**1.** **Scope of Application**

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

*Udfyld venligst ansøgningsskemaet på engelsk eller dansk.*

|  |
| --- |
| Application for authorisation of a clinical investigation of   * a non-CE marked medical device to generate clinical data for conformity assessment purposes (i.e. CE marking) (Art. 62 (1))   *or*   * a CE-marked medical device investigated for another purpose than the CE marked purpose (Art. 74 (2)) |
| Date of submission: |
| First submission |
| Re-submission  Danish Medicines Agency case number:       Date of first submission: |
| EUDAMED CIV-ID number (if known): |

|  |
| --- |
| Is the clinical investigation of the medical device also submitted to Danish Medicines Agency as an application for authorisation as a clinical trial of a *medicinal product*? Yes  No  If yes, state EudraCT number  and DKMA case number |

|  |
| --- |
| The application consists of different parts  **Signature and invoice information**  **List of documents and cross- references**  **Information**  **on device**  **Information on clinical investigation**  **Information**  **on actors and roles**  Application is to be submitted as **one mail to two recipients**; [med-udstyr@dkma.dk](mailto:med-udstyr@dkma.dk) and [dketik@dketik.dk](mailto:dketik@dketik.dk) in order for both parties to validate the application within same time frame. |

**2. Sponsor**

*The Sponsor is the individual, institution or organization who or which takes responsibility for the initiation and implementation of a clinical investigation.*

|  |  |
| --- | --- |
| Company / institution |  |
| Contact person |  |
| Title |  |
| Address |  |
| Phone number |  |
| E-mail |  |

**3. Sponsors EEC representative, if any**

*The sponsor’s legal representative within an EU/EEC country if the sponsor is not resident in an EU/EEC country.*

|  |  |
| --- | --- |
| Company / institution |  |
| Contact person |  |
| Title |  |
| Address |  |
| Phone number |  |
| E-mail |  |

**4. Monitor**

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

|  |  |
| --- | --- |
| Company/ individual/ organisation with the responsibility of the monitoring activities |  |
| Contact person |  |
| Title |  |
| Address |  |
| Phone number |  |
| E-mail |  |

**5. Contract Research Organisation (CRO), if any**

*If a CRO is used in the clinical investigation for another purpose than monitoring (submission of application, data management etc), the CRO and the related activities can be identified here.*

|  |  |
| --- | --- |
| Company |  |
| Contact person |  |
| Title |  |
| Address |  |
| Phone number |  |
| E-mail |  |
| Role of the CRO in the clinical investigation |  |

**6. Manufacturer of the medical device in clinical investigation**

*The manufacturer is the natural or legal person with responsibility for the design, manufacture, packaging and labelling of a device before it is placed on the market under his own name, regardless of whether these operations are carried out by that person himself or on his behalf by a third party. The manufacturer in this section refers to the manufacturer responsible for the IB/ statement of compliance for the investigational medical device.*

*Identification of the manufacturer’s Person Responsible for Regulatory Compliance at the time when statement of compliance is signed. Please note that MDR in article 15 has specific qualification criteria for this person.*

|  |  |
| --- | --- |
| Company / institution |  |
| Address |  |
| Contact person |  |
| Phone number |  |
| E-mail |  |
| Person responsible for regulatory compliance |  |
| Phone number |  |
| E-mail |  |

**7. Manufacturers EU representative, if any**

*The manufacturer’s legal representative in an EU/EEC country i.e., if the manufacturer is not resident in an EU/EEC country.*

|  |  |
| --- | --- |
| Company / institution |  |
| Contact person |  |
| Title |  |
| Address |  |
| Phone number |  |
| E-mail |  |

**8. Information from sponsor/manufacturer of medical device**

*Only fill in in case of a clinical investigation of a non-CE marked medical device.*

|  |  |
| --- | --- |
| 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). |  |

**9. Coordinating investigator**

*The investigator that is appointed to coordinate work in a multi-centre investigation.*

*Mandatory for multi-centre investigations.*

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

**10. Principal clinical investigator in Denmark**

*Every investigation centre has an investigator responsible for the investigation carried out at that particular site.*

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

**Principal clinical investigator in Denmark**

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

**Principal clinical investigator in Denmark**

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

**Please copy this page if there are more investigation centres11. Investigation centres outside Denmark**

*Information concerning other countries where this investigation has been or will be notified to the competent authority, including opinions received.*

|  |  |
| --- | --- |
| **Countries where authorisation has been granted** | **Countries where authorisation is pending** |
|  |  |

Have objections, study-specific conditions or supplementary comments, to the investigation been raised by other competent authorities:

**No** , **Yes**

If yes, please state where and the reasons why:

**12. Medical Device**

*Please copy this page if multiple medical devices are investigated.*

|  |  |
| --- | --- |
| Product type and generic name of device |  |
| Name of device |  |
| Model |  |
| CE-marked medical device | Yes  No |
| Proposed class of device (according to MDR) | I  IIa  IIb  III |
| Sterile medical device | Yes  No |
| Medical device with measuring function | Yes  No |
| Reusable surgical medical device | Yes  No |
| Is the device an *invasive* device (according to rule 5 in Chapter III of Annex VIII in MDR)? | Yes  No |
| Is the device implantable? | Yes  No |
| 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 |  |

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

**13. Clinical investigation**

|  |
| --- |
| Clinical investigation plan title in English (if any): |
| Clinical investigation plan title in Danish: |
| Clinical investigation plan   * reference number / code given by Sponsor: * version number * date |
| Number of subjects to be included in the investigation:  DK:      Globally: |
| Total number of the device(s) to be used in the investigation:  DK:      Globally: |
| Expected Initiation date (patient recruitment start): Global (if any)       / Denmark  Expected end date (last patient last visit): Global (if any)       / Denmark |
| **Short** summary of the design (controlled/randomised) and objective of the clinical investigation, including information on population gender/age of subjects (e.g. inclusion of subjects under 18 years) and *main* eligibility criteria for subjects: |

**14. Attached documents**

|  |  |  |
| --- | --- | --- |
|  | **Documents** | **Document, version, comments** |
| 1 | Cover letter and application form | The file name for document belonging to this part of application must be named starting with “01…xyz”, e.g.  “01.01 Cover letter”  “01.02 Application form” |
| 2 | Investigator’s Brochure | The file name for the IB and any additional documents submitted separately within this part of the application must be named starting with “02…xyz”, e.g .  “02.01 Investigator Brocure”  “02.02 Instruction for use”  “02.03 Checklist for fulfilment of general safety performance requirements” |
| 3 | Clinical investigation plan | The file name for document belonging to this part of applicatio must be named starting with “03…xyz”, e.g.  “03.01 Clinical investigation plan”  “03.02 …xyz.” |
| 4 | Patient information(s) and informed consent form(s) | The file name for document belonging to this part of applicatio must be named starting with “04.xx”, e.g.  “04.01 Subject information and consent form patients”  “04.02 Subject information and consent form legal representative” |
| 5 | Statement certifying that the device in question complies with the General safety and performance requirements, apart from those aspects covered by the investigation, and that with regard to these aspects, every precaution has been taken to protect the health and safety of the subject. The statement shall refer to the medical device regulation. | The name for this document belonging to this part of application must be named starting with “05.01 Statement of compliance”  *Please note, for CE marked devices, please attach the declaration of conformity and any EC certificates.* |
| 6 | Description of the arrangements to comply with applicable rules on the protection and confidentiality of personal data (please see MDR Annex XV, Chapter II (4.5)) | The file name for document belonging to this part of application must be named starting with “06.…xyz”, e.g.  “06.01 sponsors statement on how to comply with GDPR” |

**Documents not part Annex XV in MDR, but documents Medical Research Ethics Committees (MREC) *will* request**

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

*Link to guideline:* [*https://www.dvmk.dk/ansoger/tjekliste*](https://www.dvmk.dk/ansoger/tjekliste)

*The file name for document belonging to this part of application must be named starting with “07.01 …”, “08.01 …” etc. Please do not use special characters (-,\_,@,#, etc.).*

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**15. Overview of required information in Investigators Brochure and Clinical investigation plan according to Annex XV**

|  |  |  |  |
| --- | --- | --- | --- |
| 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):  **Investigators Brochure** (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**  (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 |

***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.*

**16. Invoice information**

*To whom the invoice for the Danish Medicines Agency’s fee and ethics committee fee shall be forwarded.*

**DKMA fee for application assessment**

*According to Executive Order no. 737 of 24 May 2022 on fees for medical devices and medical devices for in vitro diagnostics, the fee for 2022 is 52,095 DKK for class I, class IIa devices and class IIb devices (non-implantable devices or devices not suitable for long-term use), 70,017 DKK for class IIb (implantable devices or devices suitable for long-term use) and class III devices.*

|  |  |
| --- | --- |
| Clinical investigation plan title: | |
| Company |  |
| 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 annual inspection fee (clinical investigations for which authorization is granted)**

*Only fill in if different from above.*

*According to Executive Order no. 737 of 24 May 2022 on fees for medical devices and medical devices for in vitro diagnostics, the annual fee for 2022 is 11,513 DKK. The fee will be charged annually until end of trial notification is received.*

|  |  |
| --- | --- |
| Clinical investigation plan title: | |
| Company |  |
| 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 |

**Medical Research Ethics Committees fee for application assessment**

*According to Executive Order no. 713 of 24 May 2022 on “Videnskabsetisk behandling af kliniske afprøvninger af medicinsk udstyr og undersøgelse af ydeevne af medicinsk udstyr til in vitro-diagnostik”, the fee for 2022 is 18,275 DKK.*

*Fees for the ethical assessment of applications with medical devices are to be payed separately to the Medical Research Ethics Committees.*

*A separate invoice application form must be filled out and submitted together with the application to the Medical Research Ethics Committees. The invoice can be found at the* [*website*](http://www.dvmk.dk) *of the Medical Research Ethics Committees.*

**17. Sponsor’s Declaration and Signature**

*I/We are aware of the obligations in Annex XV of 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*
* *will make the clinical investigation report and a summary of the clinical investigation report (in lay man terms) publicly available in EU commissions EUDAMED database when this is made available*
* *We are aware that Danish Medicines Agency and ethics committee will contact each other and share information in relation to the assessment of this specific clinical investigation.*
* *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 MDR.*

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