HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Guide to
Clinical Investigations Carried Out in Ireland

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This guide does not purport to be an interpretation of law and/or regulations and is for guidance purposes only.

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1 SCOPE

This guide provides an overview of the legislation on clinical investigations (CIs) involving medical devices. The guide also provides guidance on how to submit applications to carry out CIs in Ireland to the Health Products Regulatory Authority (HPRA). This guide is primarily targeted towards CI sponsors (e.g. manufacturers, academic groups, clinical research organisations), who wish to carry out CIs involving medical devices in Ireland. The information may also be useful for ethics committees and other stakeholders.

This guide is not the definite interpretation of the law and/or regulations and is for guidance purposes only. You should consult the relevant legislation relating to medical devices in addition to this guide.

The Medical Devices Coordination Group (MDCG) has published a Q&A document (MDCG 2021-6) for CI sponsors. This document describes the different types of CIs and their applicable obligations in detail. MDCG has also published guidance documents on the content of clinical investigation plans (MDCG 2024-3) and investigator brochures (MDCG 2024-5) for CIs. Please read these documents before conducting a CI in Ireland.

2 WHAT IS A CLINICAL INVESTIGATION?

A CI is a systematic study involving one or more human subjects that assesses the safety or performance of a medical device. The Medical Devices Regulation (MDR) outlines specific requirements for CIs carried out in the EU. S.I. 261 of 2021 also outlines specific national requirements for CIs conducted in Ireland. There are three different types of CIs:

Article 62 studies

These are generally CIs involving non-CE marked devices, or CE marked devices used outside the scope of their intended purpose. Studies that fall under Article 62 generally include early feasibility studies, pilot studies and pivotal studies of non-CE marked devices.

Article 74 studies

These are CIs involving CE marked devices where the CI subjects study participants to additionally invasive or burdensome procedures.

Article 82 studies

This includes all other CIs. Article 82 CIs must comply with specific national requirements outlined in Part 3, Article 14 of S.I. 261 of 2021.

Please refer to the relevant articles in MDR for more detailed descriptions of the study types.

3 HOW TO CONDUCT A CLINICAL INVESTIGATION IN IRELAND

You will need to:

1. Submit an application or notification to us.
2. Apply to the National Research Ethics Committee for Medical Devices (NREC-MD).
3. Fulfil other requirements, such as adverse event reporting.

4 HOW TO SUBMIT A CLINICAL INVESTIGATION APPLICATION TO THE HPRA

These instructions only apply to CIs conducted in Ireland.

Step 1: Complete the relevant form

Depending on the type of study you plan to carry out, complete the form for an Article 62, Article 74 or Article 82 study.

Step 2: Pay the relevant fees

You can find the correct category of free for your submission in our Guide to Fees for Human Products.

This guide follows the order of the fees in our Fee Application Form. You will also need to complete and include a fee application form with your submission.

Additional details on how to pay fees by credit transfer or EFT can be found in our Payment of Fee Instructions.

Step 3: Submit documentation and contact us

Submit your application or notification form with the required documents through the Common European Submission Portal (CESP).

If you have not used CESP before, their website provides general information and frequently asked questions for study sponsors.

You can register on CESP by going to the CESP website. If you need technical support, please email cesp@hma.eu.

Step 4: Notify us of your CESP submission

Email us with confirmation of your submission and your CESP reference number at devices@hpra.ie.

Please note: Your application will not be considered to be complete or properly submitted until you complete all four steps.

5 HPRA SUBMISSION REVIEW PROCESS

Article 62 applications

Within 10 to 15 calendar days of receiving the application and proof of fee payment, we will validate your application, verify required documents and confirm the CI falls within the scope of the MDR. This may take longer if we need more information.

We will then provide you with a unique ID number (CIV-ID) for your application. If you have already received a CIV-ID for the same CI in another Member State, please say this in your application form.

We will issue the outcome of our review within 45 calendar days of validating the application. If we need help from external experts, we will add 20 calendar days to this timeline.

We may request more information during our review. We will not include time taken for the sponsor to provide information in the above timelines. Failure to provide more information may lead to a rejection or refusal of the application.

Once we have completed our assessment, we will send you a letter, either authorising or refusing to authorise the CI. You have the right to appeal a refusal decision, as outlined in our Guide to Refusals and Appeals.

Article 74 and 82 notifications

Once we receive a notification, we will conduct a high-level review to confirm it falls within the scope of MDR Article 74 or 82.

We may ask for more information during this review. Once reviewed, we will send you a letter acknowledging the notification.

You can start your CI at least 30 calendar days after submitting your notification to us, provided you have also received ethical approval from NREC-MD.

6 SHOULD I INFORM THE HPRA OF A MODIFICATION TO MY CLINICAL INVESTIGATION?

If the planned modification to the CI is substantial, you must submit a notification to us for assessment before you make the modification.

To notify us of a substantial modification, please submit a Notification of Substantial Modification form and documentation in line with the steps outlined in section 4 of this guide.

If you are unsure about whether a planned modification is substantial or not, you can find guidance in the MDCG's Q&A document (MDCG 2021-6). If you still are unsure, please email devices@hpra.ie.

7 RESEARCH ETHICS COMMITTEES AND CLINICAL INVESTIGATIONS

In Ireland, all clinical investigations must receive ethics approval from the National Research Ethics Committee – Medical Devices (NREC-MD) before the CI starts. The NREC-MD review is independent from our review. You can apply to the NREC-MD and to the HPRA at the same time or at different times, but the CI cannot start until both reviews are complete.

Please refer to the NREC website for information on how to apply.

8 SERIOUS ADVERSE EVENTS (SAE) AND DEVICE DEFICIENCY REPORTING

If an SAE or device deficiency occurs during a study, you must report it to us by email at devices@hpra.ie. To report an SAE or device deficiency to us, please follow the MDCG Guidance document for safety reporting in CIs (MDCG 2020-10/1) and use the MDCG's safety report form (MDCG 2020-10/2).

If your CI began before 26 May 2021, you do not need to reapply to us for authorisation. However, you must report SAEs and device deficiencies to us that occurred after this date, following MDCG 2020-10/1.

Sponsors must update their controlled documents relating to CIs that began before 26 May 2021, to bring the SAE reporting procedures in line with the MDR. You do not need to apply to the HPRA for a substantial modification for this update.

9 ENDING A CLINICAL INVESTIGATION IN IRELAND

If you terminate or temporarily halt a CI on safety grounds, you must notify us by email within 24 hours. Aside from this, you must notify us within 15 days of the CI ending or being temporarily halted for reasons other than safety grounds.

You must submit a CI report to us within one year of the CI ending. You can find more details about this report under Annex XV of the MDR.

If you halt or terminate your CI early, you must submit a report within three months.

You can send your report to us by email at devices@hpra.ie. Please include the CIV-ID number for your study.

10 WHAT SUPPORT DO WE OFFER DEVICE DEVELOPERS?

We offer different supports to device developers:

Innovation office

We offer regulatory support and advice. You can find more details on our innovation office webpage.

Preliminary meetings

These are typically for early stage 'start-up' companies. The aim of these meetings is to introduce our role and the regulatory requirements of the pre-market phase of device development.

Pre-submission meetings

These are typically for sponsors who plan to submit a CI application to us. These meetings allow us to answer any question you would like to ask before submitting your application. We strongly encourage sponsors to have a pre-submission meeting with us before submitting an application.

These supports are free. To apply for a preliminary or pre-submission meeting, please complete our Request for Clinical Investigation Pre-submission meeting form and send it to devices@hpra.ie.