

Ministry of health

**ORDER No. 330
of 10 February 2023**

on approval of the Methodological Rules for clinical assessment and clinical investigation with medical devices and on repeal of Order of the Minister of Public Health no. 792/2006 on conduct of the procedure for clinical investigation and the procedure for assessment of performance relating to medical devices, as amended

Published in: the Official Gazette No. 120 of 13 February 2023

***) Important note:**

For application of the Order, see the provisions of Art. 3.

On seeing approval report no. 2.698/2023 of the Pharmaceutical and Medical Devices Directorate and the notice of the National Agency for Medicines and Medical Devices of Romania no. 102.016E of 31.01.2023, registered at the Ministry of Health with no. 2/2.116 of 1.02.2023,

taking into account the provisions of:

- Art. 16 (1) of Emergency Government Ordinance no. 46/2021 on the establishment of the institutional framework and the measures necessary to ensure the direct application of the provisions of Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) no. 178/2002 and Regulation (EC) no. 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC;

- Article 932 paragraphs (1) and (2) of Law 95/2006 on healthcare reform, republished, as further amended and supplemented;

- Article 4 (4) points 1 and 15 of Law 134/2019 on reorganisation of the National Agency for Medicines and Medical Devices and amendment of further ruling provisions, as further amended and supplemented;

pursuant to Article 7 (4) of Government Decision no. 144/2010 on the organisation and operation of the Ministry of Health, as further amended and supplemented,

the minister of health hereby issues the following Order:

Art. 1 - The Methodological Rules for clinical assessment and clinical investigation with medical devices, mentioned in the Annex*) which is an integral part of this Order, are approved.

*) The Annex is published in the Official Gazette of Romania, Part I, no. 120 bis, which

can be purchased from the Public Relations Center at 1 Panduri Street, Bldg. P33, ground floor, sector 5, Bucharest.

Art. 2 - The National Agency for Medicines and Medical Devices of Romania, hereinafter referred to as the NAMMDR, is the competent authority in the field of medical devices, responsible for clinical assessment and clinical investigation with medical devices, according to the provisions of Art. 61 - 82 of Regulation (EU) 2017/745 of the European parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC, hereinafter referred to as the **Regulation**.

Art. 3 - (1) On entry into force of this Order, Order of the Minister of Public Health no. 792/2006 on the conduct of the clinical investigation procedure and the performance assessment procedure for medical devices, as amended, as further amended and supplemented, published in the Official Gazette of Romania, Part I, no. 595 of 10 July 2006, is repealed.

(2) The provisions of this Order apply to requests for clinical assessment and clinical investigation, submitted to the NAMMDR after 26 May 2021, including reports for clinical investigation with medical devices registered at the NAMMDR by 25 May 2021, in accordance with the provisions of Art. 123 paragraphs (2) and (3) point d) indents 13 - 15 of the Regulation.

Art. 4 - The NAMMDR, the National Bioethics Committee for Medicinal Products and Medical Devices (**CNBMDM**) and the specialised commissions of the Ministry of Health shall carry out the provisions of this Order.

Art. 5 - This Order shall be published in the Official Gazette of Romania, Part I.

Minister of health,
Alexandru Rafila

Annex

METHODOLOGICAL RULES for clinical assessment and clinical investigation with medical devices

Section 1 General provisions

Art. 1 - These methodological rules aim to apply the provisions of Art. 16 paragraph (1) of Government Emergency Ordinance no. 46/2021 on establishment of an institutional framework and measures for enforcement of Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No. 178/2002 and Regulation (EC) No. 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC, hereinafter referred to as the Regulation and apply to medical devices of classes I, IIa, IIb and III.

Art. 2 - The terms used in these methodological rules have the meaning established by the Regulation.

Art. 3 - (1) Clinical investigations with medical devices shall be conducted in compliance with the good clinical practice described in the EN ISO 14155:2020 standard set out in point 137 of Annex I to Commission Implementing Decision (EU) 2020/437 of 24 March 2020 on the harmonised standards for medical devices drafted in support of Council Directive 93/42/EEC and point 34 of Annex I to Commission Implementing Decision (EU) 2020/438 of 24 March 2020 on the harmonised standards for active implantable medical devices drafted in support of Council Directive 90/385/EEC.

(2) The forms used for clinical investigations with medical devices are approved by the Medical Devices Coordination Group (MDCG) of the European Commission and published on the website of the European Commission, DG SANTE (https://ec.europa.eu/health/md_sector/new_Regulations/guidance_en#sec1).

(3) The Romanian language versions of the forms provided for in paragraph (2), as well as the forms developed by the NAMMDR for the conduct of the clinical investigation procedure with medical devices are provided in Annexes 1 - 8 to these methodological rules, and their updated versions, as well as any other new document approved by the MDCG, are posted on the NAMMDR website.

Art. 4 - (1) The ethical analysis is carried out by the CNBMDM, in accordance with the provisions of Art. 2 point 56 of the Regulation, an independent body according to the provisions of Order of the Minister of Health no. 80/2023 on approval of the structure and the Regulation for organisation and operation of the National Bioethics Committee for Medicinal Products and Medical Devices.

(2) The scientific analysis is carried out by the NAMMDR within the assessment of the documents attached to the applications and to notifications of clinical investigations. For clinical investigations with new medical devices, in niche or very new fields, of particular complexity, which enrol categories of vulnerable subjects, the NAMMDR consults the specialised commissions of the Ministry of Health.

Art. 5 - The NAMMDR charges fees for the approval of the conduct of the clinical investigation procedure, according to the provisions of Art. 16 paragraph (2) of Government

Emergency Ordinance no. 46/2021, approved through Order of the Minister of Health in accordance with the provisions of Art. 9 point b) of Law no. 134 of 12 July 2019 on reorganisation of the National Agency for Medicines and Medical Devices and amendment of further ruling provisions, as further amended and supplemented.

Art. 6 - The processing of personal data in clinical investigations with medical devices carried out on the Romanian territory is carried out in accordance with the provisions of Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation).

Art. 7 - (1) In order to assume responsibility for conducting the clinical investigation, in accordance with the provisions of the EN ISO 14155:2020 standard, the investigator must:

- a) hold the necessary qualifications obtained through studies and experience, for the exercise of the profession recognized in Romania, as meeting the necessary requirements for the role of investigator, due to the scientific knowledge and the necessary experience in the field of patient care;
- b) be fully familiar with the use of the investigational medical device, as presented in the protocol, in the investigator's brochure, in the information regarding the medical device and in other sources of information provided by the sponsor;
- c) know and comply with the Good Clinical Practice rules as well as the legal Regulations in the field;
- d) allow monitoring and auditing by the sponsor and the inspection carried out by the NAMMDR;
- e) keep a list of the staff members involved in the conduct of a clinical investigation and evidence of their qualifications attesting to the specificity of the experience or qualification for that clinical investigation.

(2) Subsequent amendments to SR EN ISO 14155:2020 relating to the requirements for investigators, their duties and good clinical practice will apply to clinical investigations with medical devices even if the amendments to the standard do not entail amendments to this Order.

Art. 8 - (1) According to Art. 69 paragraph (1) of the Regulation, the sponsor must ensure a system of compensation for damage suffered directly or indirectly by a subject following participation in a clinical investigation carried out on the Romanian territory, in the form of insurance or guarantee or a similar means, which is equivalent in terms of its purpose and appropriate to the nature and extent of the risk. In the case of clinical investigations with several sponsors, the responsibility will belong equally to all sponsors.

(2) The insurance shall be concluded in accordance with the provisions of Art. 69 paragraph (2) of the Regulation, before the start of the clinical investigation on the Romanian territory, and it shall cover all liabilities that may arise during the clinical investigation, regardless of the nature of the relations between the participants in the clinical investigation, investigators and sponsors. The insurance shall include compensation for damages created depending on the risks provided, including for death situations, as well as the maximum duration of risk coverage.

(3) The assessment of the nature, extent of the risk, scope of applicability, exclusions from the applicability of the insurance policy and other relevant aspects is the responsibility of the CNBMDM.

(4) All agreements concluded by the sponsor with any party relevant to the clinical investigation must contain the responsibilities of each party involved and clearly identify the

responsibilities in terms of Regulation and making available to the NAMMDR, on the Romanian territory, the clinical investigation documentation, for situations in which the sponsor shares or delegates these responsibilities. The agreements must be concluded in written form, shall be registered, signed and dated by all parties involved, in accordance with point 6.9 of the SR EN ISO 14155:2020 standard.

(5) **Art. 9** - (1) The documentation provided for in Annex XV of the Regulation shall be kept at the disposal of the NAMMDR during the period provided for in the first paragraph of Chapter III, point 3 of Annex XV of the Regulation.

(2) The documentation provided for in paragraph (1) shall be kept at the disposal of the NAMMDR during the period provided for in paragraph (1) and in the event that the sponsor or its contact person or its legal representative in accordance with Article 62, paragraph (2) of the Regulation, established on the Romanian territory, goes bankrupt or ceases its activity before the end of the period.

Art. 10 - The NAMMDR participates in the coordinated assessment procedure for clinical investigations conducted simultaneously in several Member States, provided for in Article 78 of the Regulation.

Section 2

Clinical evaluation and clinical investigation procedures for medical devices

Art. 11 - (1) The clinical evaluation is carried out in accordance with the provisions of Art. 61 and Annex XIV part A of the Regulation, and the form provided in Annex 1 to these methodological rules is used for medical devices that require the involvement of a notified body to report the result of the clinical evaluation, in accordance with Annex VII paragraph 4.6.

(2) - As part of the clinical evaluation, the manufacturer must conduct a post-market clinical follow-up (PMCF), for this purpose we prepare the report in Annex 2 to these methodological rules according to Annex XIV Part B paragraph 7 of the Regulation.

Art. 12 - (1) To conduct a clinical investigation on a medical device, the sponsor must submit to the NAMMDR an application using the form in Annex 3 to these methodological rules, the supporting documents provided for in Annexes 4 and 5 to these methodological rules, the ethical opinion issued by the CNBMDM and the proof of payment of the fee provided for in Art. 5.

(2) In order to authorise a substantial modification to a clinical investigation, the sponsor shall submit to the NAMMDR the application provided for in Annex 6 to these methodological rules.

(3) The documents related to the clinical investigations, which accompany the applications provided for in paragraphs (1) and (2), shall be submitted to the NAMMDR in Romanian or, with the consent of the NAMMDR, in English, in accordance with Article 10 paragraph 14 of the Regulation.

(4) When assessing the documents accompanying the applications provided for in paragraphs (1) and (2), the information provided for in Annex 4 to these methodological rules shall be taken into account.

(5) The registration of the application provided for in paragraph (1) for the conduct of a clinical investigation concerning a medical device, as well as the application for the authorisation of a substantial modification to a clinical investigation provided for in

paragraph (2) is made by the sponsor into the European database on medical devices (Eudamed), according to the instructions posted by the NAMMDR on its website.

(6) Until the date of publication in the European Journal of the announcement that the European database on medical devices (Eudamed) is fully functional in line with the provisions of Art. 34 paragraph (3) of the Regulation, the sponsor shall send to the NAMMDR the documents provided for in paragraph (1), and the NAMMDR shall use the European database on medical devices, Eudamed2, to obtain a unique identification number valid in the European Union (CIV-ID), in accordance with the European Commission Communication MDCG 2021-20 Instructions for generating CIV-ID for MDR Clinical Investigations, published on the European Commission website: https://ec.europa.eu/health/sites/default/files/md_sector/docs/mdcg_2021-20_en.pdf.

(7) The sponsor shall send to the NAMMDR the documents provided for in paragraphs (1) - (4) by post, in paper format and in electronic format, via a telematic system, by electronic mail, or on CD-ROM or USB storage devices sent by post. The sponsor shall register the application into the Eudamed after the date specified in paragraph (6).

(8) Any modification of the documentation provided for in Annex XV of the Regulation shall be registered into the Eudamed within one week from the date specified in paragraph (6).

(9) By way of exemption from paragraph (7), the NAMMDR may modify the procedure for submission of the application and the documents provided for in paragraphs (1) - (3), following the functionalities of the IT system agreed by the European Commission and shall publish it on the NAMMDR website.

(10) Within 10 days of receiving the application referred to in paragraphs (1) and (2), the NAMMDR shall notify the sponsor whether the clinical investigation falls within the scope of the Regulation and whether the application file is complete in accordance with Annex XV Section II of the Regulation.

(11) If, following the verification of the file, the NAMMDR finds that the clinical investigation for which the application was submitted does not fall within the scope of the Regulation or that the file and/or the application are incomplete, the NAMMDR shall inform the sponsor accordingly and set maximum 10 days from the notification for submission of the supplementations related to the application. Depending on the complexity of the requested information, the NAMMDR may extend this period by maximum 20 days, in accordance with Art. 70 paragraph (3), first paragraph of the Regulation.

(12) If the sponsor does not supplement the application within the deadline provided for in paragraph (11), the application is considered expired, without the need to issue a decision in this regard.

(13) If the sponsor considers that the application falls within the scope of the Regulation and/or is complete and the information contained is correct, yet the NAMMDR decision remains negative, the application is considered rejected.

(14) The NAMMDR shall communicate to the sponsor the decision to reject the application within maximum 5 days from the date of submission of the additional requested supplementations, in line with paragraph (11).

(15) The NAMMDR shall notify the sponsor about the validation of the clinical investigation application within 5 days after receiving the requested supplementations, according to paragraph (10). The validation of the NAMMDR signifies the inclusion of the clinical investigation within the scope of this Regulation and the fact that the application is complete.

(16) The NAMMDR may extend, in certain cases, each of the deadlines mentioned in paragraphs (10) and (11) by 5 additional days, in line with Art. 70 paragraph (4) of the

Regulation.

(17) By the date provided for in paragraph (6), after validation of the clinical investigation application, the NAMMDR shall allocate and communicate to the sponsor the application's number of registration at the NAMMDR and the CIV-ID identification number into the Eudamed2 database. If a CIV-ID identification number has already been assigned to the clinical investigation by another Member State of the European Union for a multicentre clinical investigation, the sponsor must specify the CIV-ID identification number in the application provided for in paragraph (1).

Art. 13 - (1) For class III or classes IIa and IIb invasive medical devices, after the validation stage of the clinical investigation application for the respective medical device, the NAMMDR assesses the entire documentation of the related file, in order to issue the authorisation for the clinical investigation of the respective medical device.

(2) For the purpose of carrying out the assessment provided for in paragraph (1), the NAMMDR may consult the specialised committees of the Ministry of Health, whenever it deems necessary, regarding any type of medical device, in the process of assessing clinical investigations, depending on their complexity and to ensure the safety and health of the subjects involved, in accordance with Art. 70 paragraph (7) point a) of the Regulation. The opinions issued by the specialised committees shall be transmitted to the NAMMDR within maximum 20 days from the date of receipt of the request by the NAMMDR.

(3) For classes IIb and III medical devices, in the case of coordinated assessments for which Romania, through the NAMMDR, is appointed as the coordinating Member State, the NAMMDR may extend the 15-day period provided for in Art. 78 paragraph (4) of the Regulation by an additional 50 days in accordance with the provisions of Art. 78 paragraph (6) of the Regulation.

(4) Following the assessment and based on the favourable opinions of the consulted specialised committees, as appropriate, the NAMMDR issues the authorisation for the clinical investigation of a medical device in accordance with Annex 7 to these methodological rules.

(5) The NAMMDR shall mention in the authorisation provided for in paragraph (4) the periodicity of reporting the results of the authorised clinical investigation.

(6) For reporting serious adverse events, Annex 8 to these methodological rules shall be used.

Art. 14 - In the case of products without a proposed medical purpose listed in Annex XVI of the Regulation, for which it is necessary to conduct clinical investigations, in accordance with Art. 61 paragraph (9) of the Regulation, the provisions of Section 1 - 4 shall apply accordingly.

Art. 15 - In order to clarify some information in the clinical investigation file, as well as to verify the compliance of the investigation site with the provisions of points 7.2, 9.2, 4.3, 10.3 and Annex J.3 of the EN ISO 14155:2020 standard, the NAMMDR may carry out inspections at the sites mentioned in the file during the evaluation stage of the clinical investigation files.

Art. 16 - The sponsor may start the clinical investigation of a medical device under the following circumstances:

(1) in the case of class I medical devices or in the case of non-invasive medical devices of classes IIa and IIb, immediately after the date of validation of the application provided for in Art. 12 paragraph (1) by the NAMMDR, provided that the CNBMDM has issued a positive ethical opinion;

(2) in the case of invasive medical devices in classes III or IIa and IIb, as well as active

implantable medical devices, as soon as the NAMMDR has notified its authorisation to the sponsor for the respective clinical investigation, provided that the CNBMDM has issued a positive ethical opinion.

Section 3

Ensuring the safeguard of public health and patient safety

Art. 17 - In the event of any new event related to the conduct of the investigation that may endanger the safety of the subjects, the sponsor and the investigator are obliged to take appropriate safety measures as a matter of urgency, to protect the subjects from any immediate risk.

Art. 18 - (1) If, during the conduct of the clinical investigation, the NAMMDR has objective reasons to consider that the conditions specified in the authorisation application are no longer met or if it possesses information likely to cast doubt on the safety of the subjects or the scientific correctness of the clinical investigation, it may proceed with the suspension or prohibition of the study in question, informing the sponsor of its decision and the arguments underlying it, presenting the reasons that led to it.

(2) Before taking the decision provided for in paragraph (1), except in cases of imminent risk, the NAMMDR requests the opinion of the sponsor within 7 days.

(3) In the cases referred to in paragraphs (1) and (2), the NAMMDR shall immediately inform the other competent authorities; in the case of multicentre clinical investigations taking place in several countries, the NAMMDR shall also notify the CNBMDM of its decision to suspend or prohibit the investigation, as well as of the reasons underlying it.

Section 4

Procedure for authorising substantial modifications to a clinical investigation

Art. 19 - (1) The sponsor shall submit to the NAMMDR the request for substantial modification to the clinical investigations using the form in Annex 6 to these methodological rules.

(2) The NAMMDR shall assess any substantial modification to the clinical investigation in accordance with the procedure provided for in Articles 10 - 14, which shall be applied accordingly (G&G Errata: accordingly).

Art. 20 - (1) According to the provisions of Art. 75 paragraph (4) of the Regulation, the 38-day period from the sponsor's notification of the substantial modification, provided for in Art. 75 paragraph (3) of the Regulation, is extended by maximum 7 days in cases where the NAMMDR deems it necessary to consult the specialised committees of the Ministry of Health.

(2) The specialised committees respond within maximum 20 days from receiving the NAMMDR request, within the deadlines provided for in Art. 75 of the Regulation, and the lack of a response will be interpreted as a tacit approval.

Section 5

Clinical investigations on medical devices bearing the CE marking

Art. 21 - (1) Until the date on which the electronic system for medical devices (Eudamed), provided for in Art. 73 of the Regulation becomes operational, the notification provided for in Art. 74 paragraph (1) of the Regulation, for which Annex 3 to this Order is used, accompanied by all the documents referred to in Annex XV Section II of the Regulation, shall be sent to the NAMMDR, 30 days before the start of the investigation.

(2) The NAMMDR shall send the sponsor their confirmation of receipt of the notification provided for in paragraph (1), and the sponsor may start the clinical investigation 30 days after receiving the confirmation from the NAMMDR.

Section 6

Other clinical investigations

Art. 22 - (1) All clinical investigations with other types of devices, which are not carried out for any of the purposes listed in Art. 62 paragraph (1) of the Regulation, shall be carried out in compliance with the provisions of Art. 82 paragraph (1) of the Regulation.

(2) For registration of applications and reports of clinical outcomes of the investigations provided for in paragraph (1), the forms provided for in Annexes 1 - 8 to these methodological rules shall be used.

(3) The procedure for assessment and approval of the clinical investigations provided for in paragraph (1) shall be carried out in accordance with the provisions of Articles 11 - 15 of these methodological rules.

(4) In order to protect the rights, safety, dignity and well-being of subjects and the scientific and ethical integrity of clinical investigations provided for in Art. 82 paragraph (1) of the Regulation, depending on the specificity of the type of device and the purpose for which it is used, the NAMMDR defines additional requirements for these clinical investigations by decision of the NAMMDR President.

Art. 23 - For all clinical investigations provided for in Art. 11 - 21 of these methodological rules, the sponsor is obliged to report serious adverse effects, reports established through the authorisations issued by the NAMMDR, as well as vigilance reports, to the NAMMDR, using Annex 8 to these methodological rules.

Section 7

Surveillance

Art. 24 - Inspections for surveillance of the conduct of clinical investigations with medical devices, in compliance with the mechanisms provided for by the provisions of the Regulation and this Order, are carried out by authorised staff within the NAMMDR, with an appropriate frequency, depending on the risk, whenever necessary.

Section 8

Transitional and final provisions

Art. 25 - (1) The authorisations, decisions for rejection and suspensions issued by the NAMMDR provided for in Art.13 paragraph (4), Art. 12 paragraph (14), and Art. 18 paragraph (1) may be appealed by the sponsor to the NAMMDR within 30 days of their receipt.

(2) Within maximum 30 days of registration of the appeal with the NAMMDR, the appeals resolution committee will assemble in session to solve the appeal.

(3) The appeals resolution committee shall be appointed by decision of the NAMMDR President. It shall consist of at least 3 members and a secretary, as well as their deputies, from the NAMMDR, individuals who did not participate in the assessment process of the clinical investigation files subject to the appeals. The head of the appeals resolution committee shall be elected from among its members and shall convene the meetings through the Committee's secretariat.

(4) The convening of the members of the committee referred to in paragraph (3) or their alternates and all correspondence regarding the meeting shall be carried out by electronic mail.

(5) The agenda of the meetings shall be established by the head of the committee referred to in paragraph (3).

(6) The quorum for the assembly of the committee referred to in paragraph (3) shall be achieved by the presence of all members or their alternates, as the case may be, referred to in paragraph (3). In the event that one of the members is unable to attend the meetings, he shall immediately inform the head of the committee in order to convene the alternate to the meeting.

(7) The decisions of the appeals resolution committee shall be taken by open vote, by simple majority and shall be recorded in the minutes of the meeting.

(8) The secretary of the appeals resolution committee shall be responsible for the efficient organisation and conduct of the meetings and shall draw up the minutes.

(9) Based on the decision of the appeals resolution committee, recorded in the minutes provided for in paragraph (7), the decision of the NAMMDR president shall be issued to admit or reject the appeal, which shall be officially communicated to the sponsor, within maximum 7 days from the date of the appeals resolution committee meeting.

(10) If the sponsor does not agree with the decision to reject the appeal, they may further address the competent administrative courts.

Art. 26 - Annexes 1 - 8 are an integral part of these Methodological rules.

Annex 1

to the Methodological rules

Clinical investigation - Assessment report form (for the notified body) for clinical assessment in line with Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EE

Harmonised form - version 1.0

This Annex uses the template approved by the Medical Device Coordination Group (MDCG) of the European Commission (Article 103 of Regulation (EU) 2017/745 (Medical Device Regulation - MDR)). The use of this template is recommended for the notified body to clearly report the documented conclusions of the evaluation of the clinical evidence presented by the manufacturer in the clinical evaluation report (CER), in line with the MDR.

The template is published on the website of the European Commission, DG SANTE on the web page: https://ec.europa.eu/health/sites/default/files/md_sector/docs/md_2020-13-cea-report-template_en.pdf. Subsequent changes to this template will be taken over in updated versions of this form on the NAMMDR website.

List of acronyms

CEAR Clinical Evaluation Assessment Report

CECP Clinical Evaluation Consultation Procedure

CER Clinical Evaluation Report

CIP Clinical Investigation Plan

EUDAMED European Databank on Medical Devices

IFU Instructions for Use

MDR Medical Device Regulation (Regulation (EU) 2017/745 on medical devices)

PMCF Post-Market Clinical Follow-up

PMS Post-Market Surveillance

PSUR Post-Market Surveillance Update Report

SRN Single Registration Number

SSCP Summary of Safety and Clinical Performance

TDAR Technical Documentation Assessment Report

UDI-DI Unique Device Identification Device Identifier

Assessment report form (for the notified body) for clinical assessment (CEAR template) in line with the MDR
Harmonised form version 1.0

Section A: Administrative particulars (notified body, manufacturer, product and clinical evaluation report reference)			
Medical device name model and type: <input type="checkbox"/> Basic UDI-DI(s) (if available): <input type="checkbox"/> Certificate number (if applicable): Project number: Risk class: Applicable code(s) per Commission Implementing Regulation (EU) 2017/2185:	Manufacturer(s) name and SRN: Authorised representative (if applicable) name and SRN:	Notified body (NB): Notified body number: E-mail contact of NB: Telephone contact of NB:	Parts of this template which have been applied General considerations¹⁾ <input type="checkbox"/> Section A: Administrative particulars <input type="checkbox"/> Section B: Reviewers involved <input type="checkbox"/> Section C: Device description, classification, clinical evaluation plan, information materials supplied by the

<p>Type of assessment:</p> <p><input type="checkbox"/> Initial conformity assessment</p> <p><input type="checkbox"/> Assessment of changes ²⁾ and update of the clinical evaluation ³⁾</p> <p><input type="checkbox"/> Re-certification assessment</p> <p><input type="checkbox"/> Assessment of technical documentation for class IIa / IIb devices on a sampling basis</p> <p>According to Annex/ Section: <i>Insert the Annex and Section</i></p>	<p>Intended purpose:</p>	<p>Check of clinical evaluation report authors</p> <p><input type="checkbox"/> CER dated and signed</p> <p><input type="checkbox"/> CVs provided for CER author(s)</p> <p>Comments: <i>Confirm CVs are up to date</i> <i>Confirm CER authors have full range of required expertise represented (e.g. research methods, information management, Regulatory requirements, device technology, diagnosis and management of conditions to be treated)</i></p> <p>CVs considered acceptable: <input type="checkbox"/></p>	<p>manufacturer, common specifications and harmonised standards applied, equivalence and state of the art</p> <p><input type="checkbox"/> Section D: Clinical literature review</p> <p><input type="checkbox"/> Section E: Clinical investigations and related documentation</p> <p><input type="checkbox"/> Section F: PMS and PMCF</p> <p><input type="checkbox"/> Section G: IFU, SSCP, labelling and other information supplied with the device</p> <p><input type="checkbox"/> Section H: Summary of all available data and conclusions</p> <p><input type="checkbox"/> Overall conclusions</p> <p>Specific Considerations</p> <p><input type="checkbox"/> Section I: Clinical evaluation consultation procedure for certain class III and class IIb devices (Article 54 of the MDR)</p> <p><input type="checkbox"/> Section J: Where demonstration of conformity based on clinical data is not deemed appropriate (Article 61(10) of the MDR)</p> <p><input type="checkbox"/> Section K: The voluntary clinical consultation on the clinical development strategy (Article 61(2) of the MDR)</p>
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Technical file identification number and technical documentation assessment report (TDAR) reference if available or any other references that allow the correlation between TDAR and CEAR: Documents assessed:

For example, clinical evaluation report, clinical investigation plan, clinical investigation report, ethics committee approval, Competent Authority approval, post market surveillance data, publications. Include the title, version number/reference and date of the documents. When the CER has been updated verify that this update corresponds to the most recently updated PMS/PMCF reports and any conditions set on the first certification, if applicable. Note that references to the technical documentation should be made in order to ensure document control.

- 1) These must be completed in all cases
- 2) MDR, Annex IX Section 4.10
- 3) For instance: in line with Annex VII Section 4(10) of the MDR

Section B: Reviewers involved in the notified body assessment of the clinical evaluation

Provide the name or the employee code of the personnel with relevant clinical expertise (as per 3.2.4 of annex VII):

Relevant clinical expertise:

Have additional reviewers been involved?

Yes

No

Provide a justification:

Additional reviewers assigned to review the clinical evaluation

Number of additional reviewers Names of additional reviewers: <i>Separate the internal and external clinical reviewers. You may use employee codes</i>	Specific aspects assessed (by each additional reviewer): <i>For example, rationale for the design and chosen statistical methodology of clinical investigation etc.</i>	Competence area / codes: <i>List of relevant MDR codes or area this person is authorised to, according to the Authorisation Matrix, as of Annex VII, 3.3.2)</i> Relevant expertise:

Section C: Section C: Device description, classification, clinical evaluation plan, information materials supplied by the manufacturer, common specifications and harmonised standards applied, equivalence and state of the art

Device description

Describe the device and comment on the intended purpose, including:

- The intended patient population and medical conditions to be diagnosed, treated and/or monitored.*
- A general description of the key functional elements: its parts/components (including software if appropriate), its formulation, its composition, its functionality and, where relevant, its qualitative and quantitative composition.*
- The principles of operation of the device and its mode of action; explanation of any novel features.*

Classification

List the applicable classification rule(s) and indents

Device configurations/variants included in this application:

Include the manufacturers description of the sizes, differences in design features, different configurations etc.

Include an image of the device where possible.

If applicable, include the manufacturers description of the device history and/or changes in the device since its last assessment.

Where relevant, include the manufacturers description of the reason for differences in design variants with illustrative images where possible

Accessories or compatible devices:

Describe any accessories or compatible devices if any or state, “none”.

Include component devices in case of system/procedure pack.

If the use of accessories or compatible devices has an impact on clinical safety or performance or the scope or validity of the clinical evaluation, identify this here.

If it is necessary to understand the usage of the device, include images or other relevant information such as diagrams.

Previous generations of the device and similar devices (if applicable):

Verify that the manufacturer has provided:

- an overview of the previous generation or generations of the device produced by the manufacturer, where such devices exist.*
- an overview of identified similar devices available on the Union or international markets, where such devices exist, including length of time on the market, sales volume etc.*

Non-compliances identified and resolved for this section may be briefly described in this box

Device details, intended purpose and classification are:

Compliant with the applicable requirements of the MDR:

Include any relevant comments

Compliant with the applicable requirements of the MDR with the exception of the minor non-compliance below:

Add a clear description of any remaining minor non-compliance together with required follow-up actions to close them and timelines for their completion to be followed by the manufacturer.

Clinical evaluation plan

Briefly summarise the manufacturer’s clinical evaluation plan and confirm that it meets the requirements of Annex XIV Part A Section 1a, highlighting the areas which require particular attention for this assessment:

- an identification of the general safety and performance requirements that require support from*

relevant clinical data;

- *a specification of the intended purpose of the device;*
- *a clear specification of intended target groups with clear indications and contra-indications;*
- *a detailed description of intended clinical benefits to patients with relevant and specified clinical outcome parameters;*
- *a specification of methods to be used for examination of qualitative and quantitative aspects of clinical safety with clear reference to the determination of residual risks and side effects;*
- *an indicative list and specification of parameters to be used to determine, based on the state of the art in medicine, the acceptability of the benefit-risk ratio for the various indications and for the intended purpose(s) of the device;*
- *an indication how benefit-risk issues relating to specific components such as use of pharmaceutical, non-viable animal or human tissues, are to be addressed; and*
- *a clinical development plan indicating progression from exploratory investigations, such as first-in-man studies, feasibility and pilot studies, to confirmatory investigations, such as pivotal clinical investigations, and a PMCF as referred to in Part B of Annex XIV of MDR, with an indication of milestones and a description of potential acceptance criteria.*

A detailed description of the clinical development plan is not required for the purpose of this template unless there are specific concerns.

Add the manufacturer's reference and version and date of the clinical evaluation plan.

Clinical performance

Summarise the clinical data to demonstrate the ability of the device, resulting from any direct or indirect medical effects which stem from its technical or functional characteristics, including diagnostic characteristics, to achieve its intended purpose as claimed by the manufacturer, thereby leading to a clinical benefit for patients, when used as intended by the manufacturer.

Describe the clinical benefits.

Safety

Does the clinical evaluation adequately address the qualitative and quantitative aspects of clinical safety with clear reference to the determination of residual risks and undesirable side-effects and the confirmation of the relevant safety and performance requirements provided for in Annex I?

Summarise the clinical data regarding safety, and also describe residual risks and any undesirable side-effects.

Does the clinical evaluation specify the methods to be used for examination of qualitative and quantitative aspects of clinical safety with clear reference to the determination of residual risks and undesirable side-effects?

If relevant, briefly summarise any significant complaint, trends or vigilance issues associated with earlier device iterations, which may be equivalent or similar devices, and explain whether or not they have any impact on the clinical evaluation assessment.

Non-compliances identified and resolved for this section may be briefly described in this box

The clinical evaluation plan is:

Compliant with the applicable requirements of the MDR:

Include any relevant comments

Compliant with the applicable requirements of the MDR with the exception of the minor non-compliance below:

Add a clear description of any remaining minor non-compliance together with required follow-up actions to close them and timelines for their completion to be followed by the manufacturer

Common specifications, harmonised standards or other solutions applied

Are there common specifications relevant to the device under evaluation?

Have they been complied with?

If not:⁴⁾

- Explain any deviations and how these might affect the validity of the clinical evaluation and its conclusions, and any equivalence claims.*
- Confirm that the manufacturer has adopted solutions that ensure a level of safety and performance that is at least equivalent thereto in accordance with Article 9(3).*

Are there harmonised standards relevant to the clinical evaluation of the device under evaluation?

Have they been applied?

⁴⁾ Excluding devices listed in Annex XVI which must comply with the relevant common specifications in accordance with Article 9(4).

If partially applied add the manufacturers justification and confirm that the manufacturer has adopted solutions that ensure a level of safety and performance required by the Regulation (EU) 2017/745.

If there are deviations explain any deviations and how these might affect the validity of the clinical evaluation and its conclusions, and any equivalence claims.

Is the most up-to-date revision being used by the manufacturer? (state which revision was used)

Are there other solutions that have been applied?

Describe any standards, guidance or other solutions that have been applied, and the manufacturers justification

Non-compliances identified and resolved for this section may be briefly described in this box

The application of CS, harmonised standards or other solutions is:

Compliant with the applicable requirements of the MDR:

Include any relevant comments

Compliant with the applicable requirements of the MDR with the exception of the minor non-compliance below:

Add a clear description of any remaining minor non-compliance together with required follow-up actions to close them and timelines for their completion to be followed by the manufacturer.

The demonstration of equivalence

Is the clinical evaluation based upon clinical investigation(s) or other studies reported in scientific literature, of a device for which equivalence to the device in question can be demonstrated?

State Yes / No

Device(s) to which equivalence has been claimed:

Is the clinical evaluation based upon reports published in peer reviewed scientific literature on a device for which equivalence to the device in question can be demonstrated?

State Yes / No

If yes, specify the source(s) of the data, if it is the device in question, or an equivalent device, or both.

Device(s) to which equivalence has been claimed:

Device which is most relevant:

Assessment of equivalence:

1. Equivalence rationales:

Indicate which devices are/are not equivalent, and confirm that data relating to devices which are not equivalent have been excluded from the analysis of clinical data for the purposes for demonstrating safety and performance.

If equivalence has been claimed to more than one device, each demonstration of equivalence can only be based on a single device. Each equivalent device must meet all three equivalence criteria (clinical, technical, biological).

2. Are the devices equivalent in accordance with Section 3 of Annex XIV including technical, biological and clinical characteristics?

State Yes / No

Identify any differences in these parameters, and verify why these are not expected to adversely affect the safety and performance of the medical device under evaluation.

Non-compliances identified and resolved for this section may be briefly described in this box

The demonstration of equivalence is:

Compliant with the applicable requirements of the MDR:

Include any relevant comments

Compliant with the applicable requirements of the MDR with the exception of the minor non-compliance below:

Add a clear description of any remaining minor non-compliance together with required follow-up actions to close them and timelines for their completion to be followed by the manufacturer.

Access to data

Comment on the manufacturer's access to data, relating to devices with which they are claiming equivalence in order to justify their claims of equivalence.

For implantable and Class III devices, if equivalence is claimed with a device marketed by another manufacturer, confirm that there is a current valid contract between the two manufacturers allowing ongoing access to the technical documentation in accordance with Article 61 (5) of the MDR.

Has the original clinical evaluation been performed in compliance with the requirements of Regulation 2017/745, and has the manufacturer of the second device provided clear evidence thereof?

State Yes / No

Confirm that access to data is sufficient to provide the manufacturer with enough information about the equivalent devices to support equivalence claims, including any testing which may have been undertaken to confirm equivalence of specifications/performance/etc.

Any other limitations with respect to equivalent devices:

Comment on any other limitations with respect to the equivalent devices or manufacturer's equivalence claims, and the extent to which these limitations impact the manufacturer's clinical evaluation and conclusions.

Non-compliances identified and resolved for this section may be briefly described in this box

Manufacturer demonstration of equivalence and access to data is:

Compliant with the applicable requirements of the MDR:

Include any relevant comments

Compliant with the applicable requirements of the MDR with the exception of the minor non-compliance below:

Add a clear description of any remaining minor non-compliance together with required follow-up actions to close them and timelines for their completion to be followed by the manufacturer.

State of the art

Benchmark devices, state of the art and other available treatment options:

Describe the alternative available treatment options identified by the manufacturer which could offer comparable safety and performance for the same treatment indications / patient populations, etc. Briefly describe how benchmarks for safety and performance have been identified by the manufacturer in terms of the state of the art. Benchmarks will normally be based on aggregate data from several devices considered to have acceptable performance (e.g. systematic reviews or registry analysis); if individual devices are selected as benchmarks for safety and performance, a suitable rationale should be provided.

<p><i>Confirm that the manufacturer's description of the state of the art is based upon an appropriate literature search (see section D)?</i></p> <p><i>For devices previously marketed, is the description of the state of the art still accurate? Can the device still be considered to be state of the art?</i></p> <p>Safety, performance and benefit-risk claims - requirements in terms of the state of the art:</p>
<p><i>What performance and safety endpoints has the manufacturer identified?</i></p> <p><i>In light of the outcomes achievable with benchmark products and other treatment options, are these endpoints appropriate and clinically relevant? Have surrogate endpoints been adequately justified?</i></p> <p>Has the manufacturer adequately described an indicative list and specification of parameters used to determine, based on the state of the art in medicine, the acceptability of the benefit-risk ratio for the various indications and for the intended purpose or purposes of the device?</p>
<p>Non-compliances identified and resolved for this section may be briefly described in this box</p>
<p>Manufacturer demonstration of state of the art is:</p> <p>Compliant with the applicable requirements of the MDR: <input type="checkbox"/></p> <p><i>Include any relevant comments</i></p> <p>Compliant with the applicable requirements of the MDR with the exception of the minor non-compliance below: <input type="checkbox"/></p> <p><i>Add a clear description of any remaining minor non-compliance together with required follow-up actions to close them and timelines for their completion to be followed by the manufacturer</i></p>
<p>Novelty</p>
<p>Include the manufacturer's explanation of any novel features of the device and/or the related clinical procedures and their purpose.</p> <p>What is the possible clinical or health impact in terms of benefit/risk?</p>
<p>Is novelty adequately addressed? <input type="checkbox"/></p>

<p>Section D: Clinical literature review</p>
<p>With respect to the search criteria of the literature review, does it:</p> <p><input type="checkbox"/> Address all device sizes, variants, model and accessories?</p> <p><input type="checkbox"/> Address the same clinical condition?</p> <p><i>Further information regarding literature search methods is available in MEDDEV 2.7/1 revision 4, section A5. Searches for the device in question, equivalent devices and other devices (for example to support a description of the state of the art) should be described separately.</i></p> <p>With respect to the selection criteria of the literature review, does it relate to both below:</p> <p><input type="checkbox"/> The device under evaluation or to a device demonstrated to be equivalent?</p> <p><input type="checkbox"/> The state of the art or alternative available treatment option?</p>
<p>The clinical evaluation should clearly describe the selection criteria with respect to the Regulatory purpose to which it will apply. The CER should clearly differentiate between the two types of data referenced above. If the data does not relate to either of the above, provide a rationale with respect to its inclusion.</p>

Literature search protocol 5)

5) For general guidance on a literature search, see MEDDEV 2.7/1 revision 4, A5. Literature search and literature review protocol, key elements.

Provide a brief summary of the literature search strategy applied, commenting on:

- *The adequacy of search terms: for example, it should be sufficiently broad to establish benchmarks, determine the general state of the art, determine potential risk, adverse events, undesirable side-effects, etc.*

Note that a search which is restricted to the manufacturer's own product or the name of their chosen equivalent could miss important information and therefore is not acceptable.

- *Databases used (to minimize bias multiple databases should be used).*
- *Acceptability of inclusion and exclusion criteria.*
- *Both favourable and unfavourable data included.*
- *Strategies for avoiding duplication of data (for example, across different publications or between manufacturer and published data).*
- *Literature search and review protocol (i.e. how did the manufacturer test this protocol to ensure comprehensive identification of relevant data / demonstrate that all relevant data has been retrieved?).*
- *Any deviations from the manufacturer's literature search protocol.*
- *Overall conclusions regarding the adequacy of search methods, likelihood of having retrieved all relevant data, and methods used to avoid bias.*

Comment if systematic search and review methods such as the following have been used:

- *PICO (patient characteristics, type of intervention, control, and outcome queries).*
- *Cochrane Handbook for Systematic Reviews of Interventions.*
- *PRISMA (The Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement.*
- *MOOSE Proposal (Meta-analysis Of Observational Studies in Epidemiology)*
- *Other (specify or describe).*

Literature search documentation:

- Literature search protocol provided
- Literature search reports provided
- Full list of retrieved articles provided
- Full list of excluded articles provided, with reasons for exclusion
- Full text copies of relevant documents available

Comments:

Provide rationale if any of the above has not been provided.

Nota bene:

- *A literature search and other retrieval of data should be carried out based on a search protocol. The search protocol should document the planning of the search before execution.*
- *Once the searches have been executed, the adequacy of the searches should be verified and a literature search report should be compiled to present details of the execution, any deviations from the literature search protocol, and the results of the search.*
- *It is important that the literature search is documented to such degree that the methods can be appraised critically, the results can be verified, and the search reproduced if necessary.*

- *Abstracts lack sufficient detail to allow issues to be evaluated thoroughly and independently, but may be sufficient to allow a first evaluation of the relevance of a paper. Copies of the full text papers and documents should be obtained for the appraisal stage.*
- *The literature search protocol(s), the literature search report(s), and full text copies of relevant documents using URL links, become part of the clinical evidence and, in turn, the technical documentation for the medical device.*

Non-compliances identified and resolved for this section may be briefly described in this box

Literature search protocol and outputs are: Compliant with the applicable requirements of the MDR:

Include any relevant comments

Compliant with the applicable requirements of the MDR with the exception of the minor non-compliance below:

Add a clear description of any remaining minor non-compliance together with required follow-up actions to close them and timelines for their completion to be followed by the manufacturer

Data appraisal:

Provide a brief summary of the manufacturer’s data appraisal methods (i.e. how they determine whether the data from a given study or other source of data is of sufficient quality and relevance to be included in the clinical evaluation. This includes evaluation of criteria including study design, sources of bias, peer review, relevance to subject device, etc. Retrieved studies and data sets should be weighted on the basis of scientific quality and relevance to the scope and objectives of the clinical evaluation for the subject devices).

Justify the acceptability of the appraisal in terms of:

- *Methodological quality and scientific validity of articles retrieved and evaluated appropriately.*
- *Relevance of the information to the clinical evaluation determined and documented.*
- *Contribution of each data set to the clinical evaluation weighted according to systematic criteria.*

Non-compliances identified and resolved for this section may be briefly described in this box

Data appraisal is:

Compliant with the applicable requirements of the MDR:

Include any relevant comments

Compliant with the applicable requirements of the MDR with the exception of the minor non-compliance below:

Add a clear description of any remaining minor non-compliance together with required follow-up actions to close them and timelines for their completion to be followed by the

Section E: Clinical investigations and related documentation

Has the manufacturer conducted clinical investigation(s)?

State Yes / No

Has the manufacturer conducted pre-market or post-market clinical investigations?

Provide detail

If the manufacturer has not conducted clinical investigation:

What is the rationale?

Why is this acceptable / unacceptable?

Has the manufacturer provided a copy of all clinical investigation reports?

State Yes / No

Were all clinical investigations publicly registered?

State Yes / No

Has it been verified that clinical investigations conducted with respect to the MDR were publicly registered on EUDAMED?

State Yes / No

Provide the EUDAMED single registration number where available.

Did the clinical investigations result in a publication in a scientific journal?

State Yes / No

If yes, does the clinical investigation report reflect the results of clinical investigation(s) or other studies reported in scientific literature, or reports published in peer reviewed scientific literature on other clinical experience? If there are any differences describe these and summarise the rationale provided by the manufacturer.

Has the manufacturer provided all Competent/Regulatory Authority correspondence (from all countries, including non-EU ones)

State Yes / No

Are the conclusions drawn by the manufacturer, based upon the results of the clinical investigation, valid in the light of the approved clinical investigation plan?

Provide detail

If clinical investigations not performed under the MDR were not publicly registered or published:

- Confirm that a rationale was provided.
- Confirm that the SSCP and where relevant the IFU (for example with respect to the description of clinical benefits) adequately provide information for the intended user and if relevant, the patient.

Clinical Investigation Plan (CIP) reference

CIP complies with the MDR, Annex XV, and EN ISO 14155 Annex A
State Yes / No

CIP scope and study design

Adequacy of CIP scope and study design for demonstration of safety, performance and benefit risk of subject devices:

- Study design.
- Devices identified.
- Patient population.
- Patient numbers.
- Objectives and endpoints.
- Length of follow up and intervals.
- Study locations.
- Overall conclusions.

Non-compliances identified and resolved for this section may be briefly described in this box

Manufacturer clinical investigations and related documentation are:

Compliant with the applicable requirements of the MDR:

Include any relevant comments

Compliant with the applicable requirements of the MDR with the exception of the minor non-compliance below:

Add a clear description of any remaining minor non-compliance together with required follow-up actions to close them and timelines for their completion to be followed by the manufacturer

Section F: PMS, PMCF and the plan for updates

Documents reviewed, where relevant:

- PMS Plan
- PMS Report (where relevant)
- PMCF Plan
- PMCF Report (where relevant)
- PSUR (if available)

Include references to the above documents.

The demonstration of equivalence and the link to post-market clinical follow-up

Describe how the manufacturer will verify the presumption that there would be no clinically significant difference in the safety and clinical performance of the device under evaluation compared with the equivalent device by post market surveillance or post market clinical follow-up?

Is there a post-market clinical follow-up planned?

State Yes / No

Is this an implantable or class III device for which clinical investigations have not been performed in accordance with Article 61(4)?

State Yes / No

For these devices the PMCF plan should include post market clinical studies to demonstrate the safety and performance of the device.

Comments on appropriateness of the PMS/PMCF Plan:

If no PMCF is planned, has the manufacturer provided an acceptable justification for not conducting a PMCF?

State Yes / No

Clinical evaluation updates:

Identify when updates to the clinical evaluation report shall be assessed during the surveillance and post certification monitoring activities and which frequency should be considered.

Provide further detail taking into account the manufacturer's PMCF plan and the post-market surveillance plan.

Non-compliances identified and resolved for this section may be briefly described in this box

The PMS, PMCF and the plan for updates are:

Compliant with the applicable requirements of the MDR:

Include any relevant comments

Compliant with the applicable requirements of the MDR with the exception of the minor non-compliance below:

Add a clear description of any remaining minor non-compliance together with required follow-up actions to close them and timelines for their completion to be followed by the manufacturer

Section G: IFU, SSCP, labelling and other information supplied with the device

Information materials supplied by the manufacturer and the instructions for use:

Describe what has been reviewed – IFU, promotional materials (if available), SSCP, labelling etc. In case several documents have been assessed, identify answers to the questions below for each of the documents.⁶⁾

Intended purpose:

Does the clinical evidence support this?

Intended patient population:

Who is the intended patient population?

Does the clinical evidence support this?

Are all the appropriate/relevant restrictions, warnings or contraindications in place?

Intended users:

Is the device to be used by healthcare professionals or lay users? Does the IFU provide all the appropriate/relevant information for the intended user?

Has the manufacturer taken into account the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users).

Is any training for users required as a risk control measure? If not, is this justified with respect to the risk management file and the clinical evaluation?

Limitations:

Has the manufacturer adequately/clearly described any limitations for the device use?

Does the device require any specific limitations?

Contraindications:

Have contraindications been adequately/clearly described?

Are any further contraindications necessary?

Warnings and precautions:

Have warnings, precautions and/or measures to be taken in the event of malfunction of the device or changes in its performance that may affect safety been adequately described?

Does the information supplied by the manufacturer adequately/clearly provide the safety and performance information relevant to the user, or any other person, as appropriate/relevant?

Is the estimation of associated risks and residual risk adequate? Is this estimation quantitative (i.e. a percentage rate or rate with a confidence interval) or qualitative? Is the description appropriate for patients and users?

Is the information provided to the end user written in a clear and understandable way (instructions of use, indications, and warnings)?

Is the IFU and other information materials supplied by the manufacturer aligned with the other parts of the technical documentation?

Consider:

- *the clinical evaluation (the device description used for the clinical evaluation, other contents of the clinical evaluation report).*
- *the available clinical data (such as the public registration and results of clinical investigations, publications, PMCF studies, etc.).*
- *PMS report or PSUR.*
- *the risk management file.*

Non-compliances identified and resolved for this section may be briefly described in this box

IFU, promotional materials, labelling are:

Compliant with the applicable requirements of the MDR:

Include any relevant comments

Compliant with the applicable requirements of the MDR with the exception of the minor non-compliance below:

Add a clear description of any remaining minor non-compliance together with required follow-up actions to close them and timelines for their completion to be followed by the manufacturer.

6) Note that the SSCP requires a separate validation report.

Section H: Summary of all available data and conclusions

Has the manufacturer conducted clinical investigation(s) for the device under evaluation?

State Yes / No

Has the manufacturer demonstrated equivalence with respect to section 3 of Annex XIV of the MDR?

State Yes / No

If the manufacturer conducted CIs, does clinical data from clinical investigations of the device under evaluation adequately demonstrate compliance with the relevant general safety and performance requirements?

State Yes / No

Has the reliability of the source of clinical investigation data been assured through monitoring activities and verification of the application of appropriate clinical research standards?

State Yes / No

If the manufacturer demonstrated equivalence with respect to section 3 of Annex XIV of the MDR does the data from an equivalent device demonstrate compliance with Annex I?

State Yes / No

Provide a summary of safety data (with reference to the relevant section of the CER). Provide a summary of performance data (with reference to the relevant section of the CER)

Does the clinical data provide sufficient clinical evidence to:⁷⁾

- *Demonstrate compliance with the relevant general safety and performance requirements?*

State Yes / No and provide additional information if relevant

- *Support the intended purpose, the claims and the information in the IFU and SSCP?*

State Yes / No and provide additional information if relevant

What are the remaining unanswered questions regarding the device under evaluation?

Describe these with respect to the plan for PMS / PMCF

⁷⁾ For legacy products (legacy devices), see MDCG 2020-6

Overall conclusions:

Benefit-risk conclusions:

Summarise the clinical benefits. Describe them briefly in relation to the meaningful and measurable patient relevant clinical outcomes, including outcome(s) related to diagnosis. Describe their positive impact on patient management or public health.

Summarise the risks with clinical relevance (e.g. uncertainties or limitations of clinical data, undesirable side-effects, potential for misuse, etc) and provide a short description (e.g. incidence, severity, duration, vulnerable patient subgroups, dose-response relationship where relevant, etc).

Discuss the impact of risks (as described above) in relation to the clinical benefits taking into account the factors described and in particular the uncertainties in relation to available clinical data.

Have all the risks that could have a significant impact on the benefit-risk analysis' been identified in the clinical evaluation?

Is there alignment between the risk management and clinical evaluation?

State Yes / No

Describe how the clinical benefits outweigh the risks also considering the current state of the art.

Have all deficiencies/non-compliances been raised and satisfactorily addressed in the course of this clinical evaluation assessment?

State Yes / No

Is it possible to follow the changes that have been made to address them?

Overall conclusion on the assessment of the manufacturer's clinical evaluation including a clinical judgement of the opinion provided by any external expert.

Make a clear recommendation to the notified body's decision maker in regards to the conclusions of this assessment for the purpose of granting certification, stating in addition:

- whether the post-market surveillance plan, including the PMCF plan, is adequate.*
- specific milestones to be set for further review of the up-to-date clinical evaluation by the notified body.*
- considerations to define the period of certification.*
- additional conditions on the certification to be considered.*

Sufficient information is provided to demonstrate acceptability of benefit-risk conclusions and confirm that the relevant MDR requirements are met:

Specific considerations

Section I: Clinical evaluation consultation procedure for certain class III and class IIb devices (Article 54 of the MDR)

Is the procedure required by Article 54(1) of the MDR to be applied?

State Yes / No

Provide further information where necessary with respect to this justification

If this procedure is not to be applied, with respect to Article 54(2) of the MDR, what is the reason?⁸⁾

- (a) renewal of a certificate issued under the MDR;
- (b) the device has been designed by modifying a device already marketed by the same manufacturer for the same intended purpose, and the manufacturer has demonstrated to the satisfaction of the notified body that the modifications do not adversely affect the benefit-risk ratio of the device;

Provide a summary of the modification(s) that have been made to the device.

Provide a summary of the manufacturer's rationale demonstrating that the benefit-risk ratio of the device is not adversely affected.

Has the clinical data been provided to support the conclusions of the manufacturer regarding the benefit-risk of the modified device with respect to the previous version?

For legacy devices, verify:

- that the modifications do not adversely affect the benefit-risk ratio.
- that the device in question had a valid certificate under the Directives.
- in case the certificate has been withdrawn, suspended²⁵ or expired, if there is an impact on compliance with the general safety and performance requirements, and
- that there is no pending assessment of changes for the device or outstanding non-compliance.
- the description of modifications provided and assess if these modifications are limited only to those needed in order to comply with the new legal requirements introduced by the MDR.

Note: limitations of the intended purpose of the device should not trigger the consultation procedure in accordance to Art. 54 of the MDR.

(c) the principles of the clinical evaluation of the device type or category have been addressed in a CS referred to in Article 9 and the notified body confirms that the clinical evaluation of the manufacturer for this device is in compliance with the relevant CS for clinical evaluation of that kind of device.

Relevant scientific panel and associated competence area(s)

Indicate your opinion on the relevant scientific and associated competence area(s) for the device under assessment:

8) See MDCG 2019-3, Interpretation of Article 54(2)b

9) The devices for which the certificates were withdrawn or suspended due to lack of compliance with essential requirements will require a clinical evaluation consultation procedure as this adversely affects the benefit-risk ratio of the device.

Medical area(s)	Associated competence-related areas
<input type="checkbox"/> Orthopaedics, traumatology, rehabilitation, rheumatology	<input type="checkbox"/> Joint replacements (hip, knee, shoulder)
	<input type="checkbox"/> Spinal devices
	<input type="checkbox"/> Non-articulating devices, rehabilitation
	<input type="checkbox"/> Other
<input type="checkbox"/> Circulatory system: cardiovascular / lymphatic system	<input type="checkbox"/> Prosthetic heart valves and devices for heart valve repair
	<input type="checkbox"/> Cardiovascular stents (metallic and bioresorbable) and vascular prostheses
	<input type="checkbox"/> Active implantable cardiac devices and electrophysiological devices
	<input type="checkbox"/> Structural interventions and new devices (e.g. LAA/PFO occluders, heart failure devices)
	<input type="checkbox"/> Cardiac surgery including extracorporeal membrane oxygenation, cardiopulmonary bypass devices, artificial hearts (and left ventricular assist devices)
	<input type="checkbox"/> Other

<input type="checkbox"/>	Respiratory, anaesthesiology, intensive care	<input type="checkbox"/>	Central and peripheral nervous system devices
<input type="checkbox"/>	Neurology	<input type="checkbox"/>	Implants for hearing and vision (sensory recovery)
<input type="checkbox"/>		<input type="checkbox"/>	Neurosurgical devices
<input type="checkbox"/>		<input type="checkbox"/>	<i>Other</i>
<input type="checkbox"/>	Endocrinology and diabetes	<input type="checkbox"/>	Endocrinology and diabetes (e.g. insulin delivery systems and closed-loop systems, continuous glucose monitoring)
<input type="checkbox"/>		<input type="checkbox"/>	Implantable systems
<input type="checkbox"/>	General and plastic surgery, dentistry	<input type="checkbox"/>	Surgical implants and general surgery
<input type="checkbox"/>		<input type="checkbox"/>	Plastic surgery and wound care
<input type="checkbox"/>		<input type="checkbox"/>	Maxillofacial surgery
<input type="checkbox"/>		<input type="checkbox"/>	Dentistry (devices for dentistry (oral surgery, implantology, dental materials incl.))
<input type="checkbox"/>		<input type="checkbox"/>	<i>Other</i>
<input type="checkbox"/>	Obstetrics & gynaecology including reproductive medicine	<input type="checkbox"/>	Devices for obstetrics and gynaecology
<input type="checkbox"/>	Gastroenterology & hepatology	<input type="checkbox"/>	Devices for gastroenterology and hepatology
<input type="checkbox"/>	Nephrology & urology	<input type="checkbox"/>	Devices for nephrology and urology
<input type="checkbox"/>	Ophthalmology	<input type="checkbox"/>	Devices for ophthalmology

Provide further information necessary with respect to this justification

Conclusion for certain class III and IIb devices to be considered by the expert panel

Novel aspects

See Section C, subsection "Novelty"

Benefit-risk determination

See Section H și Section de Overall conclusions

Consistency of clinical evidence with intended purpose and PMCF

Provide an assessment of the consistency of the clinical evidence with:

(a) the intended purpose, including medical indication(s),

(b) the post-market clinical follow-up (PMCF) plan.

Section J: Where demonstration of conformity based on clinical data is not deemed appropriate (Article 61(10) of the MDR)

Has the manufacturer claimed that the demonstration of conformity with general safety and performance requirements based on clinical data is not deemed appropriate in accordance with Article 61(10) of the MDR?

State Yes / No

Nota bene: A clinical evaluation is still required and the above information and evidence-based justification shall be presented in the clinical evaluation report.

Has the manufacturer provided a justification for reliance upon Article 61(10) of the MDR?

State Yes / No

If **yes**, describe the evidence which the manufacturer is relying on, with respect to:

- Performance evaluation
- Bench testing
- Pre-clinical evaluation

Consider:

Has any available clinical data for the device or an equivalent device been searched for and/or identified by the manufacturer?

If yes – was the identified clinical data integrated in the clinical evaluation. This should include an evaluation of clinical data identified from the literature, and an appraisal of their relevance to the device under evaluation.

- Is clinical data available for similar devices, does this provide information with relevant to the safety and performance of the device under evaluation?

Has the manufacturer conducted an appropriate search of scientific literature? If clinical data for similar devices is available – this should be included in the CER and evaluated and may be of particular relevance to post-market surveillance / PMCF planning.

- The results of the manufacturer's risk management

Are the results of the manufacturer's risk management supportive of the use of non-clinical testing methods?

- Consideration of the specifics of the interaction between the device and the human body

Is the device under assessment part of a system or stand-alone? Is there sufficient information regarding this interaction available from sources other than clinical data?

- The clinical performance intended

What is the intended performance? Is it reasonable to rely upon non-clinical data for the proposed intended performance?

- The claims of the manufacturer

The manufacturer should not make any claims which are not supported by clinical data.

Overall conclusions

Non-compliances identified and resolved for this section may be briefly described in this box

The justification of the manufacturer for reliance upon Article 61(10) of the MDR is:

Compliant with the applicable requirements of the MDR:

Include any relevant comments

Compliant with the applicable requirements of the MDR with the exception of the minor non-compliance below:

Add a clear description of any remaining minor non-compliance together with required follow-up actions to close them and timelines for their completion to be followed by the manufacturer

Section K: The voluntary clinical consultation on the clinical development strategy (Article 61(2) of the MDR)

Expert Panel consultation reference:

Expert Panel recommendations:

Have the views of the expert panel been given due consideration by the manufacturer? Has this been included in the clinical evaluation report? Is there any divergence between the manufacturer's clinical development strategy and the views of the expert panel? If yes – what is the justification for this? Is this acceptable? Explain why.

Annex 2
to the Methodological rules

Post-market clinical follow-up (PMCF) form

Harmonised form, version 1.0

The post-market clinical up (PMCF) form copies the template approved by the Medical Device Coordination Group -MDCG from Article 103 of Regulation (EU) 2017/745) available on the website of the European Commission, DG SANTE: https://ec.europa.eu/health/sites/default/files/md_sector/docs/md_mdcg_2020_8_guidance_pmc_f_evaluation_en.pdf.

Subsequent changes to this template will be taken over by updated versions of this form on the NAMMDR website.

Text in italics represents general information, which is recommended to be included in the post-market clinical follow-up plan.

Post-market clinical follow- up (PMCF) plan corresponding to the present evaluation report
PMCF plan number and version:

Post-market clinical follow- up (PMCF) Evaluation Report			
PMCF report number:			
PMCF report date:			
PMCF report version:			
Revision history			
Rev	Revision date	Description of change	Revised by

Section A. Manufacturer contact details
Legal manufacturer name:
Address:
SRN:
Person responsible for Regulatory compliance:
E-mail:
Phone:
Fax:
Authorised representative (if applicable):
Address:

Contact person:
E-mail:
Phone:
Fax:

Section B. Medical Device description and specification
Refer to section B from PMCF plan, if there are no changes. If there are changes from PMCF plan, please fill in the different requested fields highlighting those changes.
Product or trade name:
Model and type:
General description of the device:
Intended purpose ¹⁾ :
Intended users
Basic UDI-DI:
Intended patient population:
Medical condition(s) ²⁾ :
Indications:
Contraindications:
Warnings:
List and description of any variants and/or configurations covered by this plan:
List of any accessories covered by this plan:
Certificate number (if available):
CND code(s) ³⁾ :
Class:
Classification rule:
Expected lifetime: ⁴⁾
Novel product: <input type="checkbox"/> yes <input type="checkbox"/> no
Novel related clinical procedure: <input type="checkbox"/> yes <input type="checkbox"/> no
Explanation of any novel features:

1) Intended purpose means the use for which a device is intended according to the data supplied by the manufacturer on the label in the instructions for use or in promotional or sales materials or statements and as specified by the manufacturer in the clinical evaluation (MDR, Article 2(12)).

2) It refers to the clinical condition that is to be diagnosed, prevented, monitored, treated, alleviated, compensated for, replaced, modified or controlled by the medical device.

3) The CND code is the code assigned in the "National Classification of Medical Devices"

4) The expected lifetime is to be defined during the design input phase by considering the current state of the art for a specific intended use and indication of a device.

Section C. Activities undertaken related to PMCF: results

In this section the manufacturer shall report all the activities described in section C of the PMCF plan which have been performed, all the collected clinical data obtained from those completed activities, as well as any justification of deviations from the plan.

The discussion shall include the analysis of the findings, whether positive or negative and also the potential impact on the different documents (clinical evaluation report, risk management file, SSCP, etc...) initially reviewed during the conformity assessment.

It is expected for each activity performed, a description in different subsections, related to the type of activities (device registry, PMCF studies, real world evidence, surveys about the use of device, etc...), and for each subsection, a description about the quality of data collected.⁵⁾

⁵⁾ For the analysis and assessment of the clinical data collected, some parts of section 9.3.1 from Meddev 2.7/1 rev.4 could be used to assess the quality of data.

Section D. Evaluation of clinical data relating to equivalent or similar devices

In this section the manufacturer shall report all the clinical data collected relating to an equivalent device or selected similar device(s), provide an analysis and conclusions, and whether changes of the state of the art, or newly identified hazards would have an impact on the devices benefit-risk determination, the clinical evaluation and/or the PMCF plan.

Product name of equivalent / similar device	Results discussed	References used to get the results (publications, part of technical documentation from this equivalent / similar device)

Section E. Impact of the results on the technical documentation

Analysis outcome to be reported in the risk management file updated:

-
-

Section F.

Reference to any common specification(s), harmonized standard(s) or guidance document(s) applied

In this section the manufacturer should point out whether the collected clinical data related the device in question still confirm adherence to applied common specifications and/or applied harmonized standards, and/or guidances listed in the PMCF plan.

Common Specification(s) applied

(Title, date and version)

Harmonised standard(s) applied

(Title, date and version)

Guidance(s) followed

(Title, date and version)

Section G. Conclusions

In this section, it is expected that the manufacturer shall provide an overall conclusion of the findings and relate them to the aims of the PMCF plan. The conclusions shall be taken into account in the following clinical evaluation and in the risk management. Finally, this conclusion shall highlight if any need for preventive and/or corrective measures has been identified. The conclusion may also give input to the next PMCF plan.

Annex 3

to the Methodological rules

Registration/notification application form for the authorisation/validation of a clinical investigation according to the MDR Harmonised form version 1.0

Section 1: Identification of the clinical investigation

Identification of the sponsor

Name:			
Address	Street name:		Number:
	Postal code:		City:
	Country:		
Telephone number:			
Email:			

Sponsor's contact person

First name:
Last name:
Telephone number:
Email:

Identification of the sponsor's authorised representative

Do you have an authorised representative?	
Yes	No
<input type="radio"/>	<input type="radio"/>
If yes, fill in the information regarding the authorised representative (Section 1.2)	

1.1. Identification of the authorised representative

Name:			
Address	Street name:		Number:
	Postal code:		City:
	Country:		
Telephone number:			
Email:			

Contact person of the authorised representative

First name:
Last name:
Telephone number:
Email:

Contact person for the clinical investigation

<input type="radio"/> Same contact person as the sponsor's <input type="radio"/> Same contact person as the authorised representative's <input type="radio"/> Other If you have selected "Other", please fill in the Section below with information regarding another contact person for this clinical investigation.
--

Other contact person for the clinical investigation

First name:			
Last name:			
Address	Street name:		Number:
	Postal code:		City:
	Country:		

1.2. Type of clinical investigation

Select the appropriate legislation for the application: <input type="radio"/> Clinical investigation request (Art. 62 paragraph (1) of the MDR) <input type="radio"/> PMCF investigation notification (Art. 74 paragraph (1) of the MDR) <input type="radio"/> Other Clinical investigation application/notification - national application (Art. 82 paragraph (1) of the MDR)

1.3. Registration type

<input type="radio"/> First registration in the EEA <input type="radio"/> First national registration (clinical investigation has already been registered in the EEA) In this case, please fill in the ID (CIV - ID) assigned to the clinical investigation

O

Re-registration

Please fill in the CIV-ID, if already available.

1.4. Countries belonging to the EU/EEA/UK (Northern Ireland), Turkey and Switzerland

Please indicate the countries participating in the clinical investigation:

1.5. Participating countries outside the EU/EEA/UK

If this study is part of a clinical investigation conducted at multiple sites outside the EU/EEA/UK, please provide a list of all countries outside the EU/EEA where the study shall be conducted, as planned.

1.6. Clinical investigation plan (CIP)

CIP code:	<input type="text"/>
CIP version:	<input type="text"/>
CIP date:	<input type="text"/>

1.7. Title of the clinical investigation

Full title:	<input type="text"/>
Short title:	<input type="text"/>
Title for lay persons:	<input type="text"/>

Section 2: Description of the clinical investigation

2.1. Scientific opinion

Has the manufacturer consulted with an expert as outlined in Art. 61(2) of the MDR?	
Yes	No
<input type="radio"/>	<input type="radio"/>

2.2. Design of the clinical investigation

<input type="radio"/> Exploratory investigation	<input type="radio"/> Confirmatory investigation
<input type="radio"/> Observational investigation	
<input type="radio"/> First in human investigation	<input type="radio"/> Not first in human

2.3. Design methodology

<input type="checkbox"/> Case control	<input type="checkbox"/> Controlled	<input type="checkbox"/> Cross-sectional	<input type="checkbox"/> Double blind
<input type="checkbox"/> Parallel	<input type="checkbox"/> Randomized	<input type="checkbox"/> Open	
<input type="checkbox"/> Other			

2.4. Development stage

<input type="radio"/> Pilot stage	<input type="radio"/> Pivotal stage	<input type="radio"/> Post-market stage
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2.5. Objectives and endpoints

Primary objective(s):
Secondary objective(s):
Other objective(s):
Primary endpoint(s):
Secondary endpoint(s):
Other endpoint(s):

2.6. Clinical investigation outcomes

Overall synopsis:

2.7. Planned number of subjects

In Europe	<input type="text"/>
In Asia:	<input type="text"/>
In Africa:	<input type="text"/>
In North America:	<input type="text"/>
In South America:	<input type="text"/>
In Oceania:	<input type="text"/>

Total planned number of subjects:

2.8. Duration of clinical investigation

Estimated start date:	<input type="text"/>
Estimated end date:	<input type="text"/>

2.9. Population

2.9.1. Medical condition

Is there an associated medical condition?	
<input type="radio"/> Yes	<input type="radio"/> No
Is the medical condition considered to be rare?	
<input type="radio"/> Yes	<input type="radio"/> No

2.9.2. Therapeutic area

<input type="checkbox"/>	Circulatory system: cardiovascular/lymphatic
<input type="checkbox"/>	Endocrinology and diabetes
<input type="checkbox"/>	Gastroenterology & hepatology
<input type="checkbox"/>	General and plastic surgery, dentistry
<input type="checkbox"/>	Nephrology & urology
<input type="checkbox"/>	Neurology
<input type="checkbox"/>	Ophthalmology
<input type="checkbox"/>	Obstetrics and gynaecology, including reproductive
<input type="checkbox"/>	Orthopaedics, traumatology & rehabilitation
<input type="checkbox"/>	Other
<input type="checkbox"/>	Respiratory, anaesthesiology, intensive care

2.9.3. Gender of subjects

<input type="checkbox"/> Female	<input type="checkbox"/> Male	<input type="checkbox"/> Other
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2.9.4. Inclusion criteria

2.9.5. Exclusion criteria

2.9.6. Type of subjects that the clinical investigation plans to recruit

Healthy Patients Vulnerable population Incapacitated subjects

Minors Pregnant women Breastfeeding women Patients in emergency situations

Other (please specify) | _____ |

2.9.7. Age range of the participants that the clinical investigation plans to include

In utero Adults (from 18 to 84 ani)

Newborns (from 0 to 27 days) Elderly (from 85 ani)

Infants and toddlers (from 28 days to 23 months)

Children (from 2 to 5 ani)

Adolescents (de la 12 la 17 ani)

2.10. Scope of the investigational device

2.10.1. Combined investigation medical device/ In Vitro diagnostic medical device?

Yes No

If yes, please provide the related IVD performance study identification number

| _____ |

2.10.2. Is the application submitted in parallel with an application for a clinical trial on medicinal products?

<input type="radio"/> Yes	<input type="radio"/> No
If Yes, please provide the EU Clinical Trial Number: <input type="text"/>	

2.11. Coordinating investigator

First name:			
Last name:			
Address	Street name:		Number:
	Postal code:		City:
	Country:		
Telephone number:			
Email:			

Section 3: Investigational device(s)*)

*) For each device, use one copy of section 3 as an appendix to this application form.

3.1. Investigational medical device

3.1.1. Device purposes

Select the therapeutic area in which the clinical investigation falls from the list below:

Alleviation of an injury or disability
Alleviation of disease
Compensation for an injury or disability
Devices for the control or support of conception
Diagnosis of an injury or disability
Diagnosis of disease
Investigation of anatomy or a physiological or pathological condition or process
Monitoring of an injury or disability
Monitoring of a condition
No medical purpose but the device belongs to a group of devices listed in Annex XVI of the MDR
Prediction of disease
Prevention of disease
Products specially intended for the cleaning, disinfection or sterilisation of devices
Prognosis of disease
Providing information by means <i>in vitro</i> examination of specimens derived from the human body,

including organ, blood and tissue donations
Replacement or modification of the anatomy or of a physiological or pathological process
Treatment of an injury or disability
Treatment of a disease

3.1.2. Device type

<input type="checkbox"/> Implantable	<input type="checkbox"/> System
<input type="checkbox"/> Active device	<input type="checkbox"/> Non-medical purpose
<input type="checkbox"/> Measuring function	<input type="checkbox"/> Sterile
<input type="checkbox"/> Reusable surgical instrument	<input type="checkbox"/> Software
<input type="checkbox"/> Intended to administer or remove medicinal substance	

3.1.3. Invasiveness

Is it an invasive medical device?
<input type="radio"/> Yes <input type="radio"/> No

3.1.4. Device identifiers

Generic denomination:					
Device trade name:	Model:				
Device name:					
European medical device nomenclature					
Medical device classification:	<table border="1"><tr><td>Class I</td></tr><tr><td>Class II A</td></tr><tr><td>Class II B</td></tr><tr><td>Class III</td></tr></table>	Class I	Class II A	Class II B	Class III
Class I					
Class II A					
Class II B					
Class III					
Classification rule:					
Rule 1 – Non invasive device and no other rules can be applied					
Rule 2 – Channelling of storing blood, liquids, cells or tissues, liquids or gases for eventual administration or introduction in the body					
Rule 3 - Devices that modify biological or chemical composition of human tissues or cells, blood, other body liquids or other liquids intended for implantation or administration into the body					
Rule 4 - Devices that come into contact with injured skin or mucous membrane					
Rule 5 - Devices invasive with respect to body orifices, Other than Surgically invasive device					
Rule 6 - Surgically invasive devices intended for transient use (< 60 minutes)					

Rule 7 - Surgically invasive devices intended for short-term use (> 60 minutes, < 30 days)

Rule 8 - Implantable devices and long-term surgically invasive devices

Rule 9 - Active therapeutic devices intended to administer or exchange energy

Rule 10 - Active devices for diagnosis and monitoring

Rule 11 - Software intended to provide information to inform decisions with diagnosis or therapeutic purposes or software intended to monitor physiological processes

Rule 12 - Active devices intended to administer and/or remove medicinal products, body liquids or other substances to or from the body

Rule 13 – All other active devices

Rule 14 - Devices incorporating, as an integral part, an ancillary medicinal product, and medicinal products derived from human blood or blood plasma

Rule 15 - Devices used for contraception or prevention of sexually transmitted diseases

Rule 16 - Specifically disinfecting, cleaning, rinsing, hydrating or sterilising devices

Rule 17 - Devices to record X-ray diagnostic images

Rule 18 - Devices manufactured utilizing tissue or cells of human or animal origin or their derivatives

Rule 19 - Devices incorporating or consisting of nanomaterial

Rule 20 - Invasive devices, intended to administer medicinal product by inhalation

Rule 21 - Devices that are composed of substances or combinations of substances that are intended to be introduced into the human body via an orifice or applied to the skin and that are absorbed by or locally dispersed in the human body

Rule 22 - Active therapeutic devices with an integrated or incorporated diagnostic function which significantly determines the patient management by the device

Device description:

Intended purpose (clinic):

Does the device contain or incorporate medicinal substance(s)?

Yes

No

If yes, please provide the medicinal substance(s) name(s):

The device incorporates, as an integral part, or it is manufactured using:

Non-viable tissues of human origin or their derivatives with an ancillary action

Non-viable cells of human origin or their derivatives with an ancillary action

Non-viable tissues of animal origin or their derivatives with an ancillary action

Non-viable cells of animal origin or their derivatives with an ancillary action

Non-viable biological substances other than those referred to in the previous points

Does the investigational device have a CE marking?

Yes No

If yes, please provide the information in the box below.

To what extent is the intended purpose of the device in the performance study covered by the CE mark?

CE marked device will be used outside the scope of its CE mark

CE marked device will be used within the scope of its CE mark and no additional procedures are foreseen in the performance study

CE marked device will be used within the scope of its CE mark, but additional procedures are foreseen in the performance study

Are those additional procedures considered to be burdensome and/or invasive?

Yes No

Please, comment why do you consider as such?

Information related to the notified body involved, if applicable:

Notified body number:

Notified body name:

3.2. Previous clinical investigation

Has this device been investigated in a clinical investigation within the EU previously?

Yes No

If yes, please provide the relevant reference number(s) (SIN, CIV-ID, other references of the previous clinical investigations)

3.3. Scientific opinion/view

Has the investigational study/device been subject to a national scientific view/opinion from an expert panel?

Yes No

3.4. Manufacturer of the investigational device

Is the manufacturer the same as the sponsor?

Yes No

If no, please fill in the requested information in sections 3.4.1 and 3.4.2.

3.4.1. Manufacturer information

Organisation name:			
Address	Street name:		Number:
	Postal code:		City:
	Country:		
Telephone number:			
Email:			

Contact person of the manufacturer

First name:
Last name:
Telephone number:
Email:

3.4.2. Authorised representative

Organisation name:			
Address	Street name:		Number:
	Postal code:		City:
	Country:		
Telephone number:			
Email:			

Contact person of the authorised representative

First name:
Last name:
Telephone number:
Email:

Section 4: Comparator*)

*) For each comparator, use one copy of Section 4 as an Annex to this application form.

4.1. Allocability of section 4

Is there a comparator included in a clinical investigation?

Yes No

If yes, Section 4.2 needs to be completed.

4.2. Type of comparator

<p><input type="radio"/> Therapy</p> <p><input type="radio"/> Placebo</p> <p><input type="radio"/> No treatment</p> <p><input type="radio"/> Medical device</p>

4.2.1. Medical device as comparator

Is the comparator medical device CE marked?
 Yes No

If yes, will the CE marked comparator medical device be used in the clinical investigation within the scope of its CE mark?
 Yes No

Generic denomination:

Device trade name:

Model:

Device name:

European Medical Device Nomenclature:

Medical device classification:

Class I

Class IIA

Class IIB

Class III

Device description:

Intended (clinical) purpose:

Does the comparator device contain or incorporate medicinal substance(s)?
 Yes No

If yes, please provide the medicinal substance(s) names:

The comparator device incorporates, as an integral part, or it is manufactured using:

Non-viable tissues of human origin or their derivatives with an ancillary action

Non-viable cells of human origin or their derivatives with an ancillary action

Non-viable tissues of animal origin or their derivatives with an ancillary action

Non-viable cells of animal origin or their derivatives with an ancillary action

Non-viable biological substances other than those referred to in the previous points

None of these proposals / Not applicable

Section 5: National information

5.1. Study site information*)

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

Name of institution	Site address	Investigator attached to this site	Contact information of investigators

*) Additional sites could be added by using a duplicated section 5.1, in appendix to this application form

5.2. Ethics committee information

Select the applicable option: <input type="radio"/> Ethics committee opinion available <input type="radio"/> Ethics committee opinion under review <input type="radio"/>			
Ethics committee opinion is not mandatory before submission to the competent authority. If an ethics committee has to be selected by the sponsor before submission, please provide the ethics committee information's below.			
Organisation name:			
Address	Street name:		Number:
	Postal code:		City:
	Country:		
Telephone number:			
Email:			

5.3. Status of the clinical investigation

Is the sponsor considered as commercial according to national legislation? <input type="radio"/> Yes <input type="radio"/> No
--

5.4. Expected number of subjects recruited within the Member State

How many subjects are expected to be recruited?

I hereby certify that the information and documentation submitted with this application/notification is correct in detail and all the information requested has been supplied. The investigated medical device complies with the applicable general safety and performance requirements, apart from those covered by the investigation and that every precaution has been taken to protect the health and safety of the patient and/or user.

I confirm that all the clinical investigations information collected for this application, has been done in compliance with the European data protection legislation (GDPR).

Name:

Position:

Where necessary, for:

- providing information for additional medical devices, Section 3 may be used several times, whenever necessary.
- adding more comparators, Section 4 may be used several times, whenever necessary.
- adding more sites/centers where the investigation takes place, Section 5 may be used several times, whenever necessary.

Annex 4

to the Methodological rules

**Clinical investigation - Supporting documents according to the MDR Harmonised list of documents to be attached to the application registration forms for the authorisation of clinical evaluations, clinical investigations or substantial modifications thereof
- Harmonised form -**

Version 1.0

Document	Version/Date [DD-MM-YY] At time of NAMMDR application	Version / Date [DD-MM-YY] At time of NAMMDR authorisation / refusal	Summary of changes made	Amended as a result of NAMMDR / CE/CS assessment
Mandatory				
Cover letter				<input type="checkbox"/>
Registration form				
Investigator's brochure (including all annexes, if applicable)				<input type="checkbox"/>
Clinical investigation plan (CIP)				<input type="checkbox"/>
Clinical assessment plan				<input type="checkbox"/>
CIP summary				<input type="checkbox"/>
Declaration of conformity				<input type="checkbox"/>
Example of labels				<input type="checkbox"/>
Description of the arrangements to comply with the applicable rules on the protection and confidentiality of personal data/ personal information				<input type="checkbox"/>
List of General Safety and Performance Requirements				<input type="checkbox"/>
As applicable				

Description of the arrangements to comply with the applicable rules on the protection and confidentiality of personal data/ personal information				☐
Risk management documentation				☐
Test reports				☐
Proof of Clinical Investigation Insurance				☐
Suitability of investigational sites and investigation site team				☐
Manufacturer's Instructions for Use				☐
Suitability of the investigators				☐
Recruitment procedures and advertising materials				☐
Documents to obtain informed consent, informed consent procedure, all written information to participants, payments and compensation of participants				☐
Notified Body Certificates				☐
Decisions form other countries				☐
PMCF plan				☐
Expert panel opinion				☐
Other documents				☐

Note

This template has been developed by the European Commission Working Group on Clinical Assessment and Investigations to ensure the traceability of documents in the absence of the EUDAMED.

This template in this Annex must be used together with the Harmonised Registration Form for the application for authorisation of a clinical evaluation or investigation for a medical device, in line with the MDR (Annex 2 to this Order). The use of this template is not mandatory, only recommended.

The fields marked as "mandatory" are required for the registration of a clinical investigation in line with the MDR, and those marked "as appropriate" may be required, depending on the clinical investigation. In the column " Summary of modifications", a brief description of the changed sections and the type of change shall be entered.

Acronyms

ANMDMR (NAMMDR)	The National Agency for Medicines and Medical Devices of Romania
CE	Ethics Committee (The National Bioethics Committee of Medicines and Medical Devices)
CS	Specialised Commission of the Ministry of Health
PMCF	Post-market clinical follow-up
CIP	Clinical Investigation Plan
MDR	Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (Medical Device Regulation - MDR).

Annex 5

to the Methodological rules

Clinical investigation - Checklist of general safety and performance requirements, Standards, common specifications and scientific advice for the authorisation of a clinical evaluation or investigation for a medical device - Information on investigational medical devices according to section 2.7 of chapter II of annex XV MDR¹⁰ - Harmonised form – Version 1.0

¹⁰) Regulation (EU) 2017/745 (Medical device Regulation, MDR)

Investigational device (name, size, model):

Manufacturer:

Date:

A. Standards, common specifications, scientific advice

B.

Standards, common specifications, scientific advice obtained from expert panels according to article 106 MDR		Compliance information (with the exception of clinical requirements that will be assessed during the clinical investigation)		
Identification number and title of the document	Version/Year	Full	Partial	Description of all deviations, reasons, alternative solutions adopted to meet the General safety and performance requirements of the MDR
		<input type="checkbox"/>	<input type="checkbox"/>	
		<input type="checkbox"/>	<input type="checkbox"/>	
		<input type="checkbox"/>	<input type="checkbox"/>	
		<input type="checkbox"/>	<input type="checkbox"/>	
		<input type="checkbox"/>	<input type="checkbox"/>	
		<input type="checkbox"/>	<input type="checkbox"/>	
		<input type="checkbox"/>	<input type="checkbox"/>	

C. Matrix of General safety and performance requirements

General safety and performance requirement (GSPR)	Does ER apply to the invest. device? Yes/No	Standards and common specifications used in full or in part	Evidence of conformance, documentation	Justification/comment in case of deviation

CHAPTER I, GENERAL REQUIREMENTS

<p>1. Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose. They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.</p>				
<p>2. The requirement in this Annex to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.</p>				
<p>3. Manufacturers shall establish, implement, document and maintain a risk management system. Risk management shall be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring Ruler systematic updating. In carrying out risk management manufacturers shall:</p>				
<p>(a) establish and document a risk management plan for each device;</p>				
<p>(b) identify and analyse the known and foreseeable hazards associated with each device;</p>				
<p>(c) estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse;</p>				
<p>(d) eliminate or control the risks referred to in point (c) in accordance with the requirements of Section 4;</p>				
<p>(e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, benefit-risk ratio and risk acceptability; and</p>				
<p>(f) based on the evaluation of the impact of the</p>				

<p>information referred to in point (e), if necessary amend control measures in line with the requirements of Section 4.</p>				
<p>4. Risk control measures adopted by manufacturers for the design and manufacture of the devices shall conform to safety principles, taking account of the generally acknowledged state of the art. To reduce risks, Manufacturers shall manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. In selecting the most appropriate solutions, manufacturers shall, in the following order of priority:</p> <p>(a) eliminate or reduce risks as far as possible through safe design and manufacture;</p> <p>(b) where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; and</p> <p>(c) provide information for safety (warnings/precautions/contra-indications) and, where appropriate, training to users.</p> <p>Manufacturers shall inform users of any residual risks.</p>				
<p>5. In eliminating or reducing risks related to use error, the manufacturer shall:</p> <p>(a) reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety), and</p> <p>(b) give consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users).</p>				
<p>6. The characteristics and performance of a device shall not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.</p>				

7. Devices shall be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer.				
8. All known and foreseeable risks, and any undesirable side-effects, shall be minimised and be acceptable when weighed against the evaluated benefits to the patient and/or user arising from the achieved performance of the device during normal conditions of use.				
9. For the devices referred to in Annex XVI, the general safety requirements set out in Sections 1 and 8 shall be understood to mean that the device, when used under the conditions and for the purposes intended, does not present a risk at all or presents a risk that is no more than the maximum acceptable risk related to the product's use which is consistent with a high level of protection for the safety and health of persons.				
CHAPTER II, REQUIREMENTS REGARDING DESIGN AND MANUFACTURE				
10. Chemical, physical and biological properties				
10.1. Devices shall be designed and manufactured in such a way as to ensure that the characteristics and performance requirements referred to in Chapter I are fulfilled. Particular attention shall be paid to:				
(a) the choice of materials and substances used, particularly as regards toxicity and, where relevant, flammability;				
(b) the compatibility between the materials and substances used and biological tissues, cells and body fluids, taking account of the intended purpose of the device and, where relevant, absorption, distribution, metabolism and excretion;				
(c) the compatibility between the different parts of a device which consists of more than one implantable part;				
(d) the impact of processes on material properties;				
(e) where appropriate, the results of biophysical or modelling research the validity of which has been demonstrated beforehand;				

(f) the mechanical properties of the materials used, reflecting, where appropriate, matters such as strength, ductility, fracture resistance, wear resistance and fatigue resistance;				
(g) surface properties; and				
(h) the confirmation that the device meets any defined chemical and/or physical specifications.				
10.2. Devices shall be designed, manufactured and packaged in such a way as to minimise the risk posed by contaminants and residues to patients, taking account of the intended purpose of the device, and to the persons involved in the transport, storage and use of the devices. Particular attention shall be paid to tissues exposed to those contaminants and residues and to the duration and frequency of exposure.				
10.3. Devices shall be designed and manufactured in such a way that they can be used safely with the materials and substances, including gases, with which they enter into contact during their intended use; if the devices are intended to administer medicinal products they shall be designed and manufactured in such a way as to be compatible with the medicinal products concerned in accordance with the provisions and restrictions governing those medicinal products and that the performance of both the medicinal products and of the devices is maintained in accordance with their respective indications and intended use.				
10.4. Substances				

<p>10.4.1. Design and manufacture of devices</p> <p>Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks posed by substances or particles, including wear debris, degradation products and processing residues, that may be released from the device.</p> <p>Devices, or those parts thereof or those materials used therein that:</p> <ul style="list-style-type: none"> — are invasive and come into direct contact with the human body, — (re)administer medicines, body liquids or other substances, including gases, to/from the body, or — transport or store such medicines, body fluids or substances, including gases, to be (re)administered to the body, <p>shall only contain the following substances in a concentration that is above 0,1 % weight by weight (w/w) where justified pursuant to Section 10.4.2:</p> <p>(a) substances which are carcinogenic, mutagenic or toxic to reproduction ('CMR'), of category 1A or 1B, in accordance with Part 3 of Annex VI to Regulation (EC) No 1272/2008 of the European Parliament and of the Council (5), or</p> <p>(b) substances having endocrine-disrupting properties for which there is scientific evidence of probable serious effects to human health and which are identified either in accordance with the procedure set out in Article 59 of Regulation (EC) No 1907/2006 of the European Parliament and of the Council (6) or, once a delegated act has been adopted by the Commission pursuant to the first subparagraph of Article 5(3) of Regulation (EU) No 528/2012 of the European Parliament and the Council (7), in accordance with the criteria that are relevant to human health amongst the criteria established therein.</p>				
<p>10.4.2. Justification regarding the presence of CMR and/or endocrine-disrupting substances</p> <p>The justification for the presence of such substances shall be based upon:</p>				

<p>(a) an analysis and estimation of potential patient or user exposure to the substance;</p> <p>(b) an analysis of possible alternative substances, materials or designs, including, where available, information about independent research, peer-reviewed studies, scientific opinions from relevant scientific committees and an analysis of the availability of such alternatives;</p> <p>(c) argumentation as to why possible substance and/ or material substitutes, if available, or design changes, if feasible, are inappropriate in relation to maintaining the functionality, performance and the benefit-risk ratios of the product; including taking into account if the intended use of such devices includes treatment of children or treatment of pregnant or breastfeeding women or treatment of other patient groups considered particularly vulnerable to such substances and/or materials; and</p> <p>(d) where applicable and available, the latest relevant scientific committee guidelines in accordance with Sections 10.4.3. and 10.4.4.</p>				
<p>10.4.3. Guidelines on phthalates</p> <p>For the purposes of Section 10.4., the Commission shall, as soon as possible and by 26 May 2018, provide the relevant scientific committee with a mandate to prepare guidelines that shall be ready before 26 May 2020. The mandate for the committee shall encompass at least a benefit-risk assessment of the presence of phthalates which belong to either of the groups of substances referred to in points (a) and (b) of Section 10.4.1. The benefit-risk assessment shall take into account the intended purpose and context of the use of the device, as well as any available alternative substances and alternative materials, designs or medical treatments. When deemed appropriate on the basis of the latest scientific evidence, but at least every five years, the guidelines shall be updated.</p>				
<p>10.4.4. Guidelines on other CMR and endocrine-disrupting substances</p> <p>Subsequently, the Commission shall mandate the relevant scientific committee to prepare guidelines as referred to in Section 10.4.3. also for other substances referred to in points (a) and (b) of Section 10.4.1., where appropriate.</p>				

<p>10.4.5. Labelling</p> <p>Where devices, parts thereof or materials used therein as referred to in Section 10.4.1. contain substances referred to in points (a) or (b) of Section 10.4.1. in a concentration above 0,1 % weight by weight (w/w), the presence of those substances shall be labelled on the device itself and/or on the packaging for each unit or, where appropriate, on the sales packaging, with the list of such substances. If the intended use of such devices includes treatment of children or treatment of pregnant or breastfeeding women or treatment of other patient groups considered particularly vulnerable to such substances and/or materials, information on residual risks for those patient groups and, if applicable, on appropriate precautionary measures shall be given in the instructions for use</p>				
<p>10.5. Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks posed by the unintentional ingress of substances into the device taking into account the device and the nature of the environment in which it is intended to be used.</p>				
<p>10.6. Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks linked to the size and the properties of particles which are or can be released into the patient's or user's body, unless they come into contact with intact skin only. Special attention shall be given to nanomaterials.</p>				
<p>11. Infection and microbial contamination</p>				
<p>11.1. Devices and their manufacturing processes shall be designed in such a way as to eliminate or to reduce as far as possible the risk of infection to patients, users and, where applicable, other persons. The design shall:</p> <ul style="list-style-type: none"> (a) reduce as far as possible and appropriate the risks from unintended cuts and pricks, such as needle stick injuries, (b) allow easy and safe handling, (c) reduce as far as possible any microbial leakage from the device and/or microbial exposure during use, and (d) prevent microbial contamination of the device or its content such as specimens or fluids. 				
<p>11.2. Where necessary devices shall be designed to facilitate their safe cleaning, disinfection, and/or re-sterilisation.</p>				

<p>11.3. Devices labelled as having a specific microbial state shall be designed, manufactured and packaged to ensure that they remain in that state when placed on the market and remain so under the transport and storage conditions specified by the manufacturer.</p>				
<p>11.4. Devices delivered in a sterile state shall be designed, manufactured and packaged in accordance with appropriate procedures, to ensure that they are sterile when placed on the market and that, unless the packaging which is intended to maintain their sterile condition is damaged, they remain sterile, under the transport and storage conditions specified by the manufacturer, until that packaging is opened at the point of use. It shall be ensured that the integrity of that packaging is clearly evident to the final user.</p>				
<p>11.5. Devices labelled as sterile shall be processed, manufactured, packaged and, sterilised by means of appropriate, validated methods.</p>				
<p>11.6. Devices intended to be sterilised shall be manufactured and packaged in appropriate and controlled conditions and facilities.</p>				
<p>11.7. Packaging systems for non-sterile devices shall maintain the integrity and cleanliness of the product and, where the devices are to be sterilised prior to use, minimise the risk of microbial contamination; the packaging system shall be suitable taking account of the method of sterilisation indicated by the manufacturer.</p>				
<p>11.8. The labelling of the device shall distinguish between identical or similar devices placed on the market in both a sterile and a non-sterile condition additional to the symbol used to indicate that devices are sterile.</p>				
<p>12. Devices incorporating a substance considered to be a medicinal product and devices that are composed of substances or of combinations of substances that are absorbed by or locally dispersed in the human body.</p>				
<p>12.1. In the case of devices referred to in the first subparagraph of Article 1(8), the quality, safety and usefulness of the substance which, if used separately, would be considered to be a medicinal product within the meaning of point (2) of Article 1 of Directive 2001/83/EC, shall be verified by analogy with the methods specified in Annex I to Directive 2001/83/EC,</p>				

as required by the applicable conformity assessment procedure under this Regulation.				
12.2. Devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body, and that are absorbed by or locally dispersed in the human body shall comply, where applicable and in a manner limited to the aspects not covered by this Regulation, with the relevant requirements laid down in Annex I to Directive 2001/83/EC for the evaluation of absorption, distribution, metabolism, excretion, local tolerance, toxicity, interaction with other devices, medicinal products or other substances and potential for adverse reactions, as required by the applicable conformity assessment procedure under this Regulation.				
13. Devices incorporating materials of biological origin				
13.1. For devices manufactured utilising derivatives of tissues or cells of human origin which are non-viable or are rendered non-viable covered by this Regulation in accordance with point (g) of Article 1(6), the following shall apply:				
(a) donation, procurement and testing of the tissues and cells shall be done in accordance with Directive 2004/23/EC;				
(b) processing, preservation and any other handling of those tissues and cells or their derivatives shall be carried out so as to provide safety for patients, users and, where applicable, other persons. In particular, safety with regard to viruses and other transmissible agents shall be addressed by appropriate methods of sourcing and by implementation of validated methods of elimination or inactivation in the course of the manufacturing process;				
(c) the traceability system for those devices shall be complementary and compatible with the traceability and data protection requirements laid down in Directive 2004/23/EC and in Directive 2002/98/EC.				
13.2. For devices manufactured utilising tissues or cells of animal origin, or their derivatives, which are non-viable or rendered non-viable the following shall apply:				

<p>(a) where feasible taking into account the animal species, tissues and cells of animal origin, or their derivatives, shall originate from animals that have been subjected to veterinary controls that are adapted to the intended use of the tissues. Information on the geographical origin of the animals shall be retained by manufacturers;</p>				
<p>(b) sourcing, processing, preservation, testing and handling of tissues, cells and substances of animal origin, or their derivatives, shall be carried out so as to provide safety for patients, users and, where applicable, other persons. In particular safety with regard to viruses and other transmissible agents shall be addressed by implementation of validated methods of elimination or viral inactivation in the course of the manufacturing process, except when the use of such methods would lead to unacceptable degradation compromising the clinical benefit of the device;</p>				
<p>(c) in the case of devices manufactured utilising tissues or cells of animal origin, or their derivatives, as referred to in Regulation (EU) No 722/2012 the particular requirements laid down in that Regulation shall apply.</p>				
<p>13.3. For devices manufactured utilising non-viable biological substances other than those referred to in Sections 13.1 and 13.2, the processing, preservation, testing and handling of those substances shall be carried out so as to provide safety for patients, users and, where applicable, other persons, including in the waste disposal chain. In particular, safety with regard to viruses and other transmissible agents shall be addressed by appropriate methods of sourcing and by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.</p>				
<p>14. Construction of devices and interaction with their environment</p>				
<p>14.1. If the device is intended for use in combination with other devices or equipment the whole combination, including the connection system shall be safe and shall not impair the specified performance of the devices. Any restrictions on use applying to such combinations shall be indicated on the label and/or in the instructions for use. Connections which the user has to handle, such as fluid, gas transfer, electrical or mechanical coupling, shall be designed and constructed in such a way as to minimise all possible risks, such as misconnection.</p>				

<p>14.2. Devices shall be designed and manufactured in such a way as to remove or reduce as far as possible:</p> <p>(a) the risk of injury, in connection with their physical features, including the volume/pressure ratio, dimensional and where appropriate ergonomic features;</p>				
<p>(b) risks connected with reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, temperature, variations in pressure and acceleration or radio signal interferences;</p>				
<p>(c) the risks associated with the use of the device when it comes into contact with materials, liquids, and substances, including gases, to which it is exposed during normal conditions of use;</p>				
<p>(d) the risks associated with the possible negative interaction between software and the IT environment within which it operates and interacts;</p>				
<p>(e) the risks of accidental ingress of substances into the device;</p>				
<p>(f) the risks of reciprocal interference with other devices normally used in the investigations or for the treatment given;</p>				
<p>(g) risks arising where maintenance or calibration are not possible (as with implants), from ageing of materials used or loss of accuracy of any measuring or control mechanism.</p>				
<p>14.3. Devices shall be designed and manufactured in such a way as to minimise the risks of fire or explosion during normal use and in single fault condition. Particular attention shall be paid to devices the intended use of which includes exposure to or use in association with flammable or explosive substances or substances which could cause combustion.</p>				
<p>14.4. Devices shall be designed and manufactured in such a way that adjustment, calibration, and maintenance can be done safely and effectively.</p>				
<p>14.5. Devices that are intended to be operated together with other devices or products shall be designed and manufactured in such a way that the interoperability and compatibility are reliable and safe.</p>				

<p>14.6 Any measurement, monitoring or display scale shall be designed and manufactured in line with ergonomic principles, taking account of the intended purpose, users and the environmental conditions in which the devices are intended to be used.</p>				
<p>14.7. Devices shall be designed and manufactured in such a way as to facilitate their safe disposal and the safe disposal of related waste substances by the user, patient or other person. To that end, manufacturers shall identify and test procedures and measures as a result of which their devices can be safely disposed after use. Such procedures shall be described in the instructions for use</p>				
<p>15. Devices with a diagnostic or measuring function</p>				
<p>15.1. Diagnostic devices and devices with a measuring function, shall be designed and manufactured in such a way as to provide sufficient accuracy, precision and stability for their intended purpose, based on appropriate scientific and technical methods. The limits of accuracy shall be indicated by the manufacturer.</p>				
<p>15.2. The measurements made by devices with a measuring function shall be expressed in legal units conforming to the provisions of Council Directive 80/181/EEC (4).</p>				
<p>16. Protection against radiation</p>				
<p>16.1. General (a) Devices shall be designed, manufactured and packaged in such a way that exposure of patients, users and other persons to radiation is reduced as far as possible, and in a manner that is compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for therapeutic and diagnostic purposes.</p>				
<p>(b) The operating instructions for devices emitting hazardous or potentially hazardous radiation shall contain detailed information as to the nature of the emitted radiation, the means of protecting the patient and the user, and on ways of avoiding misuse and of reducing the risks inherent to installation as far as possible and appropriate. Information regarding the acceptance and performance testing, the acceptance criteria, and the maintenance procedure shall also be specified.</p>				

<p>16.2. Intended radiation</p> <p>(a) Where devices are designed to emit hazardous, or potentially hazardous, levels of ionizing and/or nonionizing radiation necessary for a specific medical purpose the benefit of which is considered to outweigh the risks inherent to the emission, it shall be possible for the user to control the emissions. Such devices shall be designed and manufactured to ensure reproducibility of relevant variable parameters within an acceptable tolerance.</p>				
<p>(b) Where devices are intended to emit hazardous, or potentially hazardous, ionizing and/or non-ionizing radiation, they shall be fitted, where possible, with visual displays and/or audible warnings of such emissions.</p>				
<p>16.3. Devices shall be designed and manufactured in such a way that exposure of patients, users and other persons to the emission of unintended, stray or scattered radiation is reduced as far as possible. Where possible and appropriate, methods shall be selected which reduce the exposure to radiation of patients, users and other persons who may be affected.</p>				
<p>16.4. Ionising radiation</p> <p>(a) Devices intended to emit ionizing radiation shall be designed and manufactured taking into account the requirements of the Directive 2013/59/Euratom laying down basic safety standards for protection against the dangers arising from exposure to ionising radiation.</p>				
<p>(b) Devices intended to emit ionising radiation shall be designed and manufactured in such a way as to ensure that, where possible, taking into account the intended use, the quantity, geometry and quality of the radiation emitted can be varied and controlled, and, if possible, monitored during treatment.</p>				
<p>(c) Devices emitting ionising radiation intended for diagnostic radiology shall be designed and manufactured in such a way as to achieve an image and/or output quality that are appropriate to the intended medical purpose whilst minimising radiation exposure of the patient and user.</p>				
<p>(d) Devices that emit ionising radiation and are intended for therapeutic radiology shall be designed and manufactured in such a way as to enable reliable monitoring and control of the delivered dose, the beam</p>				

type, energy and, where appropriate, the quality of radiation.				
17. Electronic programmable systems — devices that incorporate electronic programmable systems and software that are devices in themselves				
17.1. Devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, shall be designed to ensure repeatability, reliability and performance in line with their intended use. In the event of a single fault condition, appropriate means shall be adopted to eliminate or reduce as far as possible consequent risks or impairment of performance.				
17.2. For devices that incorporate software or for software that are devices in themselves, the software shall be developed and manufactured in accordance with the state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation.				
17.3. Software referred to in this Section that is intended to be used in combination with mobile computing platforms shall be designed and manufactured taking into account the specific features of the mobile platform (e.g. size and contrast ratio of the screen) and the external factors related to their use (varying environment as regards level of light or noise).				
17.4. Manufacturers shall set out minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.				
18. Active devices and devices connected to them				
18.1. For non-implantable active devices, in the event of a single fault condition, appropriate means shall be adopted to eliminate or reduce as far as possible consequent risks.				
18.2. Devices where the safety of the patient depends on an internal power supply shall be equipped with a means of determining the state of the power supply and an appropriate warning or indication for when the capacity of the power supply becomes critical. If necessary, such warning or indication shall be given prior to the power supply becoming critical.				

18.3. Devices where the safety of the patient depends on an external power supply shall include an alarm system to signal any power failure.				
18.4. Devices intended to monitor one or more clinical parameters of a patient shall be equipped with appropriate alarm systems to alert the user of situations which could lead to death or severe deterioration of the patient's state of health.				
18.5. Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks of creating electromagnetic interference which could impair the operation of the device in question or other devices or equipment in the intended environment.				
18.6. Devices shall be designed and manufactured in such a way as to provide a level of intrinsic immunity to electromagnetic interference such that is adequate to enable them to operate as intended.				
18.7. Devices shall be designed and manufactured in such a way as to avoid, as far as possible, the risk of accidental electric shocks to the patient, user or any other person, both during normal use of the device and in the event of a single fault condition in the device, provided the device is installed and maintained as indicated by the manufacturer.				
18.8. Devices shall be designed and manufactured in such a way as to protect, as far as possible, against unauthorised access that could hamper the device from functioning as intended.				
19. Particular requirements for active implantable devices				
19.1. Active implantable devices shall be designed and manufactured in such a way as to remove or minimize as far as possible: (a) risks connected with the use of energy sources with particular reference, where electricity is used, to insulation, leakage currents and overheating of the devices,				
(b) risks connected with medical treatment, in particular those resulting from the use of defibrillators or high-frequency surgical equipment, and				
(c) risks which may arise where maintenance and calibration are impossible, including: — excessive increase of leakage currents, — ageing of the materials used, — excess heat generated by the device, — decreased accuracy of any measuring or control				

mechanism.				
19.2. Active implantable devices shall be designed and manufactured in such a way as to ensure: — if applicable, the compatibility of the devices with the substances they are intended to administer, and — the reliability of the source of energy.				
19.3. Active implantable devices and, if appropriate, their component parts shall be identifiable to allow any necessary measure to be taken following the discovery of a potential risk in connection with the devices or their component parts				
19.4. Active implantable devices shall bear a code by which they and their manufacturer can be unequivocally identified (particularly with regard to the type of device and its year of manufacture); it shall be possible to read this code, if necessary, without the need for a surgical operation.				
20. Protection against mechanical and thermal risks				
20.1. Devices shall be designed and manufactured in such a way as to protect patients and users against mechanical risks connected with, for example, resistance to movement, instability and moving parts.				
20.2. Devices shall be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from vibration generated by the devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.				
20.3. Devices shall be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance.				
20.4. Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user or other person has to handle, shall be designed and constructed in such a way as to minimise all possible risks.				

<p>20.5. Errors likely to be made when fitting or refitting certain parts which could be a source of risk shall be made impossible by the design and construction of such parts or, failing this, by information given on the parts themselves and/or their housings. The same information shall be given on moving parts and/or their housings where the direction of movement needs to be known in order to avoid a risk.</p>				
<p>20.6. Accessible parts of devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings shall not attain potentially dangerous temperatures under normal conditions of use.</p>				
<p>21. Protection against the risks posed to the patient or user by devices supplying energy or substances</p>				
<p>21.1. Devices for supplying the patient with energy or substances shall be designed and constructed in such a way that the amount to be delivered can be set and maintained accurately enough to ensure the safety of the patient and of the user.</p>				
<p>21.2. Devices shall be fitted with the means of preventing and/or indicating any inadequacies in the amount of energy delivered or substances delivered which could pose a danger. Devices shall incorporate suitable means to prevent, as far as possible, the accidental release of dangerous levels of energy or substances from an energy and/or substance source.</p>				
<p>21.3. The function of the controls and indicators shall be clearly specified on the devices. Where a device bears instructions required for its operation or indicates operating or adjustment parameters by means of a visual system, such information shall be understandable to the user and, as appropriate, the patient.</p>				
<p>22. Protection against the risks posed by medical devices intended by the manufacturer for use by lay persons</p>				

<p>22.1. Devices for use by lay persons shall be designed and manufactured in such a way that they perform appropriately for their intended purpose taking into account the skills and the means available to lay persons and the influence resulting from variation that can be reasonably anticipated in the lay person's technique and environment. The information and instructions provided by the manufacturer shall be easy for the lay person to understand and apply.</p>				
<p>22.2. Devices for use by lay persons shall be designed and manufactured in such a way as to: — ensure that the device can be used safely and accurately by the intended user at all stages of the procedure, if necessary after appropriate training and/or information, — reduce, as far as possible and appropriate, the risk from unintended cuts and pricks such as needle stick injuries, and — reduce as far as possible the risk of error by the intended user in the handling of the device and, if applicable, in the interpretation of the results.</p>				
<p>22.3. Devices for use by lay persons shall, where appropriate, include a procedure by which the lay person:</p>				
<p>— can verify that, at the time of use, the device will perform as intended by the manufacturer, and — if applicable, is warned if the device has failed to provide a valid result.</p>				
<p>CHAPTER III - REQUIREMENTS REGARDING THE INFORMATION SUPPLIED WITH THE DEVICE</p>				
<p>23. Label and instructions for use</p>				
<p>23.1. General requirements regarding the information supplied by the manufacturer Each device shall be accompanied by the information needed to identify the device and its manufacturer, and by any safety and performance information relevant to the user, or any other person, as appropriate. Such information may appear on the device itself, on the packaging or in the instructions for use, and shall, if the manufacturer has a website, be made available and kept up to date on the website, taking into account the following:</p>				

<p>(a) The medium, format, content, legibility, and location of the label and instructions for use shall be appropriate to the particular device, its intended purpose and the technical knowledge, experience, education or training of the intended user(s). In particular, instructions for use shall be written in terms readily understood by the intended user and, where appropriate, supplemented with drawings and diagrams.</p>				
<p>(b) The information required on the label shall be provided on the device itself. If this is not practicable or appropriate, some or all of the information may appear on the packaging for each unit, and/or on the packaging of multiple devices.</p>				
<p>(c) Labels shall be provided in a human-readable format and may be supplemented by machine-readable information, such as <i>radio-frequency identification</i> ('<i>RFID</i>') or bar codes.</p>				
<p>(d) Instructions for use shall be provided together with devices. By way of exception, instructions for use shall not be required for class I and class IIa devices if such devices can be used safely without any such instructions and unless otherwise provided for elsewhere in this Section.</p>				
<p>(e) Where multiple devices are supplied to a single user and/or location, a single copy of the instructions for use may be provided if so agreed by the purchaser who in any case may request further copies to be provided free of charge.</p>				
<p>(f) Instructions for use may be provided to the user in non-paper format (e.g. electronic) to the extent, and only under the conditions, set out in Regulation (EU) No 207/2012 or in any subsequent implementing rules adopted pursuant to this Regulation.</p>				
<p>(g) Residual risks which are required to be communicated to the user and/or other person shall be included as limitations, contra-indications, precautions or warnings in the information supplied by the manufacturer.</p>				
<p>(h) Where appropriate, the information supplied by the manufacturer shall take the form of internationally recognised symbols. Any symbol or identification colour used shall conform to the harmonised standards or CS. In areas for which no harmonised standards or CS exist, the symbols and colours shall be described in the documentation supplied with the device.</p>				

23.2. Information on the label: The label shall bear all of the following particulars:				
(a) the name or trade name of the device;				
(b) the details strictly necessary for a user to identify the device, the contents of the packaging and, where it is not obvious for the user, the intended purpose of the device;				
(c) the name, registered trade name or registered trade mark of the manufacturer and the address of its registered place of business;				
(d) if the manufacturer has its registered place of business outside the Union, the name of the authorised representative and address of the registered place of business of the authorised representative;				
(e) where applicable, an indication that the device contains or incorporates: — a medicinal substance, including a human blood or plasma derivative, or — tissues or cells, or their derivatives, of human origin, or — tissues or cells of animal origin, or their derivatives, as referred to in Regulation (EU) No 722/2012;				
(f) where applicable, information labelled in accordance with Section 10.4.5.;				
(g) the lot number or the serial number of the device preceded by the words LOT NUMBER or SERIAL NUMBER or an equivalent symbol, as appropriate;				
(h) the UDI carrier referred to in Article 27(4) and Part C of Annex VII;				
(i) an unambiguous indication of the time limit for using or implanting the device safely, expressed at least in terms of year and month, where this is relevant;				
(j) where there is no indication of the date until when it may be used safely, the date of manufacture. This date of manufacture may be included as part of the lot number or serial number, provided the date is clearly identifiable;				
(k) an indication of any special storage and/or handling condition that applies;				
(l) if the device is supplied sterile, an indication of its sterile state and the sterilisation method;				

(m) warnings or precautions to be taken that need to be brought to the immediate attention of the user of the device, and to any other person. This information may be kept to a minimum in which case more detailed information shall appear in the instructions for use, taking into account the intended users;				
(n) if the device is intended for single use, an indication of that fact. A manufacturer's indication of single use shall be consistent across the Union;				
(o) if the device is a single-use device that has been reprocessed, an indication of that fact, the number of reprocessing cycles already performed, and any limitation as regards the number of reprocessing cycles;				
(p) if the device is custom-made, the words 'custom-made device';				
(q) an indication that the device is a medical device. If the device is intended for clinical investigation only, the words 'exclusively for clinical investigation';				
(r) in the case of devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body via a body orifice or applied to the skin and that are absorbed by or locally dispersed in the human body, the overall qualitative composition of the device and quantitative information on the main constituent or constituents responsible for achieving the principal intended action;				
(s) for active implantable devices, the serial number, and for other implantable devices, the serial number or the lot number.				
23.3. Information on the packaging which maintains the sterile condition of a device ('sterile packaging')				
The following particulars shall appear on the sterile packaging:				
(a) an indication permitting the sterile packaging to be recognised as such,				
(b) a declaration that the device is in a sterile condition,				
(c) the method of sterilisation,				
(d) the name and address of the manufacturer,				
(e) a description of the device,				
(f) if the device is intended for clinical investigations, the words 'exclusively for clinical investigations',				

(g) if the device is custom-made, the words ‘custom-made device’,				
(h) the month and year of manufacture,				
(i) an unambiguous indication of the time limit for using or implanting the device safely expressed at least in terms of year and month, and				
(j) an instruction to check the instructions for use for what to do if the sterile packaging is damaged or unintentionally opened before use.				
23.4 Information in the instructions for use The instructions for use shall contain all of the following particulars: (a) the particulars referred to in points (a), (c), (e), (f), (k), (l), (n) and (r) of Section 23.2;				
(b) the device's intended purpose with a clear specification of indications, contra-indications, the patient target group or groups, and of the intended users, as appropriate;				
(c) where applicable, a specification of the clinical benefits to be expected.				
(d) where applicable, links to the summary of safety and clinical performance referred to in Article 32;				
(e) the performance characteristics of the device;				
(f) where applicable, information allowing the healthcare professional to verify if the device is suitable and select the corresponding software and accessories;				
(g) any residual risks, contra-indications and any undesirable side-effects, including information to be conveyed to the patient in this regard;				
(h) specifications the user requires to use the device appropriately, e.g. if the device has a measuring function, the degree of accuracy claimed for it;				
(i) details of any preparatory treatment or handling of the device before it is ready for use or during its use, such as sterilisation, final assembly, calibration, etc., including the levels of disinfection required to ensure patient safety and all available methods for achieving those levels of disinfection;				
(j) any requirements for special facilities, or special training, or particular qualifications of the device user and/or other persons;				
(k)				

<p>the information needed to verify whether the device is properly installed and is ready to perform safely and as intended by the manufacturer, together with, where relevant:</p> <ul style="list-style-type: none"> — details of the nature, and frequency, of preventive and Ruler maintenance, and of any preparatory cleaning or disinfection, — identification of any consumable components and how to replace them, — information on any necessary calibration to ensure that the device operates properly and safely during its intended lifetime, and — methods for eliminating the risks encountered by persons involved in installing, calibrating or servicing devices; 				
<p>(l) if the device is supplied sterile, instructions in the event of the sterile packaging being damaged or unintentionally opened before use;</p>				
<p>(m) if the device is supplied non-sterile with the intention that it is sterilised before use, the appropriate instructions for sterilisation;</p>				
<p>(n) if the device is reusable, information on the appropriate processes for allowing reuse, including cleaning, disinfection, packaging and, where appropriate, the validated method of re-sterilisation appropriate to the Member State or Member States in which the device has been placed on the market. Information shall be provided to identify when the device should no longer be reused, e.g. signs of material degradation or the maximum number of allowable reuses;</p>				
<p>(o) an indication, if appropriate, that a device can be reused only if it is reconditioned under the responsibility of the manufacturer to comply with the general safety and performance requirements;</p>				

<p>(p) if the device bears an indication that it is for single use, information on known characteristics and technical factors known to the manufacturer that could pose a risk if the device were to be re-used. This information shall be based on a specific section of the manufacturer's risk management documentation, where such characteristics and technical factors shall be addressed in detail. If in accordance with point (d) of Section 23.1. no instructions for use are required, this information shall be made available to the user upon request;</p>				
<p>(q) for devices intended for use together with other devices and/or general purpose equipment:</p>				
<p>— information to identify such devices or equipment, in order to obtain a safe combination, and/or — information on any known restrictions to combinations of devices and equipment;</p>				
<p>(r) if the device emits radiation for medical purposes: — detailed information as to the nature, type and where appropriate, the intensity and distribution of the emitted radiation, — the means of protecting the patient, user, or other person from unintended radiation during use of the device;</p>				

- information that allows the user and/or patient to be informed of any warnings, precautions, contraindications, measures to be taken and limitations of use regarding the device. That information shall, where relevant, allow the user to brief the patient about any warnings, precautions, contra-indications, measures to be taken and limitations of use regarding the device. The information shall cover, where appropriate:

- warnings, precautions and/or measures to be taken in the event of malfunction of the device or changes in its performance that may affect safety,
- warnings, precautions and/or measures to be taken as regards the exposure to reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, or temperature,
- warnings, precautions and/or measures to be taken as regards the risks of interference posed by the reasonably foreseeable presence of the device during specific diagnostic investigations, evaluations, or therapeutic treatment or other procedures such as electromagnetic interference emitted by the device affecting other equipment,
- if the device is intended to administer medicinal products, tissues or cells of human or animal origin, or their derivatives, or biological substances, any limitations or incompatibility in the choice of substances to be delivered,
- warnings, precautions and/or limitations related to the medicinal substance or biological material that is incorporated into the device as an integral part of the device; and
- precautions related to materials incorporated into the device that contain or consist of CMR substances or endocrine-disrupting substances, or that could result in sensitisation or an allergic reaction by the patient or user;

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<p>(t) in the case of devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body and that are absorbed by or locally dispersed in the human body, warnings and precautions, where appropriate, related to the general profile of interaction of the device and its products of metabolism with other devices, medicinal products and other substances as well as contraindications, undesirable side-effects and risks relating to overdose;</p>				
<p>(u) in the case of implantable devices, the overall qualitative and quantitative information on the materials and substances to which patients can be exposed;</p>				
<p>(v) warnings or precautions to be taken in order to facilitate the safe disposal of the device, its accessories and the consumables used with it, if any. This information shall cover, where appropriate:</p> <ul style="list-style-type: none"> — infection or microbial hazards such as explants, needles or surgical equipment contaminated with potentially infectious substances of human origin, and — physical hazards such as from sharps. <p>If in accordance with the point (d) of Section 23.1 no instructions for use are required, this information shall be made available to the user upon request;</p>				
<p>(w) for devices intended for use by lay persons, the circumstances in which the user should consult a healthcare professional;</p>				
<p>(x) for the devices covered by this Regulation pursuant to Article 1(2), information regarding the absence of a clinical benefit and the risks related to use of the device;</p>				
<p>(y) date of issue of the instructions for use or, if they have been revised, date of issue and identifier of the latest revision of the instructions for use;</p>				
<p>(z) a notice to the user and/or patient that any serious incident that has occurred in relation to the device should be reported to the manufacturer and the competent authority of the Member State in which the user and/or patient is established;</p>				
<p>(aa) information to be supplied to the patient with an implanted device in accordance with Article 18;</p>				
<p>(ab) for devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.</p>				

Annex 6

to the Methodological rules

Application for substantial modification of clinical investigation under Medical Device Regulation

Harmonised form version 1.0

Section 1. Identification of the clinical investigation

Please provide the clinical investigation ID (CIV - ID)	
Does this substantial modification relate to a clinical investigation that is currently suspended/stopped?	Yes No
How many patients have been recruited in the clinical investigation in the EU/EEA: In the Member State you are submitting this substantial modification: outside the EU/EEA:	
Specify the Member State where this clinical investigation takes place:	

Section 2. Subject of the substantial modification

Please provide a short rationale of this substantial modification	
This substantial modification refers to <input type="checkbox"/> the subjects' rights <input type="checkbox"/> the subjects' safety <input type="checkbox"/> the subjects' health <input type="checkbox"/> Other	
This substantial modification shall impact the following: <input type="checkbox"/> the robustness of the clinical data generated by the investigation <input type="checkbox"/> the reliability of the clinical data generated by the investigation <input type="checkbox"/> Other <input type="checkbox"/> no impact on the subjects	

The documents that must be completed and attached and that best reflect the effects generated by the proposed substantial modification shall be identified in Annex 3 to this Order of the Minister of Health (containing the harmonised list of documents which must be attached to the registration form of an application for authorisation of a clinical evaluation or investigation for a medical device).

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I hereby certify that the information and documentation submitted with this substantial modification is correct in detail and all the information requested has been supplied. The investigated (medical) device complies with the applicable general safety and performance requirements, apart from those covered by the investigation and that every precaution has been taken to protect the health and safety of the patient and/or user. I confirm that all the clinical investigations information collected for this notification has been done in compliance with the European data protection legislation (GDPR).

Date:

Name:

Position:

Annex 7

to the Methodological rules

Authorisation/validation form for clinical investigation of a medical device

**AUTHORISATION/VALIDATION OF THE CLINICAL
INVESTIGATION**

of medical device

no. of

In line with the provisions of Art. 932 of Law 95/2006 on healthcare reform, republished, as further amended and supplemented, of Law no. 134 of 12 July 2019 on reorganisation of the National Agency for Medicines and Medical Devices and amendment of further ruling provisions, as further amended and supplemented, of Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC and of Emergency Government Ordinance no. 46/2021 on the establishment of the institutional framework and the measures necessary to ensure the direct application of the provisions of Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) no. 178/2002 and Regulation (EC) no. 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC as well as on the basis of the submitted documentation, the National Agency for Medicines and Medical Devices of Romania authorizes the conduct of the clinical investigation/validates the clinical investigation file for:

- medical device (name, type):
- trial name:
- sponsor:
- manufacturer
- protocol number:
- CIV-ID:

Any modification of the conditions established by the aforementioned Regulations that formed the basis of the authorisation/validation, as well as the failure to submit periodic reports*) of the results of the clinical investigation, shall lead to the cancellation of this document.

*) the frequency of reporting (quarterly, biannually or annually) shall be determined depending on the degree of risk of the medical device

President,
.....

Annex 8
to the Methodological rules

Clinical investigation - Form for reporting serious adverse events (SAEs) and medical device deficiencies (MDD) according to the MDR

In order to protect your data, we recommend converting this document to PDF format. Please submit the documents related to this document in their original format, not converted to this format. This form shall be amended after the European Commission has approved the harmonised form for reporting serious adverse reactions and deficiencies of medical devices subject to clinical evaluation/investigation.

1. Clinical investigation/evaluation identification data

Administrative information		
Date (day, month, year)		
"SAE/DD" Reporting	<input type="radio"/> Serious adverse event <input type="radio"/> Device deficiency	
Reference number of the Member State/competent authority		
Clinical investigation (CI) data		
EUDAMED number <i>(if available)</i>		
Registration number at the NAMMDR		
Trial name		
Sponsor		
Manufacturer		
Name of sponsor representative (EU, EEA) <i>(if available)</i>		
Contact person <i>(name, address, e-mail, telephone number)</i>		
Device under investigation <i>Name, product ID, version, type</i>		
Clinical investigation plan <i>Number/code</i>		
Trial site		
Event trigger date		
Current recruitment status	in Romania	outside Romania
• number of already recruited patients		
• (total) planned number of patients		
Total number of investigational devices used to date		
Number of devices used in the investigation to date per country		
Patient data		
Patient identifier		
Patient's age at the time of the event		
Patient's gender		

Classification of the event	<input type="radio"/> Death <input type="radio"/> Life-threatening illness or injury <input type="radio"/> Permanent impairment/chronic disease <input type="radio"/> Hospitalisation <input type="radio"/> Medical or surgical intervention <input type="radio"/> Foetal distress, foetal death or a congenital physical or mental impairment or birth defect <input type="radio"/> Not applicable	
Description of the event		
Arm	<input type="radio"/> Testing group <input type="radio"/> Comparator group <input type="radio"/> Blind <input type="radio"/> Not applicable	
Corrective action/treatment/patient response to treatment		
Connection of the event with the procedure	Sponsor	Investigator
	<input type="radio"/> No connection <input type="radio"/> Possible <input type="radio"/> Probable <input type="radio"/> Causal	<input type="radio"/> No connection <input type="radio"/> Possible <input type="radio"/> Probable <input type="radio"/> Causal
Connection of the event with the device	Sponsor	Investigator
	<input type="radio"/> No connection <input type="radio"/> Possible <input type="radio"/> Probable <input type="radio"/> Causal	<input type="radio"/> No connection <input type="radio"/> Possible <input type="radio"/> Probable <input type="radio"/> Causal
Status of the event	<input type="radio"/> Solved <input type="radio"/> Solved with sequelae <input type="radio"/> Ongoing <input type="radio"/> Death	
Event resolution date		