Notification of Substantial Modification of a Clinical Investigation of a Medical Device

As described in Article 75 of EU Regulation 2017/745 (MDR), if the sponsor wishes to introduce modifications to a clinical investigation in Ireland that are likely to have a substantial impact on the safety, health or rights of the subjects or on the robustness or reliability of the clinical data generated by the investigation, they are required to notify the HPRA of these modifications at least 38 days prior to implementation.

This requirement applies to all clinical investigations that fall under Article 62 or Article 74 of the MDR. In Ireland, this also applies to clinical investigations that fall under Article 82 of the MDR and national legislation (Part 3 of the Medical Devices Regulations 2021, S.I. 261 of 2021), if stated as an additional requirement in the HPRA’s letter of acknowledgement of notification of an Article 82 study.

Sponsors are required to complete this notification form and provide an updated version of relevant documentation referred to in Chapter II of Annex XV as part of this notification. All changes and modifications to the relevant documentation must be clearly identifiable. Refer to section 4.2 and appendix 2 of the [HPRA Guide to Clinical Investigations Carried Out in Ireland](https://www.hpra.ie/homepage/about-us/publications-forms/guidance-documents/item?id=60230126-9782-6eee-9b55-ff00008c97d0&t=/docs/default-source/publications-forms/guidance-documents/aut-g0095-guide-to-clinical-investigations-carried-out-in-ireland-v5) for details on the HPRA’s expectations regarding documentation of changes.

Notifications will only be accepted via the Common European Submission Portal (CESP), unless previously agreed with the HPRA. Please submit the completed form and all accompanying documents at <https://cespportal.hma.eu/>. Following submission of documents via this portal, please send an email to devices@hpra.ie to advise that a substantial modification notification has been submitted.

For guidance on what may be considered a substantial modification, please refer to the Medical Device Coordination Group (MDCG) guidance document [MDCG 2021-6: Questions & Answers regarding clinical investigation](https://ec.europa.eu/health/sites/default/files/md_sector/docs/mdcg_2021-6_en.pdf).

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| **SECTION A: Administrative Information** |
| 1 | Enter the contact details of the sponsor who is responsible for this application.Name      Address      Telephone      Email  |
| 2 | Is this the first substantial modification notification regarding this clinical investigation?[ ]  First substantial modification[ ]  Other, please specify:       |
| 3 | Details of the original clinical investigation to which this substantial modification relates: Full title of clinical investigation:      HPRA reference no. (CI number):      EUDAMED CIV ID:       Date of previous authorisation/notification:       |
| 4 | Clinical Investigation Plan (CIP) details (latest version)CIP code      CIP version number      CIP version date       |
| 5 | Does this substantial modification relate to a clinical investigation that is currently suspended/stopped?[ ]  Yes[ ]  NoIf yes, please provide details:       |
| 6 | How many patients have been recruited in the clinical investigation to date?Ireland      European Union      Worldwide       |
| 7 | Enter start date and proposed completion date of the clinical investigation.Start date      Completion date       |
| 8 | Since the previous application/notification, are there any changes to the following?[ ]  Principal investigator(s) in Ireland [ ]  Clinical investigation site(s) in Ireland [ ]  Clinical investigation site(s) outside of Ireland[ ]  Principal investigator(s) conducting a multi-site study [ ]  Manufacturer’s name, address, contact details [ ]  Authorised representative, if applicable[ ]  None of the abovePlease provide details of any changes made to the above:      |
| 9 | Has an Ethics Committee in Ireland provided an opinion with respect to this proposed clinical investigation substantial modification? [ ]  Yes[ ]  No If yes, please provide a copy of the opinion.If no, please provide details:       |

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| **SECTION B: device information** |
| 1 | Name of device:       |
| 2 | Device description:       |
| 3 | Are there any changes or modifications in relation to the device or its components since the previous application/notification to the HPRA?[ ]  Yes[ ]  NoIf yes, please provide a description, including rationale, of these changes.      |

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| **SECTION C: Summary Of Modifications** |
| Using the below table format, please provide a summary of the proposed modification(s) and rationale for the changes.*(Alternatively, please attach a separate document with this information, using the format below.)* |
| **Document and location reference** | **Original text** | **Amended text** | **Rationale** |
| *e.g. CIP001 Page 2**Section 1.11* | *e.g. The study will be performed at the following sites: Hospital A* *Hospital B* | *e.g. The study will be performed at the following sites: Hospital A* *Hospital B* *Hospital C* | *e.g. An additional investigational site will be added due to….* |
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| Will the proposed modification(s) likely have an impact on the rights, safety or health of the subjects participating in the clinical investigation?[ ]  Yes [ ]  NoIf yes, please explain:      Will the proposed modification(s) likely have an impact on the robustness or reliability of clinical data generated by the investigation?[ ]  Yes[ ]  NoIf yes, please explain:       |

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| **SECTION D: Documentation to be attached** |
| The following list is for guidance only and is not exhaustive. Additional requests for documentation and information may be made following submission. If a document has been modified or changed since the previous application/notification, please include the document in the below list and ensure a copy of this document is provided with this form. Please ensure to include a copy of any document that has been listed in Section C.Please include a copy of the latest version of the Clinical Investigation Plan (CIP), Investigator’s Brochure (IB) (if applicable), and Instructions For Use (IFU) in your application. The content and structure of documents submitted should be in line with relevant regulatory requirements and associated standards. Please provide section/page references for items in the CIP or document reference and page numbers for items not described in the CIP. |
| [ ]  | Clinical investigation plan (CIP) Version number      Date       |
| [ ]  | Investigator’s brochure (IB) (if applicable) Version number      Date       |
| [ ]  | Instructions for use (IFU) for the deviceVersion number      Date       |
| [ ]  | A copy of the opinion of the National Research Ethics Committee for Medical Devices (NREC-MD) concerned on the details of the aspects covered by its opinion (if available) |
| [ ]  | A copy of any document listed in Section C of this form, and any other relevant documents (please list here):       |

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| **SECTION E: Declaration** |

Signed on behalf of **<sponsor>** (*if applicable)*.

I, *(please print full name in block capital letters)* \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_,

1. As the natural or legal person responsible for the manufacture of the investigational device, confirm that the investigational device(s) in question conform(s) to the applicable general safety and performance requirements set out in Annex I of the MDR.
2. Certify that the information and documentation submitted with this notification is correct in detail and all relevant information has been supplied. Any further information requested by the competent authority will be submitted on request.
3. Undertake to keep available for the competent authority for a period of 10 years (15 years for implantable devices) after the end of the clinical investigation, or, where the device is subsequently placed on the market, from the time the device was last placed on the market, all the documentation referred to in Annex XV of Regulation (EU) 2017/745.
4. Certify that the sponsor consents to allow the final letter detailing the outcome of the HPRA review to be copied to the Irish based investigators and the relevant Ethics Committee(s).
5. Certify that the sponsor consents to the HPRA contacting the National Research Ethics Committee for Medical Devices (NREC-MD) during the course of the review if required.
6. Certify that the sponsor consents to the HPRA utilising external experts, when necessary, during the assessment of this application. (Experts used will be subject to the HPRA’s procedures for protection of confidentiality and impartiality.)

**Signature:** \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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**Position:** \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Company name:** \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Date:** \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_