of a new IMPD	SM other
Proposed fees (Part I only or Parts I & II)						
Mono national	€980	€510	**€400**	**€400**	€1,280	€910
Reporting member state (RMS)	€1200	€810	**€400**	**€400**	€1,600	€1,210
Member state concerned (MSC)	€925	€430	**€400**	**€400**	€1,325	€830
SM non-commercial	€50	€50	**€50**	**€50**	€100	€100
Proposed fees (Part II only)						
Commercial	-	-	**€400**	**€400**	€400	€400
Non-commercial	-	-	**€50**	**€50**	€50	€50