NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Public Consultation on
Proposal for HPRA and NREC Clinical Trial Fees – Financial Year 2022

CONTENTS

1 INTRODUCTION

A new Clinical Trial Regulation (CTR) (Regulation No 536/2014) was adopted on 16 April 2014, and becomes applicable on 31 January 2022. The CTR is designed to benefit patients and medical research in Europe by streamlining the approval of clinical trials across the Member States. Once implemented, the key features of the new Clinical Trial Regulation will include:

- Single submission and approval of multinational clinical trial applications through an EU 'Clinical Trial portal and database' (known as the Clinical Trial Information System (CTIS);
- A single fee per Member State
- Identical rules for conducting clinical trials throughout the European Union (EU)
- Strictly defined timelines for assessment
- Increase in the efficiency in approval process for clinical trials

These features will assist the CTR in achieving its aim of creating a favourable environment for conducting trials in the EU while also ensuring that the highest standards of safety for participants are maintained (further information: www.hpra.ie).

2 CHANGES IN IRELAND

In Ireland, a coordinated procedure for scientific and research ethics assessment of clinical trials is being developed by the HPRA and the newly formed National Office for Research Ethics Committees (hereafter 'the National Office'; www.nrecoffice.ie) in conjunction with the Department of Health. This coordinated procedure will lead to a single national administrative decision for Ireland on the scientific and ethical aspects of a clinical trial application, within EU-mandated timelines. This is a positive development for sponsors conducting research in Ireland, and clinical trial participants.

Following implementation, sponsors intending to conduct a clinical trial in Ireland will apply via CTIS, including a single fee with the application. This fee will be collected by the HPRA and a portion transferred to the National Office to cover the independent process of research ethics review by the National Research Ethics Committee (NREC).

Sponsors can continue to submit new clinical trial applications under the current legislation during the first year post-implementation, and can submit substantial amendments during the three-year transition period. Separate applications to the HPRA and the National Office will continue to be required for clinical trials submitted under the current legislation, and the usual fees will be charged.

This consultation document provides details of the fees intended to be charged for clinical trial applications under the CTR, and background information.

To ensure that we manage the business properly, we have agreed to review our fees on an annual basis to reflect changes to our cost base and service levels. This document summarises

the outcome of our review of fees and it sets out the current operating environment, the service levels and activities and expected changes in service levels and activities for 2022.

3 CLINICAL TRIAL FEES UNDER THE CLINICAL TRIAL REGULATIONS – KEY POINTS

a) A single fee will be charged by Ireland (the HPRA and the National Office) for each clinical trial application (CTA) or substantial modification (previously known as substantial amendments). Fee details will be published on the HPRA and National Office websites.

b) The HPRA and the National Office consider the proposed fees reflect the work involved, but are competitive, in order to encourage research in Ireland. This is in line with the CTR (Article 86), which requires that the level of the fee is set in a transparent manner and on the basis of cost recovery principles. However, given that it is a new regulation with new working methodologies, European co-ordination and timelines, there is a level of uncertainty on the scope and volume of work. Therefore we commit to reviewing the fees after one year and they will be adjusted up or down, based on our experience of CTR implementation. This review will be transparent and subject to a public consultation.

c) For new applications, the sponsor will pay the fee to the HPRA at the time of application to CTIS, and following validation the HPRA will transfer the corresponding portion to the National Office. There are two parts to the assessment: Part I (protocol and investigator's brochure, proof of payment of fees, etc.), and Part II (informed consent documents, suitability of the investigator/facilities etc.). The assessment will be conducted by the HPRA and the NREC in line with their organisational roles. Part I can be submitted alone, and Part II submitted up to two years later. The following principles will apply:

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

d) For substantial modifications (SM) 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.

e) The separate fee for additional trial sites has been replaced by the fee for substantial modification to Part II documents.

f) A small administrative fee will be charged to non-commercial/academic sponsors.

g) The current system whereby the amount of the fee is predominantly based on the presence or otherwise of an investigational medicinal product dossier (IMPD), a substantial document for assessment, will continue to apply.

h) A 'low intervention trial' is defined in the CTR, and is confirmed by the reporting Member State (RMS) at the time of validation. It corresponds with the current HPRA fee code for the use of a medicine within the terms of its marketing authorisation, and is reflected in the fee proposals.

i) The fee proposals take account of the HPRA's role as the competent authority for clinical trials, and also the additional responsibilities associated with the RMS role, versus the concerned MS (CMS) role. New activities include coordination at national level for both roles, and in the case of the RMS, liaising with other MSs, and the preparation of assessment reports.

4 IMPLICATIONS FOR CLINCAL TRIALS AND THE FEES FROM THE NEW REGULATIONS

The HPRA, the National Office and NRECs are committed to supporting innovation, and facilitating sponsors to avail of the opportunities under the CTR, and manage their regulatory responsibilities. A coordinated rigorous and efficient review of clinical trials should encourage quality research and ultimately lead to better access to medicines for Irish and EU patients. Significantly the CTR will allow multicentre trials to be authorised simultaneously across Europe, benefitting both patients and research.

The CTR will make a profound change to the regulatory system and significant work is ongoing in this area at national and international level. In the past, the HPRA and ethics committees have provided clinical trial services on a non-recovery basis, particularly in the area of academic trials. We do not expect that the new proposed fee model will cover the costs of assessing and authorising all clinical trials in 2022, but none-the-less it is necessary to increase the fees to reflect the new structures and coordinated approach, which in turn will result in a significantly increased workload.

5 PROPOSED HPRA AND NREC FEES (SEE TABLES IN APPENDIX I)

5.1 New Clinical Trial Applications (Table 1)

5.1.1 Proposal: Mono–National Trials

HPRA fee: It is proposed to increase the current fee by €300 for trials submitted to Ireland only. These trials will require the generation of an assessment report for external access under transparency rules.

NREC fee: It is proposed to increase the current fee by 25%.

5.1.2 Proposal: Clinical Trials where IE is the RMS

HPRA fee: It is proposed to introduce a new fee of €6,700 (with IMPD) and €5,500 (without IMPD) for multinational trials with IE as RMS.

NREC fee: It is proposed to apply a fee of €1,250.

5.1.3 Proposal: Clinical Trials where IE is the CMS

HPRA fee: It is proposed to increase the current fee by 5% for the CMS role due to administrative activities at national and EU level.

NREC fee: It is proposed to increase the current fee by 25%.

5.1.4 Proposal: Supplement fee for authorised mono-national trials where IE subsequently becomes the RMS

HPRA fee: It is proposed to apply a supplement fee to authorised mono nation trials where IE subsequently becomes the RMS - €4,780 (with IMPD), €4,595 (without IMPD).

5.1.5 Proposal: Second and Subsequent waves

HPRA fee: A fee of €500 is proposed for the second and subsequent waves as RMS.

5.1.6 Non-Commercial/Academic Trials

HPRA fee: A fee of €150 is proposed to be charged for non-commercial/academic trials.

NREC fee: It is proposed to continue to charge €150 for these trials.

5.2 Substantial Modifications (Table 2)

5.2.1 Proposal: Modifications to Mono–National Trials

HPRA fee: It is proposed to increase the current fee by €100 for mono-national trials.

NREC fee: It is proposed to increase the current fee by 25%.

5.2.2 Proposal: Modifications to trials where IE is the RMS

HPRA fee: A new fee for substantial modifications where IE is the RMS of €1,200 for the addition of a new IMPD and €810 for other substantial modifications. Only a single fee will be charged even if there are multiple new IMPDs added via a substantial modification.

NREC fee: It is proposed to apply a fee of €250.

5.2.3 Proposal: Modifications to trials where IE is the CMS

HPRA fee: An increase of 5% is proposed for the CMS role due to administrative activities at national and EU level.

NREC fee: It is proposed to increase the current fee by 25%.

5.3 Safety Assessment – DSUR/ASR/SUSAR

It is proposed that there will be no changes to the current fees as the implementing regulation for safety is still under discussion.

6 CONSULTATION

The HPRA and 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 HPRA by 8th October 2021. Contributions should be sent by email to feesconsultation@hpra.ie.

APPENDIX I CLINICAL TRIAL PROPOSED FEE TABLES

TABLE 1- NEW CLINICAL TRIAL FEES

	Proposed HPRA Fees		Proposed NREC Fees		Total Fees	
New Clinical Trial Applications	**CTA with IMPD**	**CTA with no IMPD or with simplified IMPD or a low intervention trial**	**CTA with IMPD**	**CTA with no IMPD or with simplified IMPD or a low intervention trial**	**CTA with IMPD**	**CTA with no IMPD or with simplified IMPD or a low intervention trial**
Current Fee	*1,620*	*605*	*1,000*	*1,000*	*2,620*	*1,605*
Proposed Fees						
Mono National	1,920	905	1,250	1,250	3,170	2,155
RMS	6,700	5,500	1,250	1,250	7,950	6,750
CMS	1,700	635	1,250	1,250	2,950	1,885
Supplement – where IE subsequently becomes the RMS for Mono National trial	4,780	4,595	-	-	4,780	4,595
RMS – 2nd & subsequent waves	500	500	-	-	500	500
Non-commercial/academic Trials	150	150	150	150	300	300

TABLE 2 - SUBSTANTIAL MODIFICATIONS

	Proposed HPRA Fees		Proposed NREC Fees		Total Fees	
Clinical Trial Substantial Modifications (SM)	**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**
Current Fee	*880*	*410*	*200*	*200*	*1,080*	*610*
Proposed fees (Part I only or Parts I & II)						
Mono National	980	510	250	250	1,230	760
RMS	1200	810	250	250	1,450	1,060
CMS	925	430	250	250	1,175	680
SM non-commercial/academic	50	50	50	50	100	100
Proposed fees (Part II only)						
SM (including new trial site)			250	250	250	250
SM - non-commercial/academic			50	50	50	50