Application for a Clinical Investigation of Non-CE Marked Medical Devices (Article 62 MDR)

For instructions on how to complete this application form, please see the ‘Guide to Clinical Investigations carried out in Ireland’.

Sponsors who wish to submit an application to the HPRA for a clinical investigation falling under Article 62 of EU Regulation 2017/745 (MDR) are required to complete this application form and submit it with the relevant supporting documentation as described below.

Validation of this application will be completed and review will commence only once all relevant application documentation is submitted. If completed documentation is not received within the timeframe specified in a notification of an incomplete application from the HPRA, the application will be deemed lapsed.

Applications 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 new clinical investigation application has been submitted.

|  |
| --- |
| SECTION A: Administrative Information |
| 1 | Is this a first submission or resubmission?[ ]  First submission[ ]  Resubmission |
| 2 | If resubmission, state previous submission date and HPRA reference number.Date      Reference no.       |
| 3 | Enter the contact details of the sponsor who is responsible for this application.Name      Address      Telephone      Email       |
| 4 | Where the sponsor referred to in point 3 above is not established in the Union, enter the contact details of a legal representative who is established in the Union (c.f. Art 62(2) MDR 2017/745).Name      Address      Telephone      Email       |
| 5 | Clinical investigator responsible for the conduct of the clinical investigation in Ireland.*If more than two clinical investigators are involved, please attach these details as an appendix. This appendix should include details and roles for members of the investigator’s team who will be directly involved in the conduct of the investigation.*(i) Name      Qualification      Address      Telephone      Email      (ii) Name      Qualification      Address      Telephone      Email       |
| 6 | Please list the clinical investigation sites in Ireland.*If more than two sites, please attach details in an appendix.**Irish site 1* Name      Address      *Irish site 2* Name      Address       |
| 7 | Please confirm that the investigators, together with the investigation sites listed above, have the capability to conduct the clinical investigation in accordance with the proposed clinical investigation plan.[ ]  Yes[ ]  No |
| 8 | Is this part of a multi-site clinical investigation outside Ireland? [ ]  Yes[ ]  NoIf yes, enter details of other sites. *If more than two sites, please attach details in an appendix.**Non-Irish site 1* Name      Address      *Non-Irish site 2* Name      Address       |
| 9 | Principal clinical investigator appointed to coordinate the work in a multi-site study:Name      Qualification      Address      Telephone      Email       |
| 10 | Manufacturer's name, address and contact details including site where the manufacture of the device is taking place:Name      Address      Telephone      Email       |
| 11 | If the manufacturer is not based in a European state, please provide the name, address and contact details of authorised representative.Name      Address      Telephone      Email       |
| 12 | Enter the details of notified body/bodies who approved the quality system at the site referred to in point 10 above (if applicable).*Notified body 1*Name      Address      Identification no.      *Notified body 2*Name      Address      Identification no.       |
| 13 | Is this application submitted in parallel with an application for a clinical trial in accordance with EU Regulation 536/2014? If so, please provide the reference number.[ ]  Yes[ ]  NoClinical trial reference no.       |
| 14 | Please confirm that an application has been submitted to the National Research Ethics Committee – Medical Devices (NREC-MD). [ ]  Yes[ ]  NoIf so, indicate the date on which this application was made.      |
| 15 | Payment details (please include documentary confirmation of payment with your application, where applicable):[ ]  Cheque[ ]  Bank transfer[ ]  Bank draft[ ]  Credit on account |

|  |
| --- |
| SECTION B: device information |
| 1 | Name of device:       |
| 2 | Nomenclature or generic name of device:       |
| 3 | Device description:       |
| 4 | 1. Does the device incorporate a medicinal substance, including a human blood or plasma derivative?

 [ ]  Yes [ ]  No1. Has the device been manufactured using non-viable tissue or cells of human or animal origin, or their derivatives?

 [ ]  Yes [ ]  No |
| 5 | Proposed device classification:[ ]  Class III[ ]  Class IIb[ ]  Class IIa[ ]  Class I |
| 6 | Will a comparator device be used during this clinical investigation?[ ]  Yes[ ]  NoIf yes, please provide details of the comparator device, including its classification and any information necessary for the identification of the comparator device. |

|  |
| --- |
| SECTION C: Clinical Investigation information |
| 1 | Full title of clinical investigation:  |
| 2 | Short title of clinical investigation (if applicable):  |
| 3 | Title for lay persons:  |
| 4 | Summary of the Clinical Investigation Plan (CIP), including the objectives of the clinical investigation, the number and gender of subjects, criteria for subject selection, whether there are any subjects under 18 years of age, design of the investigation and planned dates of commencement and completion of the clinical investigation: |
| 5 | CIP code:  |
| 6 | CIP version number:  |
| 7 | CIP version date:  |
| 8 | Has this CI been the subject of a scientific review/opinion from a regulatory authority?[ ]  Yes[ ]  No |
| 9 | Device development stage[ ]  Pilot stage[ ]  Pivotal stage[ ]  Post market stage |
| 10 | In the case of a resubmission, have any changes been made to address the conclusions of previous Competent Authority or Ethics Committee reviews?[ ]  Yes[ ]  No(If yes, please ensure that all changes are identified and a rationale for those changes is provided in accompanying documentation.) |

|  |
| --- |
| SECTION D: documentation to be attached |
| The following list is guidance only and is not exhaustive. Annex XV of the MDR 2017/745 sets out the full description of documentation required for a clinical investigation. Additional requests for documentation and information may be made following submission of the application. The below list outlines the minimum level of information required for this application to be validated. Please ensure that all questions are answered. 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 clinical investigation plan or document reference and page numbers for items not described in the clinical investigation plan. |
| 1 | **Clinical Investigation Plan (CIP)** (*which sets out the rationale, objectives, design, methodology, monitoring, conduct, record-keeping and the method of analysis for the clinical investigation)*Version number      Date       |
|  | References |
| 2 | Statement of compliance with the recognised ethical principles for medical research involving humans and the principles of good clinical practice in the field of clinical investigations of devices and with applicable regulatory requirements |       |
| 3 | Identification and contact details of the sponsor and, where applicable, the contact details of the person listed in question 4 in section A above |       |
| 4 | Identification of the principal investigator at each investigational site, the coordinating investigator, address details for each investigational site, emergency contact details for the principal investigator at each site. The roles, responsibilities and qualifications of the investigators must also be specified in the CIP |       |
| 5 | Brief description of how the clinical investigation is funded and a brief description of the agreement between the sponsor and the site |       |
| 6 | Overall synopsis of the clinical investigation, in English |       |
| 7 | Identification and description of the device, any other comparator device and any other device or medication to be used in the clinical investigation |       |
| 8 | Risks and benefits of the device to be examined, with justification of the corresponding expected clinical outcomes in the CIP |       |
| 9 | Description of the relevance of the clinical investigation in the context of the state of the art of clinical practice |       |
| 10 | Objectives and hypotheses of the clinical investigation |       |
| 11 | Full description and justification of investigation design with evidence of its scientific robustness and validity, including criteria used for decision making, e.g. meeting end point, stopping criteria |       |
| 12 | Description of informed consent process |       |
| 13 | Information about any amendment to the CIP |       |
| 14 | Policy regarding follow-up and management of any deviations from investigation protocol |       |
| 15 | Details on device accountability |       |
| 16 | Proposed clinical and procedural follow-up protocols for participants, both during and after the clinical investigation, if applicable |       |
| 17 | Details of criteria and procedures for subjects following the end of a clinical investigation and for those who have withdrawn from the clinical investigation, including, at a minimum for implantable devices, procedures for device traceability |       |
| 18 | Description of data management plan |       |
| 19 | Investigation monitoring plan |       |
| 20 | Safety reporting provisions |       |
| 21 | Details of the policy regarding the clinical investigation report |       |
| **Investigator’s Brochure (IB)** | References |
| 22 | An identification and description of the device including information on: the intended purpose, the risk classification and applicable classification rule (Annex VIII), design and manufacturing of the device and reference to previous and similar generations of the device. Data allowing identification of device (i) generic name, (ii) model name, (iii) model number |       |
| 23 | Instructions for installation, maintenance, hygiene and use including storage and handling requirements and relevant training required. Also, to the extent available, information to be placed on label and instructions for use to be provided when device placed on the market |       |
| 24 | Existing clinical data, including from relevant scientific literature and other relevant clinical data related to equivalent or similar devices of the same manufacturer including length of time on the market, review of performance, clinical benefit and safety-related issues and any corrective actions taken |       |
| 25 | Comment on the overall clinical development strategy for the medical device |       |
| 26 | Summary of risk-benefit analysis and risk management, including information on known or foreseeable risks, any undesirable effects, contraindications and warnings |       |
| 27 | For devices where question 4 in section B is answered ‘Yes’: detailed information on the medicinal substance or tissues, cells or their derivatives and on the compliance with the relevant GSPRs and the specific risk management in relation to the substance, tissues, cells or their derivatives as well as the evidence for the added value of incorporating such constituents |       |
| 28 | Where applicable, a statement indicating whether or not the device is manufactured utilising tissues of animal origin as referred to in EU Regulation 722 of 2012 |       |
| 29 | If the device is manufactured utilising tissues of animal origin as referred to in Regulation 722 of 2012, the risk management measures which have been applied to reduce the risk of infection. (Please submit the EDQM certificate where available.) |       |
| 30 | A list detailing the relevant GSPRs, including the standards and common specifications applied (specify whether applied in whole or in part). Also a description of the solutions for fulfilling the relevant GSPRs, insofar as those standards and CS have not or have only been partly fulfilled, or are lacking |       |
| 31 | Design drawings methods of manufacture envisaged, in particular regarding sterilisation and diagrams of components, sub-assemblies, circuits, etc. |       |
| 32 | The descriptions and explanations necessary to understand the above mentioned drawings and the operation of the device. Photos of relevant components |       |
| **Preclinical Testing** | References |
| 33 | Description and rationale for bench/technical testing conducted and associated results/data obtained |       |
| 34 | Validation testing |       |
| 35 | The results of the design calculation and of the inspection tests, such as biocompatibility/biological testing |       |
| 36 | Where applicable, results of electrical and/or radiation safety testing |       |
| 37 | Where applicable, software verification and validation testing and results |       |
| 38 | Description and details of material and/or chemical composition of device components |       |
| 39 | Details of new or previously untested features of the device including, where applicable, functions and principles of operation |       |
| 40 | Detailed description of the clinical procedures and diagnostic tests used during the clinical investigation and information on any deviation from normal clinical practice |       |
| **Documents and statements** | References |
| 41 | A copy of the opinion of the relevant Ethics Committee concerned on the details of the aspects covered by its opinion |       |
| 42 | Documents used to obtain informed consent |       |
| 43 | Confirmation of insurance of subjects |       |

|  |
| --- |
| SECTION E: Declaration |

Signed on behalf of **<company name>**

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

1. As the natural or legal person responsible for the manufacture of the investigational device, certify that the device in question conforms to the general safety and performance requirements apart from the aspects covered by the clinical investigation and that, with regard to those aspects, every precaution has been taken to protect the health and safety of the subject.
2. Certify that the information and documentation submitted with this notification is correct in detail and all the information requested 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 relevant Ethics Committee(s) 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:** \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Print name:** \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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

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

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