**1.** **Scope of application**

*Please fill in the application form in English or Danish.*

|  |
| --- |
| **Clinical investigation under MDR**  Application for authorisation of a clinical investigation of a non-CE marked medical device, or CE marked device investigated for another purpose, in order to generate clinical data of a medical device, as part of a clinical evaluation for conformity assessment purposes (i.e. CE marking  Application is to be submitted as **one e-mail to two recipients**;  DKMA: [med-udstyr@dkma.dk](mailto:med-udstyr@dkma.dk) and MREC: [dketik@dketik.dk](mailto:dketik@dketik.dk) in order for both authorities to validate and assess the application within the same time frame. |

|  |
| --- |
| First submission in Denmark |
| *or*  Re-submission in Denmark  Date of first submission:  DKMA case number:       MREC case number: |
| EUDAMED CIV-ID number (if known): |

|  |
| --- |
| Is the clinical investigation of the medical device also submitted via CTIS to Danish Medicines Agency and MREC as an application for authorisation as a clinical trial of a *medicinal product*?  Yes  No  If yes, state EU trial number / CTIS number: |

**2. Contact information**

**2.1 Sponsor**

*The sponsor is the individual, company, institution or organisation who or which takes responsibility for the initiation, management and financing of the clinical investigation.*

|  |  |
| --- | --- |
| Individual / company / institution / organisation |  |
| Address |  |
| Phone number |  |
| E-mail |  |

**Sponsor’s contact person**

|  |  |
| --- | --- |
| Name |  |
| Title |  |
| Address |  |
| Phone number |  |
| E-mail |  |

**Sponsor’s EU representative (if located outside of EU/EEC)***The sponsor’s legal representative within an EU/EEC country if sponsor is not established in EU.*

|  |  |
| --- | --- |
| Individual / company / institution / organisation |  |
| Address |  |
| Phone number |  |
| E-mail |  |

**Contact person for sponsor’s EU representative**

|  |  |
| --- | --- |
| Name |  |
| Title |  |
| Address |  |
| Phone number |  |
| E-mail |  |

**2.2 Monitor**

*Sponsor shall appoint a monitor, independent of the investigation site, to ensure that the investigation is conducted in accordance with the clinical investigation plan, good clinical practice and legislation (MDR Annex XV, Chapter III, 4).*

*Please note that the monitor needs to be independent of the investigation site. Monitor must be able to understand source documents written in Danish, hence it is expected that Danish (or Scandinavian monitors) will be monitoring the investigation.*

|  |  |
| --- | --- |
| Individual / company / institution / organisation responsible for monitoring activities | **Please confirm that monitor is able to read and**  **understand Danish** |
| Contact person |  |
| Title |  |
| Address |  |
| Phone number |  |
| E-mail |  |

**2.3 Manufacturer of the medical device(s) under investigation**

*The manufacturer is the natural or legal person who manufactures or fully refurbishes a device or has a device designed, manufactured or fully refurbished by a third party, and markets that device under its name or trademark. The manufacturer in this section refers to the manufacturer responsible for the investigator’s brochure / statement of compliance for the investigational medical device.*

|  |  |
| --- | --- |
| Company / institution |  |
| Address |  |
| Phone number |  |
| E-mail |  |

**Contact person for manufacturer**

|  |  |
| --- | --- |
| Name |  |
| Title |  |
| Phone number |  |
| E-mail |  |

**Person responsible for regulatory compliance for manufacturer**

*Please note that the MDR Article 15 specifies the qualification criteria for the manufacturer’s person responsible for regulatory compliance at the time when statement of compliance is signed.*

|  |  |
| --- | --- |
| Name |  |
| Title |  |
| Phone number |  |
| E-mail |  |

**Manufacturer’s EU representative (if located outside of EU/EEC)**

*The manufacturer’s legal representative within an EU/EEC country if manufacturer is not established in EU.*

|  |  |
| --- | --- |
| Company / institution |  |
| Address |  |
| Phone number |  |
| E-mail |  |

**Contact person for manufacturer’s EU representative**

|  |  |
| --- | --- |
| Name |  |
| Title |  |
| Phone number |  |
| E-mail |  |

**2.4 Coordinating investigator (if multicentre investigation)**

*The investigator that is appointed to coordinate work in a multicentre investigation.*

|  |  |
| --- | --- |
| Name |  |
| Institution |  |
| Title |  |
| Address |  |
| Phone number |  |
| E-mail |  |

**3. Investigation site information and information on principal clinical investigator(s) in Denmark**

*Please provide the list of sites taking part in the clinical investigation*

|  |  |  |  |
| --- | --- | --- | --- |
| Name of institution and department | Site address | Name and title of principal investigator | Contact information of principal investigator  (e-mail and phone number) |
|  |  |  |  |
|  |  |  |  |
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|  |  |  |  |
|  |  |  |  |

**Please copy this page if there are additional study sites**

**4. Investigation sites outside Denmark**

*Information concerning other countries where the investigation has been or will be submitted.*

|  |
| --- |
| **Countries where the clinical investigation will be/is being conducted** |
|  |

|  |
| --- |
| **Have objections, conditions or supplementary comments to the investigation been raised by other competent authorities?**  **No**  **Yes** |
| If yes, please state where and the reasons why: |

**5. Clinical evaluation information**

|  |
| --- |
| Brief information and/or reference to the clinical evaluation plan for the non-CE marked medical device (e.g. how this specific clinical investigation fits into the clinical development plan for the product). |
|  |

**6. Expert panel**

|  |
| --- |
| Has the manufacturer consulted with an expert panel on the manufacturer's intended clinical development strategy and proposals for clinical investigation as outlined in Article 61(2) of the MDR?  Yes  No  If yes, please confirm that the expert opinion document is attached to the application |

**7. Clinical investigation information**

|  |
| --- |
| Official title of clinical investigation: |
| Clinical investigation title in Danish (if any): |
| Short title/acronym for the clinical investigation (if any): |
| Clinical investigation plan  reference number / code given by sponsor:  version number:  date: |
| Please state clinical development stage:  Pilot stage  Pivotal stage  Post-market stage  (*Reference: Annex I of EN ISO 14155:2020*)  Please state type of design:  Exploratory investigation  Confirmatory investigation  *(Reference: Annex I of EN ISO 14155:2020)* |
| Is the clinical investigation “first in human”? Yes  No  If yes, please specify whether this type of device/technology has been used in humans before |
| Investigational design:  Does the clinical investigation constitute a controlled design? Yes  No  If yes, please specify design:  Randomised  Open label  Single-blinded  Double-blinded  Parallel-group  Cross-over  Historic data/control  Cohort study  Case-Control  Cross-sectional  Other  please specify |
| Primary objective(s) of the clinical investigation: |
| Secondary objective(s) of the clinical investigation: |
| Primary endpoint(s): |
| Secondary endpoint(s): |
| Number of subjects to be included in the investigation:  DK:       EU/EEA:       Globally (in total): |
| Expected initiation date (start of recruitment): Global (if any)       / Denmark  Expected end date (last patient last visit): Global (if any)       / Denmark |
| Main eligibility criteria for subjects: |

**8. Information on study population**

|  |
| --- |
| Healthy participants  Patients  Are subjects from vulnerable populations included in the investigation? Yes  No  If yes, please specify which vulnerable population(s) is included:  Incapacitated subjects  Pregnant women  Minors (<18 years)  Breastfeeding women  Participants in emergency situations  Other (e.g. military personnel, institutionalised, employees/students)  please specify |
| Is there an associated medical condition? Yes  No  If yes, is the medical condition considered to be rare? Yes  No  *EU defines a rare disease as one that affects no more than 1 person in 2,000.*  [*https://research-and-innovation.ec.europa.eu/research-area/health/rare-diseases\_en*](https://research-and-innovation.ec.europa.eu/research-area/health/rare-diseases_en) |
| Please specify the gender of the study subjects:  Female  Male  Other |
| Please specify the age range of the study subjects:  In utero  New-borns (0-27 days)  Infants and toddlers (28 days – 23 months)  Children (2-11 years)  Adolescents (12-14 years)  Adolescents (15-17 years)  Adults (18-84 years)  Elderly (85+ years) |

**9. Medical device characteristics**

|  |  |
| --- | --- |
| Product type and generic name of device |  |
| Name of device |  |
| Model |  |
| Proposed class of device  (according to the MDR) | Class I  Class IIa  Class IIb  Class III |
| CE marked medical device | Yes  No |
| Sterile medical device  Medical device with measuring function  Reusable surgical medical device  Active medical device  Medical device software  Invasive device (according to rule 5 in Chapter III of Annex VIII in the MDR)  Implantable device | |
| Does the device incorporate a medicinal substance or a human blood or plasma derivate? | Yes  No |
| If yes, specify the component |
| Does the device incorporate any non-viable tissues or cells of human or animal origin or their derivates? | Yes  No |
| If yes, specify the component |
| Notified body, if relevant |  |

**Please copy this page if there are more medical devices under investigation (i.e. a comparator device)**

**10. Attached application documents**

*I have read and attached documents according to the MREC guideline*

*Link to* [*MREC’s guideline*](https://researchethics.dk/information-for-researchers/clinical-investigations-of-medical-devices-under-the-mdr/checklist-for-reporting-clinical-investigations-of-medical-devices-under-the-mdr)*.*

*Please note: documents marked with \* indicate that the document is not required according to the MDR, but will be requested in order for MREC to assess the application.*

|  |  |  |
| --- | --- | --- |
|  | **Documents** | **Document, version** |
| 1 | Cover letter \* | The file name for the document belonging to this part of the application must be named starting with:  “01.01 Cover letter” |
| 2 | Application form | The file name for the document belonging to this part of the application must be named starting with:  “02.01 Application form” |
| 3 | Clinical investigation plan | The file name for the document belonging to this part of the application must be named starting with:  “03.01 Clinical investigation plan”  “03.02 …xyz.” |
| 4 | Synopsis/summary of clinical investigation plan if not part of clinical investigation plan  *The synopsis may be written in English* | The file name for the document belonging to this part of the application must be named starting with:  “04.01 Synopsis of clinical investigation plan” |
| 5 | National addendum to clinical investigation plan, if any (according to national legislation) \*  *Please tick this box if there is* ***no*** *Danish addendum to the clinical investigation plan* | The file name for the document belonging to this part of the application must be named starting with:  “05.01 “National addendum to clinical investigation plan” |
| 6 | Participant information sheet(s) including informed consent form(s) | The file name for the document belonging to this part of the application must be named starting with:  “06.01 Participant information sheet including informed consent form”  “06.02 Dine rettigheder som forsøgsperson i forsøg med medicinsk udstyr” ([link](https://videnskabsetik.dk/deltagelse-i-kliniske-forsoeg/dine-rettigheder-som-forsoegsperson/dine-rettigheder-som-forsoegsperson-i-forsoeg-med-medicinsk-udstyr)) |
| 7 | Recruitment material\*  (e.g. advertisements, postings, recruitment letters, text on sundhed.dk or social media)  *Please tick this box if there is* ***no*** *recruitment material in the clinical investigation* | The file name for the document belonging to this part of the application must be named starting with:  “07.01 Invitation letter” |
| 8 | Questionnaires\*  (that are linked to the endpoint(s) of the clinical investigation)  *Please tick this box if there are* ***no*** *questionnaires in the clinical investigation* | The file name for the document belonging to this part of the application must be named starting with:  “08.01 Questionnaire\_Quality of life”  (possibly in a combined file or if separate documents, numbered e.g. 08.01, 08.02 etc.) |
| 9 | Investigator’s Brochure (IB) | The file name for the document belonging to this part of the application must be named starting with:  “09.01 Investigator’s brochure”  “09.02 Instructions for use”  “09.03 Labels” |
| 10 | General Safety and Performance Requirements (GSPR) checklist  [Link to template](https://laegemiddelstyrelsen.dk/da/udstyr/klinisk-afproevning-af-medicinsk-udstyr/ansoegning-om-klinisk-afproevning/~/media/C267F5C228BB4CB8BD757822E6CCF513.ashx) | The file name for the document belonging to this part of the application must be named starting with:  “10.01 GSPR checklist” |
| 11 | Statement certifying that the non-CE marked medical device(s) complies with the general safety and performance requirements in Annex I of Regulation (EU) 2017/745 (MDR), apart from those aspects covered by the investigation.  [Link to template](https://laegemiddelstyrelsen.dk/da/udstyr/klinisk-afproevning-af-medicinsk-udstyr/ansoegning-om-klinisk-afproevning/~/media/C311C6251EFA46B0B6A26C7B56B418C8.ashx) | The file name for the document belonging to this part of the application must be named starting with  “11.01 Statement of compliance” |
| 12 | Description of the arrangements to comply with applicable rules on the protection and confidentiality of personal data, cf. MDR, Annex XV, Chapter II (4.5)) | The file name for the document belonging to this part of the application must be named starting with:  “12.01 Sponsor’s description of how to comply with GDPR” |
| 13 | Curriculum Vitae of investigator(s) on Danish investigational sites\* | The file name for the document belonging to this part of the application must be named starting with:  “13.01 CV last name investigator\_name of site”  “13.02 Print from STPS authorisation database” |
| 14 | Danish version of relevant parts of the sponsor contract\*  (about publishing conditions and compensation for researchers/subjects as well as researcher's access to data) | The file name for the document belonging to this part of the application must be named starting with:  “14.01 Sponsor contract” |
| 15 | Proof of insurance cover or indemnification\* (if not covered by the Danish Patient Compensation)  *Please tick this box if there is* ***no*** *insurance cover/indemnification as the investigation is covered by the Danish Patient Compensation* | The file name for the document belonging to this part of the application must be named starting with:  “15.01 Proof of insurance” |

**11. Overview of required information in investigator’s brochure and clinical investigation plan according to Annex XV of the MDR**

***Note:*** *The application shall contain information concerning all items in the MDR Annex XV. In exceptional cases, a required item is considered irrelevant for a specific clinical investigation, the covering letter must contain a list of these items as well as the justification for the omissions.*

|  |  |  |  |
| --- | --- | --- | --- |
| LIST / CROSS-REFERENCES BETWEEN REQUIREMENT IN ANNEX XV CHAPTER II AND SUBMISSION PACKAGE | | | |
| Requirement | | Description of requirement | Location within submission package |
| Annex XV Chapter II (2):  **Investigator’s brochure (IB)** (information in IB or in *exceptional* cases enclosed as separate documents.  If enclosed as separate documents, a clear reference within the IB shall be made to the enclosed documents) | 2.1 | Identification and description of the device | Document Page |
| 2.1 | information on the intended purpose | Document Page |
| 2.1 | the risk classification and applicable classification rule pursuant to Annex VIII | Document Page |
| 2.1 | design and manufacturing of the device | Document Page |
| 2.1 | Reference to previous and similar generations of the device. | Document Page |
| 2.2 | Manufacturer's instructions for installation, maintenance, maintaining hygiene standards and for use, including storage and handling requirements | Document Page |
| 2.2 | Information to be placed on the label | Document Page |
| 2.2 | Instructions for use to be provided with the device. | Document Page |
| 2.2 | Information relating to any relevant training required. | Document Page |
| 2.3 | Pre-clinical evaluation based on pre-clinical testing and experimental data in particular as applicable;  in-design calculations, in-vitro test, ex-vivo test, animal test, mechanical test, electrical test, reliability test, sterilization validation, software verification and validation, performance test  evaluation of biocompatibility and biological safety.  Summary and evaluation of pre-clinical/ non-clincal data:  Have all relevant pre-clinical test been completed: Yes  No  If no, provide justification for why the investigation can be initiated. | Document(s) Page |
| 2.4 | Existing clinical data, in particular available literature or other clinical data available relating to safety, performance and clinical benefit | Document Page |
| 2.5 | Summary of the benefit risk analysis and risk management | Document Page |
| 2.5 | Information regarding known or foreseeable risks, any undesirable side effects, contraindications and warnings | Document Page |
| 2.6 | In case of devices that contains:  **medicinal substance**  Detailed information om the substance, and the risk management in relation to the substance, and evidence for the added value of incorporation of such constituents in relation to the clinical benefit and safety of the device | Document Page |
| 2.6 | In case of devices that contains:  **human blood / plasma or derivate**  Detailed information om the substance, and the risk management in relation to the substance, and evidence for the added value of incorporation of such constituents in relation to the clinical benefit and safety of the device | Document Page |
| 2.6 | In case of devices that contains  **non-viable tissues or cells of human or animal origin, or their derivatives**  Detailed information on the tissue/cell their derivate, and the risk management in relation to the tissue, cell or their derivate, and evidence for the added value of incorporation of such constituents in relation to the clinical benefit and safety of the device | Document Page |
| 2.7 | List of fulfilment of the General Safety and Performance Requirements (GSPR).  A list detailing the fulfilment of the relevant general safety and performance requirements set out in Annex I, including the standards and CS applied, in full or in part, as well as a description of the solutions for fulfilling the relevant general safety and performance requirements, in so far as those standards and CS have not or have only been partly fulfilled or are lacking. | Document Page |
| 2.8 | A detailed description of the clinical procedures and diagnostic tests used in the course of the clinical investigation and in particular information on any deviation from normal clinical practice. | Document Page |
| Annex XV Chapter II (3):  **Clinical Investigation Plan (CIP)**  (information in CIP or in exceptional cases enclosed as separate documents) | 3.1.2 | Identification of sponsor, and sponsors contact person and/or legal representative in CIP | Document Page |
| 3.1.3 | Information on Coordinating investigator | Document Page |
| 3.1.3 | Principal investigator at each site, and contact details | Document Page |
| 3.1.3 | Specification of roles, responsibilities and qualifications of the different kinds of investigators (coordinating investigator, principal investigator, sub-investigator) | Document Page |
| 3.1.4 | A brief description on how the clinical investigation is financed | Document Page |
| 3.1.4 | A brief description of the agreement between sponsor and the site | Document Page |
| 3.1.5 | Synopsis of the clinical investigation in Danish language | Document Page |
| 3.2 | Identification and description of the device, including its intended purpose and the target population, | Document Page |
| 3.2 | Identification of manufacturer | Document Page |
| 3.2 | Identification and description of the device’s traceability | Document Page |
| 3.2 | Identification and description of materials coming into contact with the human body, | Document Page |
| 3.2 | Identification and description of the medical or surgical procedures involved in its use. | Document Page |
| 3.2 | Identification and description of and the necessary training and experience for its use | Document Page |
| 3.2 | Identification and description of background literature review | Document Page |
| 3.2 | Identification and description of the current state of the art in clinical care in the relevant field of application and the proposed benefits of the new device | Document Page |
| 3.3 | Risks and clinical benefits of the device to be examined, with justification of the corresponding expected clinical outcomes in the clinical investigation plan | Document Page |
| 3.4 | Description of the relevance of the clinical investigation in the context of the state of the art of clinical practice | Document Page |
| 3.5 | Objectives and hypotheses of the clinical investigation. | Document Page |
| 3.6.1 | General information such as type of investigation with rationale for choosing it, for its endpoints and for its variables as set out in the clinical evaluation plan | Document Page |
| 3.6.2 | Information on the investigational device, on any comparator and on any other device or medication to be used in the clinical investigation. | Document Page |
| 3.6.3 | Information on subjects, selection criteria, size of investigation population, representativeness of investigation population in relation to target population and, if applicable, information on vulnerable subjects involved such as children, pregnant women, immuno-compromised or, elderly subjects. | Document Page |
| 3.6.4 | Details of measures to be taken to minimise bias, such as randomisation, and management of potential confounding factors. | Document Page |
| 3.6.5 | Description of the clinical procedures and diagnostic methods relating to the clinical investigation and in particular highlighting any deviation from normal clinical practice. | Document Page |
| 3.6.6 | Monitoring plan.  (The *general* outline of the monitoring plan in the CIP, as the detailed study specific detailed monitoring plan is finalized at a later point in time) | Document Page |
| 3.7 | Statistical considerations, with justification, including a power calculation for the sample size, if applicable | Document Page |
| 3.8 | Data management. | Document Page |
| 3.9 | Information about any amendments to the CIP. | Document Page |
| 3.10 | Policy regarding follow-up and management of any deviations from the CIP at the investigational site and clear prohibition of use of waivers from the CIP | Document Page |
| 3.11 | Accountability regarding the device, in particular control of access to the device, follow-up in relation to the device used in the clinical investigation and the return of unused, expired or malfunctioning devices | Document Page |
| 3.12 | Statement of compliance with the recognised ethical principles for medical research involving humans (i.e. declaration of Helsinki) | Document Page |
| 3.12 | Statement of compliance with the principles of good clinical practice in the field of clinical investigations of devices (ISO 14155) | Document Page |
| 3.12 | Statement of compliance with as with the applicable regulatory requirements | Document Page |
| 3.13 | Description of the Informed consent process. | Document Page |
| 3.14 | Safety reporting, including definitions of adverse events and serious adverse events, device deficiencies, procedures and timelines for reporting. | Document Page |
| 3.15 | Criteria and procedures for follow-up of subjects following the end, temporary halt or early termination of an investigation, for follow-up of subjects who have withdrawn their consent and procedures for subjects lost to follow-up. Such procedures shall for implantable devices, cover as a minimum traceability. | Document Page |
| 3.16 | A description of the arrangements for taking care of the subjects after their participation in the clinical investigation has ended, where such additional care is necessary because of the subjects' participation in the clinical investigation and where it differs from that normally expected for the medical condition in question | Document Page |
| 3.17 | Policy as regards the establishment of the clinical investigation report and publication of results in accordance with the legal requirements and the ethical principles referred to in Section 1 of Chapter I. | Document Page |
| 3.18 | List of the technical and functional features of the device, with specific mention of those covered by the investigation. | Document Page |

**12. Invoice information**

**DKMA’s fee for application assessment**

*DKMA’s fee for assessment of applications of clinical investigations of medical devices can be found on DKMA’s* [*website*](https://laegemiddelstyrelsen.dk/en/devices/clinical-investigations/fees/)*.*

|  |  |
| --- | --- |
| Clinical investigation plan title: | |
| Individual / company / institution / organisation |  |
| Contact person |  |
| Company invoice ref. number |  |
| Address |  |
| Phone number |  |
| E-mail |  |
| CVR / VAT number  and EAN number | CVR / VAT number:  EAN number for Danish invoice recipients, if any: |

**DKMA’s annual inspection fee (clinical investigations for which authorisation is granted)**

*Only fill in if different from above. DKMA’s annual inspection fee for clinical investigations of medical devices can be found on DKMA’s* [*website*](https://laegemiddelstyrelsen.dk/en/devices/clinical-investigations/fees/)*.*

|  |  |
| --- | --- |
| Clinical investigation plan title: | |
| Individual / company / institution / organisation |  |
| Contact person |  |
| Company invoice ref. number |  |
| Address |  |
| Phone number |  |
| E-mail |  |
| CVR / VAT number  and EAN number | CVR / VAT number:  EAN number for Danish invoice recipients, if any: |

**MREC’s fee for application assessment**

*Fees for the ethical assessment of applications with medical devices are to be paid separately to the Medical Research Ethics Committees. The Medical Research Ethics Committees’ fee for assessment of applications of clinical investigations of medical devices can be found on the Medical Research Ethics Committees’* [*website*](https://researchethics.dk/information-for-researchers/clinical-investigations-of-medical-devices-under-the-mdr/fees-for-review-of-applications-under-the-mdr)*. A* ***separate invoice application form*** *must be filled out and submitted together with the application to the Medical Research Ethics Committees. The invoice form can be found in both Danish and English at the* [*website*](https://researchethics.dk/information-for-researchers/clinical-investigations-of-medical-devices-under-the-mdr/fees-for-review-of-applications-under-the-mdr) *of the Medical Research Ethics Committees.*

**13. Sponsor’s declaration and signature**

*I/We are aware of the obligations in Annex XV of the MDR to*

* *conduct study according to ethical principles (declaration of Helsinki), the principles for good clinical practice in clinical investigation of medical devices (ISO 14155) and according to national legislation,*
* *make the clinical investigation report and a summary of the clinical investigation report publicly available in EU Commission’s EUDAMED database when this is made available,*
* *keep available for the Danish Medicines Agency for a period of 10 years (15 years for implantable devices) after the end of the clinical investigation all documentation referred to in Annex XV of the MDR.*
* *We are aware that the Danish Medicines Agency and the Medical Research Ethics Committees will contact each other and share information in relation to the assessment of this specific clinical investigation.*
* *All information collected for this application, has been done in compliance with the European data protection legislation (GDPR).*
* *The information and documentation submitted with this application/notification are correct in detail and all the information requested has been supplied.*

|  |  |
| --- | --- |
| Date |  |
| Name |  |
| Sponsor’s signature |  |