GUIDE

MEDICAL DEVICES
CLINICAL EVALUATION
SUMMARY OF SAFETY AND CLINICAL PERFORMANCE (SSCP)
REGULATION (EU) 2017/745

AUGUST 2020 EDITION

GUIDANCE FOR GMED CUSTOMERS
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GMED
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CONTENTS

REFERENCE DOCUMENTS

ORIGIN	REFERENCE	TITLE
European Union	Regulation (EU) 2017/745	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
European Union	MEDDEV 2.7/1 rev.4	Evaluation of clinical data: a guide for manufacturers and notified bodies
European Union	MEDDEV 2.12/2 rev.2	Guidelines on post-market clinical follow-up
CEN ISO	NF EN ISO 13485: 2016	Medical devices Quality management systems – Requirements for regulatory purposes
CEN ISO	NF EN ISO 14971: 2013	Medical devices – Application of risk management to medical devices.
CEN ISO	NF EN ISO 14155: 2012	Clinical investigation of medical devices for human subjects
GHTF	SG5/N1R8 (2007)	Clinical Evidence – Key definitions and concepts
GHTF	SG5/N2R8 (2007)	Clinical Evaluation
MDCG	MDCG 2019-9	Summary of safety and clinical performance A guide for manufacturers and notified bodies
MDCG	MDCG 2020-1	Guidance on Clinical Evaluation (MDR) / Performance Evaluation (IVDR) of Medical Device Software
MDCG	MDCG 2020-5	Clinical evaluation – Equivalence A guide for manufacturers and notified bodies
MDCG	MDCG 2020-6	Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC A guide for manufacturers and notified bodies
MDCG	MDCG 2020-7	Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies
MDCG	MDCG 2020-8	Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies
MDCG	MDCG 2020-13	Clinical evaluation assessment report template

NOTE

The European Regulation is published in the Official Journal of the European Union.
MEDDEV guidelines are available on the European Commission website:
https://ec.europa.eu/growth/sectors/medical-devices/current-directives/guidance_en
MDCG guidelines are available on the European Commission website:
https://ec.europa.eu/growth/sectors/medical-devices/new-regulations/guidance_en
Standards are available at AFNOR www.afnor.org
GHTF (Global Harmonization Task Force) guidelines are available on the following website:
http://www.imdrf.org/documents/documents.asp

II DEFINITIONS

Bias: bias is a systematic deviation of an outcome measure from its true value, leading to either an overestimation or underestimation of a treatment's effect. It can originate from, for example, the way patients are allocated to treatment, the way treatment outcomes are measured and interpreted, and the way data are recorded and reported.
[Adapted from GHTF SG5/N2R8:2007]

Clinical data: information concerning safety or performance that is generated from the use of a device and is sourced from the following:

- clinical investigation(s) of the device concerned,
- clinical investigation(s) or other studies reported in scientific literature, of a device for which equivalence to the device in question can be demonstrated,
- reports published in peer reviewed scientific literature on other clinical experience of either the device in question or a device for which equivalence to the device in question can be demonstrated,
- clinically relevant information coming from post-market surveillance, in particular the post-market clinical follow-up.

[Regulation (EU) 2017/745]

Clinical evaluation: a systematic and planned process to continuously generate, collect, analyse and assess the clinical data pertaining to a device in order to verify the safety and performance, including clinical benefits, of the device when used as intended by the manufacturer.
[Regulation (EU) 2017/745]

Clinical evidence: clinical data and clinical evaluation results pertaining to a device of a sufficient amount and quality to allow a qualified assessment of whether the device is safe and achieves the intended clinical benefit(s), when used as intended by the manufacturer.
[Regulation (EU) 2017/745]

Clinical investigation: a document that describes the rationale, objectives, design, methodology, monitoring, statistical considerations, organisation and conduct of a clinical investigation.
[Regulation (EU) 2017/745]
Note: "Clinical trial" or "clinical study" are synonymous with "clinical investigation" [EN ISO 14155:2011]

Equivalent device: a device for which equivalence to the device in question can be demonstrated *(See the explanation in this guidance document).*

Feasibility study: a clinical investigation that is commonly used to capture preliminary information on a medical device (at an early stage of product design) to adequately plan further steps of device development, including needs for design modifications or parameters for a pivotal study.
[MEDDEV 2.7/2 revision 2]

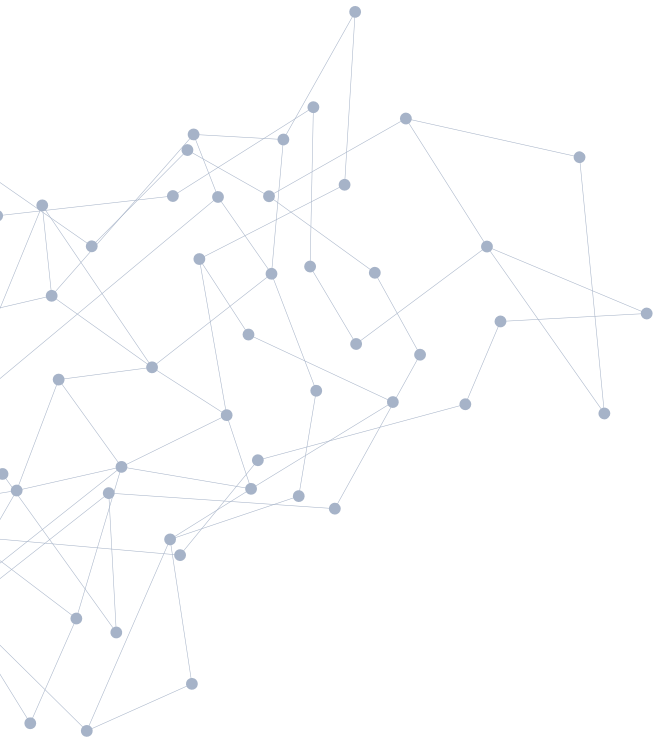
Clinical performance: the ability of a device, resulting from any direct or indirect medical effects which stem from its technical or functional characteristics, including diagnostic characteristics, to achieve its intended purpose as claimed by the manufacturer, thereby leading to a clinical benefit for patients, when used as intended by the manufacturer.
[Regulation (EU) 2017/745]

Clinical benefit: the positive impact of a device on the health of an individual, expressed in terms of a meaningful, measurable, patient-relevant clinical outcome(s), including outcome(s) related to diagnosis, or a positive impact on patient management or public health.
[Regulation (EU) 2017/745]

Clinical safety: freedom from unacceptable clinical risks, when using the device according to the manufacturer's Instructions for Use.
[MEDDEV 2.7/2 revision 2]
Note: In exceptional cases where an instruction for use (IFU) is not required, the collection, analysis and assessment are conducted taking into account generally recognised modalities of use.

Intended purpose: the use for which a device is intended according to the data supplied by the manufacturer on the label, in the instructions for use (IFU) or in promotional or sales materials or statements and as specified by the manufacturer in the clinical evaluation.
[Regulation (EU) 2017/745]

Post-market surveillance: all activities carried out by manufacturers in cooperation with other economic operators to institute and keep up to date a systematic procedure to proactively collect and review experience gained from devices they place on the market, make available on the market or put into service for the purpose of identifying any need to immediately apply any necessary corrective or preventive actions.
[Regulation (EU) 2017/745]



Post-market clinical follow-up (PMCF): means all activities carried out by manufacturers in cooperation with other economic operators to institute and keep up to date a systematic procedure to proactively collect and review experience gained from devices they place on the market, make available on the market or put into service for the purpose of identifying any need to immediately apply any necessary corrective or preventive actions.
[Regulation (EU) 2017/745]

PMCF study: a study carried out following the CE marking of a device and intended to answer specific questions relating to clinical safety or performance (i.e. residual risks) of a device when used in accordance with its approved labelling.
[MEDDEV 2.12/2 rev.2]

Sufficient clinical evidence: an amount and quality of clinical evidence to guarantee the scientific validity of the conclusions.
[MEDDEV 2.7/1 revision 4]

Indication/Indication for use: refers to the clinical condition that is to be diagnosed, prevented, monitored, treated, alleviated, compensated for, replaced, modified or controlled by the medical device. It should be distinguished from 'intended purpose/intended use', which describes the effect of a device. All devices have an intended purpose/intended use, but not all devices have an indication (e.g. medical devices with an intended purpose of disinfection or sterilisation of devices).
[MDCG 2020-6]

Similar device: devices belonging to the same generic device group. The Regulation (EU) 2017/745 defines this as a set of devices having the same or similar intended purposes or a commonality of technology allowing them to be classified in a generic manner not reflecting specific characteristics.
[MDCG 2020-6]

III PART A: CLINICAL EVALUATION

Confirmation of conformity with relevant general safety and applicable performance requirements to Regulation (EU) 2017/745, under the normal conditions of the device intended use, as well as the evaluation of the undesirable side-effects and of the acceptability of the benefit-risk ratio is based on clinical data providing sufficient clinical evidence.

It is the manufacturer's responsibility to specify and justify the level of clinical evidence necessary to demonstrate conformity with the relevant general safety and performance requirements. That level of clinical evidence shall be appropriate in view of the characteristics of the device and its intended purpose.

To that end, manufacturers plan, perform and document a clinical evaluation.

The purpose of this section, to the attention of medical device manufacturers, is to describe the different elements to be included in:

- The clinical evaluation plan
- The clinical evaluation report
- The post-market surveillance plan including the post-market clinical follow-up (PMCF) plan
- The PMCF evaluation report.

All these documents are part of the technical documentation that the manufacturer must establish to demonstrate the conformity of its device with the relevant provisions of Regulation (EU) 2017/745.

Preamble:

- In case of the devices concerning by the specific procedure of article 54 in Regulation (EU) 2017/745, namely class III implantable devices and class IIb active devices intended to administer in the organism and / or remove medicinal products, body liquids or other substance to /of from the body, the manufacturer is requested to send the clinical evaluation report in duplicate and in English.
- In case of devices that have used the provisions of article 61, paragraph 2, in Regulation (EU) 2017/745, namely a prior consultation with a group of experts, the manufacturer is requested to transmit the opinion issued by the group of experts, as part of the clinical data evaluation.
- In case of medical device software, the manufacturer is requested to use the MDCG guide: « MDCG 2020-1 Guidance on Clinical Evaluation (MDR) / Performance Evaluation (IVDR) of Medical Device Software » in order to carry out the clinical data evaluation.

1 → Principles of clinical evaluation

1.1 What is a clinical evaluation?

Clinical evaluation is a methodologically sound ongoing procedure to collect, appraise and analyse clinical data pertaining to a device and to analyse whether there is sufficient clinical evidence to confirm compliance with relevant essential requirements for safety and performance when using the device according to the manufacturer's instructions for use.

Clinical evaluation is a requirement of Regulation (EU) 2017/745 which applies to all classes and types of devices, including devices for which demonstration of conformity with the general safety and performance requirements based on clinical data is not deemed appropriate as well as device without an intended medical purpose listed in Annex XVI to Regulation (EU) 2017/745. The evaluation should be appropriate to the device assessed, its specific properties, and its intended purpose.

Please note that the article 61, paragraph 10, of Regulation (EU) 2017/745 which allows the use of non-clinical data to demonstrate the conformity with the general safety and performance requirements does not apply to implantable devices or class III devices.

Conformity to the essential requirements for safety and performance can only be assumed when the following items are aligned with each other:

1. The information supplied by the manufacturer (the labelling, instructions for use, available promotional materials, including accompanying documents foreseen by the manufacturer),
2. The clinical evaluation (the device description used for the clinical evaluation, results of clinical investigations, publications, post-market clinical follow-up studies, other content of the clinical evaluation report),
3. The risk management file,
4. The usability demonstration.

1.2. When clinical evaluation is to be performed?

Clinical evaluation is conducted throughout the life cycle of a device, as an ongoing process.

Usually, it is first performed during the development of a medical device in order to identify data that need to be generated for market access. Clinical evaluation is mandatory to obtain CE marking and it must be actively updated thereafter.
As reminder, it addresses the section 7.3.7 of the ISO 13485 standard, current version.

- **During device development**
  Typically, manufacturers carry out clinical evaluations to:

1. Define needs regarding clinical safety and clinical performance (including clinical benefit) of the device;
2. In case of possible equivalence to an existing device, evaluate if there are clinical data available and determine equivalence;
3. Carry out a gap analysis and define which data still need to be generated for the device under assessment, whether clinical investigations are necessary and if so, to define the study.

- **Clinical evaluation for CE marking**
  Clinical evaluation is required to be carried out for the conformity assessment process leading to the CE marking and placing on the market of a device. The purpose is to:

1. document that there is sufficient clinical evidence to demonstrate conformity with the relevant general safety and performance requirements;
2. identify aspects that need to be systematically addressed during post-market surveillance, e.g. the required post-market clinical follow-up studies (PMCF). Typically, these aspects include estimation of residual risks and uncertainties or unanswered questions (such as rare complications, uncertainties regarding long-term performance, safety under wide-spread use).

- **Updating the clinical evaluation: frequency and consideration**
  The manufacturer should define and justify the frequency at which the clinical evaluation needs to be actively updated.

It should ensure that the clinical evaluation and the documentation relating thereto are updated throughout the life cycle of the device concerned using clinical data obtained following the application of its post-market surveillance plan, including the PMCF plan.

For class III devices and implantable devices, the PMCF evaluation report and, where applicable, the summary of safety and clinical performance, are updated at least annually by adding the relevant data.

Please note that for each update of the summary of safety and clinical performance, the manufacturer must send the summary to GMED for validation and upload of the summary in the European database on medical devices (EUDAMED) as soon as EUDAMED will be fully functional.

At the end of the conformity assessment process, GMED decides a specific frequency for review the updated clinical evaluation. The frequency at which the clinical evaluation will be updated by the manufacturer must be coordinated with the timeline set by GMED.

1.3. Clinical investigation in the case of implantable devices and class III devices

As a general rule, in case of implantable devices and class III devices, clinical investigations shall be performed.

However, there is no need to conduct clinical investigations in the following cases:

Case 1:
- The device has been designed by modifications of a device already marketed by the same manufacturer,
- The manufacturer has demonstrated that the modified device is equivalent (see part IV) to the device marketed, and this demonstration has been approved by GMED, and
- The clinical evaluation of the marketed device is sufficient to demonstrate conformity of the modified device with the relevant safety and performance requirements.

Case 2:
- The manufacturer has demonstrated that its device is equivalent to a device already on the market and not manufactured by itself,
- The two manufacturers have a contract in place that explicitly allows the manufacturer of the second device full access to the technical documentation on an ongoing basis, and
- The original clinical evaluation has been performed in compliance with the requirements of the Regulation (EU) 2017/745, and
- The manufacturer of the second device provides clear evidence thereof to GMED.

Case 3:
- The device has been lawfully placed on the market or put into service in accordance with Directive 90/385/EEC or Directive 93/42/EEC,
- The clinical evaluation is based on sufficient clinical data, and
- The clinical evaluation complies with the relevant product-specific common specification (CS) for the clinical evaluation of that kind of device, where such CS is available.

Case 4:
- The device belongs to the following list: sutures, staples, dental filling products, orthodontic appliances, dental crowns, screws, wedges, plates, guides, pins, clips, connection devices,
- The clinical evaluation is based on sufficient clinical data, and
- The clinical evaluation complies with the relevant product-specific CS for the clinical evaluation of that kind of device, where such a CS is available.

In cases 1 and 2, GMED verifies that the PMCF plan is appropriate and includes post-market studies to demonstrate the safety and performance of the device.

In cases 3 and 4, the manufacturer justifies his decision not to conduct clinical investigations in the clinical evaluation report. GMED shall also justify this decision in the clinical evaluation report assessment.

1.4. How is Clinical Evaluation performed?

There are distinct stages in performing a clinical evaluation:

- **Preliminary stage** – clinical evaluation planning
  - Establishes the clinical evaluation plan.

- **Stage 0** – Scope of clinical evaluation:
  - Explains the scope and context of the evaluation, including which products/ models/ sizes/ settings are covered by the clinical evaluation report, and the technology on which the medical device is based.

- **Stage 1** – Identification of pertinent data:
  - Describes the literature search strategy;
  - Presents the nature and extent of the clinical data and relevant pre-clinical data that have been identified.

- **Stage 2** – Appraisal of pertinent data:
  - Evaluates the clinical data identified in the previous step, their methodological quality, their scientific validity, the relevance for the evaluation, the weighting attributed to the evidence, and any limitations.

The clinical data sets should be subject to an appraisal with respect to their relative contribution to the overall clinical evaluation. It is important to perform analysis of the methodological quality of data obtained from different sources to identify and assess the level of evidence, bias, other inherent weakness or other possible shortcomings. Indeed, clinical investigations, scientific literature, post-market clinical data and other sources of clinical data can be of variable methodological quality and therefore an appraisal of the design of these studies is important.

Clinical data appraisal should be conducted using verified/validated assessment tools. Among these methodological quality assessment tools, we find the tools described in Appendix F of IMDRF MDCE WG/N56 on Clinical Evaluation, Cochrane Collaboration's tool for Randomized Controlled Trials (RCT), MINORS (Methodological index for non-randomized studies), Reisch tool (for non-randomized interventional studies), Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomised studies in meta-analyses. This list is not exhaustive. Additional validated tools may be used.

  - Presents justifications for rejecting certain data or documents.

- **Stage 3** – Summary and analysis of data:
  - Summarizes the relevant data provided
  - Analyses relevant data provided to demonstrate:
    . The conformity to the safety requirements;
    . The conformity to the performance and clinical benefit requirements;
    . The conformity to the requirement related to acceptable benefit/risk, including acceptability of undesirable side-effects.

It is noted that the utilisation of post-market surveillance data, such as data from customer complaints, vigilance, incidence report or any other vigilance, for the purpose of conformity assessment cannot always provide reliable data with respect to the incidence of risks due to limitations of complaints reporting, misuse... Therefore, the use of ratio [number of incidents or complaints] / [number of device sales] cannot be considered sufficient to provide proof of device safety. Their use should be limited to cases where data from pre-market or post-market clinical investigations are not deemed appropriate.

- **Stage 4** – Finalise the clinical evaluation report:
  - Provides clear statement concerning compliance to general safety and performance requirements;
  - Takes into account the opinion of the expert group, when applicable;
  - Justifies the acceptability of the benefit/risk profile according to current knowledge/ the state of the art in the medical fields concerned and according to available medical alternatives;
  - Declares suitability of the device, including its IFU, for the intended users and usability aspects; discrepancies;
  - Evaluates if there is consistency between the clinical data, the information materials supplied by the manufacturer, the risk management documentation for the device under assessment; discrepancies.

1.5. What is the post-market surveillance plan?

The post-market surveillance plan relates to the collection and usage of available information, in particular:

- Information concerning serious incidents, including information from PSURs, and field safety corrective actions;
- Records referring to non-serious incidents and data on any undesirable side-effects;
- Information from trend reporting;
- Relevant specialist or technical literature, databases and/or registries;
- Information, including feedbacks and complaints, provided by users, distributors and importers, and
- Publicly available information about similar medical devices.

1.6. What is the post-market clinical follow-up plan?

The PMCF plan specifies the methods and procedures for proactively collecting and evaluating clinical data with the aim of:

- Confirming the safety and performance of the device throughout its expected lifetime;
- Identifying previously unknown side-effects and monitoring the identified side-effects and contraindications;
- Identifying and analysing emergent risks on the basis of factual evidence;
- Ensuring the continued acceptability of the benefit-risk ratio referred to in Annex I, sections 1 and 9 of Regulation (EU) 2017/745; and
- Identifying possible systematic misuse or off-label use of the device, with a view to verifying that the intended purpose is correct.

The MDCG 2020-7 « Post-market clinical follow-up (PMCF) Plan template – A guide for manufacturers and notified bodies » provides a PMCF plan template to meet the requirement of Regulation (EU) 2017/745. GMED advises the manufacturer to use this template to build the PMCF plan.

1.7. Who should perform a clinical evaluation?

The clinical evaluation should be conducted by a suitably qualified individual or a team.

The manufacturer should take the following aspects into consideration:

1. The manufacturer defines requirements for the product reviewers that are in line with the nature of the device under evaluation and its clinical performance and risks;
2. The manufacturer should be able to justify the choice of the product reviewers through reference to their qualifications and documented experience, and to present a declaration of interest for each product reviewer.

As a general principle, the product reviewers should possess knowledge of the following:

1. Research methodology (including clinical investigation design and biostatistics);
2. Information management (e.g. scientific background or librarianship qualification; experience with relevant databases such as Embase and Medline);
3. Regulatory requirements;
4. Medical writing (e.g. post-graduate experience in a relevant science or in medicine; training and experience in medical writing, systematic review and clinical data appraisal).

With respect to the particular device under evaluation, the product reviewers should in addition have knowledge of:

1. The device technology and its application;
2. The diagnosis and management of the conditions for which the device is intended to be used, knowledge of medical alternatives, treatment standards and technology (e.g. specialist clinical expertise in the relevant medical specialty).

The product reviewers should have at least the following training and experience in the relevant field:

1. A degree from higher education (undergraduate degree) in the relevant field and 5 years of documented professional experience; or
2. 10 years of documented professional experience if a degree is not a prerequisite for a given task, related to the clinical evaluation.

There may be circumstances where the level of product reviewer expertise may be less or different; this should be documented and duly justified. It is understood that the competences can be shared on a team, knowing that the plan and the report need to be signed by all the members of the team.

2. → Equivalence

Clinical, technical and biological characteristics shall be taken into consideration for the demonstration of equivalence:

- Clinical, the device shall be:
  - used for the same clinical condition or purpose, including similar severity and stage of disease,
  - used at the same site in the body,
  - used in a similar population, including as regards age, anatomy and physiology, possibly other aspects,
  - used by the same kind of user, and
  - have similar relevant critical performance in view of the expected clinical effect for a specific intended purpose.
- Technical, the device shall:
  - be similar design,
  - used under similar conditions of use,
  - have similar specifications and properties including physicochemical properties such as intensity of energy, tensile strength, viscosity, surface characteristics, wavelength and software algorithms,
  - used similar deployment methods, where relevant, and,
  - have similar principles of operation and critical performance requirements.
- Biological, the device shall:
  - use the same materials or substances in contact with the same human tissues or body fluids for a similar kind and duration of contact and similar release characteristics of substances, including degradation products and leachables.

Different aspects of equivalence and conformity of different general safety and performance requirements can be affected by materials. Assessors should consider biological safety (e.g. in compliance to ISO 10993) as well as other aspects necessary for a comprehensive demonstration of equivalence. A justification explaining the situation should be provided for any differences.

For assuming equivalence:

- Equivalence can only be based on a single device;
- all three characteristics (clinical, technical, biological) need to be fulfilled;
- similar means that no clinically significant difference in the performance and safety of the device would be triggered by the differences between the device under evaluation and the device presumed to be equivalent;
- the differences between the device under evaluation and the device presumed to be equivalent need to be identified, fully disclosed, and evaluated; explanations should be given why the differences are not expected to significantly affect the clinical performance and clinical safety of the device under evaluation.

- The manufacturer should investigate if the medical device presumed to be equivalent has been manufactured via a special treatment (e.g. a surface modification, a process that modifies material characteristics); if this is the case, the treatment could cause differences in respect to technical and biological characteristics; this should be taken into account for the demonstration of equivalence and documented in the clinical evaluation report;

- if measurements are possible, clinically relevant specifications and properties should be measured both in the device under evaluation and the device presumed to be equivalent, and presented in comparative tabulations;

- comparative drawings or pictures should be included in order to compare shapes and sizes of elements that are in contact with the body.

- The manufacturer is expected to:
  - include the supporting non-clinical information (e.g. pre-clinical study reports) in the technical documentation of the device; and
  - in the clinical evaluation report, summarise the information and cite its location in the technical documentation.

- For the evaluation of the technical characteristics, devices that achieve the same therapeutic result by different means cannot be considered equivalent.

- For the evaluation of the biological characteristics:
  - when a detailed chemical characterisation of materials in contact with the body is needed, ISO 10993-18 Annex C can be used to show toxicological equivalence but this is just one part of the evaluation of the biological criteria;
  - sourcing and manufacturing procedures may adversely affect impurity profiles; analytical methods chosen to characterise medical devices should appropriately take into consideration knowledge concerning expected impurity profiles (tests may have to be repeated when production methods or sourcing are modified);
  - it may be necessary to show from histopathological studies that the same host response is achieved in vivo in the intended application and the intended duration of contact;
  - for animal tests, differences between species may limit the predictive value of the test; the choice of the test and its predictive value should be justified;
  - abrasion, if relevant, and host response to particles may also need to be considered.

- For the clinical characteristics evaluation:
  - the only clinical data that are considered relevant are the data obtained when the equivalent device is a CE marked medical device used in accordance with its intended purpose as documented in the IFU.

- For implantable devices and class III devices:
  - when the equivalence concerns implantable devices and class III devices already marketed and not manufactured by the manufacturer itself and this equivalence allows the manufacturer to not conduct clinical investigations, the manufacturer must provide a contract concluded between the two manufacturers who explicitly allows the manufacturer of the device under clinical evaluation full access to the technical documentation on an ongoing basis as well as clear evidence that the original clinical evaluation has been performed in accordance with the requirements of Regulation (EU) 2017/745.

- For devices other than implantable devices and class III devices:
  - when the equivalence concerns devices other than implantable devices and class III devices already marketed and not manufactured by the manufacturer itself and this equivalence allows the manufacturer to not conduct clinical investigations, the Regulation (EU) 2017/745 does not require a contract between the two manufacturers allowing full access to the technical documentation. However, the manufacturer must have a sufficient level of access to data relating to the devices with which it claims equivalence and document this access.

  - **Note:** Exceptions can be considered. When the equivalent device is not a CE marked device, information concerning the regulatory status of the equivalent device and a justification for the use of its data shall be included in the clinical evaluation report. All applicable (EU) 2017/745 requirements on equivalence and clinical evaluation shall be met. The justification shall explain if the clinical data is transferrable to the European population, and include an analysis of any gaps to good clinical practices and relevant harmonised standards (such as ISO 14155).

- For device without an intended medical purpose:
  - In case of products without an intended medical purpose listed in Annex XVI of Regulation (EU) 2017/745, clinical investigations shall be performed for those products unless reliance on existing clinical data from an analogous medical device is duly justified. An analogous device, in this context, is understood as a medical device which is similar in terms of functioning and risks profile and has a medical purpose.

To duly justify reliance on existing clinical data from an analogous device, the principles of demonstration of equivalence should be applied with the acceptance that the device under evaluation will only have an aesthetic or another non-medical purpose whereas the analogous device has a medical purpose. The general requirement to demonstrate a clinical benefit shall be understood as a requirement to demonstrate the performance of the device.

In addition, since the common specifications (CS) for the products without an intended medical purpose may have requirements related to the clinical evaluation regarding safety, these requirements must be taken into consideration when demonstrating equivalence and concluding whether there would be no clinically significant difference in the safety.

There shall be no significant difference in the safety and performance between the product and the presumed analogous medical device.

3. → Clinical evaluation plan

The manufacturer must establish a clinical evaluation plan which, at least:

- identifies the general safety and performance requirements that require support from relevant clinical data;
- specifies the device intended purpose;
- specifies clearly the intended target groups with clear indications and contra-indications;
- describes in detail the intended clinical benefits to patients with relevant and specified clinical outcome parameters;
- specifies 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 side-effects;
- provides 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 device intended purpose(s);
- indicates how benefit-risk issues relating to specific components such as use of pharmaceutical, non- viable animal or human tissues, are to be addressed; and
- includes 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 with an indication of milestones and a description of potential acceptance criteria.

The clinical evaluation plan must be systematically attached to the clinical evaluation report.

Note that for the devices covered by a CE marking certificate under Directive 93/42/EEC or 90/385/EEC (legacy devices), the content of the clinical evaluation plan can be adapted to this type of devices.

Consequently, the clinical evaluation plan expected for this type of device should include at least:

- 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 contraindications;
- A detailed description of intended clinical benefits to patients with relevant and specified clinical outcome parameters;
- A strategy to identify, analyse and assess alternative treatments;
- 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 device intended purpose(s);
- 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;
- A strategy and methodology to identify, analyse and assess all relevant available clinical data in light of the changed definition for clinical data;
- Evidence for equivalence, if clinical data from an equivalent device is included in the clinical evaluation;
- A definition of the required level of clinical evidence, which shall be appropriate in view of the characteristics of the device and its intended purpose;
- A strategy and methodology to systematically collect, summarise and assess post-market surveillance data to demonstrate continuing safety and performance, and to what extent complaints with regards to safety and performance have been observed with the legacy devices.

4. → Clinical evaluation report (CER)

The elements of the clinical evaluation report are records of the process that the manufacturer applies to the identification, selection, evaluation and critical analysis of clinical data in order to meet the relevant provisions of Regulation (EU) 2017/745.

The table below gives an example of the clinical evaluation report possible content. It is recommended that the manufacturer follows this template.

TABLE OF CONTENTS	EXAMPLE OF CONTENTS
Section A : *Manufacturer, product and clinical evaluation report reference, type of assessment*	– **Medical device name model and type** – **Risk class** – **Basic UDI-DI(s)** (if available) – **Applicable code(s)** per Commission Implementing Regulation (EU) 2017/2185 – **CND code** (code of the CND nomenclature, with the maximum digits, corresponding to the device) – **For class IIb and implantable IIb class devices limited to sutures, dental fillings, dental braces, tooth crowns, screws, wedges, plates, wires, pins, clips and connectors, provide generic device group** – **For class IIa devices, provide category of device** – **Certificate number** (if applicable) – **Manufacturer's clinical evaluation report reference**
	– **Manufacturer(s) name and SRN** – **Authorized representative name** (if applicable) **and SRN**
	– **Type of assessment:** • Initial conformity assessment, or • Assessment of changes and clinical evaluation update, or • Re-certification assessment, or • Technical documentation assessment for class IIa/ IIb devices on a sampling basis – **Conformity assessment route under Regulation (EU) 2017/745:** • Annex IX Chapters I, II and III, or • Annex X + Annex XI Part A, or • Annex X + Annex XI Part B, or • Annex IX Chapters I and III with sampling of technical documentation assessment as specified in section 4 of Annex IX, or • Annex XI - Part A - Including section 10, or • Annex XI - Part B - Including section 18
	– **Intended purpose as claimed**
	– **Type of clinical evaluation:** • The scientific literature currently available and/or • Clinical investigations carried out by the manufacturer Or • Demonstration of compliance with general safety and performance requirements based on clinical data is not considered appropriate
	– **CVs of CER author(s)** – **Report's author(s) declaration of interests**

4. → Clinical evaluation report (CER) (afterparts)

TABLE OF CONTENTS	EXAMPLE OF CONTENTS
Section B : *Device description, classification, clinical evaluation plan , manufacturer's claim, common specifications and harmonized standards applied, equivalence and state of the art*	**1. Device description:** Describe the device and comment on the intended use, 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 device operation principles and its mode of action; explanation of any novel features • Intended application of the device: single use/reusable, invasive/non-invasive, implantable • The duration of use or contact with the body, the maximum number of repeated applications • The identification of organs, tissues or bodily fluids in contact by the device. **2. Classification:** Applicable classification rule(s) and indents. **3. Device configurations/variants:** • Description of the sizes, differences in design features, different configurations etc. • Image of the device where possible • If applicable, description of the device history and/or changes in the device since its last assessment • Where relevant, description of the reason for differences in design variants with illustrative images where possible **4. Accessories or compatible devices:** Description, images or other relevant information such as diagrams if necessary **5. Previous and similar generations of the device (if applicable):** • Whether the device is already CE marked, whether it is on the market, since when, in what regions, history of the device, including date of past modifications with reasons and description, sales volumes • 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 in the European Union or international markets, where such devices exist, including length of time on the market, sales volume etc **6. Clinical evaluation plan:** • Clinical evaluation plan • Exact description of indications and contra-indications • Identification of target patient population and target user group • Describe the claims on clinical performance and clinical safety foreseen by the manufacturer • Describe the clinical benefits sought for the patients, using relevant and precise parameters in terms of clinical results

4. → Clinical evaluation report (CER) (afterparts)

TABLE OF CONTENTS	EXAMPLE OF CONTENTS
Section B : *Device description, classification, clinical evaluation plan , manufacturer's claim, common specifications and harmonized standards applied, equivalence and state of the art*	**7. Common specifications and harmonized standards applied:** If Common Specifications are not applied: • Identification of any deviations and how these might affect the validity of the clinical evaluation and its conclusions, and any equivalence claims • Identification of adopted solutions that ensure a level of safety and performance that is at least equivalent thereto in accordance with Article 9(3) of Regulation (EU) 2017/745 If harmonized standards not applied or partially applied: • Identification of adopted solutions that ensure a level of safety and performance required by the Regulation (EU) 2017/745 • Identification of any deviations and how these might affect the validity of the clinical evaluation and its conclusions, and any equivalence claims **8. The demonstration of equivalence:** a) Device(s) to which equivalence has been claimed: • Identification of the equivalent device(s) and its manufacturer: – Exact name, models, sizes, software versions, accessories, etc. – Name of the manufacturer – Relationship to the device under evaluation (predecessor/ successor, others). If the device is not CE marked, justification for the use of the data, based on the other regulatory status b) Equivalence: • Comparative tables for device(s) under evaluation compared to the equivalent device showing the parameters relating to the evaluation of the three characteristics in accordance with Annex XIV, section 3, of Regulation (EU) 2017/745 • Justification of equivalence in accordance with section 3 of Annex XIV, description of relevant clinical, biological and technical characteristics that affect clinical properties of the device. Comparative diagrams or photos of the device and equivalent device(s) showing the elements in contact with the body • Identification of any testing which may have been undertaken to confirm equivalence of specifications/performance,etc • Conclusions whether equivalence is demonstrated or not; if it is demonstrated, confirmation that the differences are not expected to affect the clinical performance and clinical safety of the device under evaluation; description of any limitations and gaps **9. Access to data:** • For implantable and Class III devices, if equivalence is claimed with a device marketed by another manufacturer, a current valid contract between the two manufacturers allowing ongoing access to the technical documentation in accordance with Article 61(5) of Regulation (EU) 2017/745, as well as clear evidence that the original clinical evaluation was carried out in accordance with the requirements of Regulation (EU) 2017/745.

4. → Clinical evaluation report (CER) (afterparts)

TABLE OF CONTENTS	EXAMPLE OF CONTENTS
Section B : *Device description, classification, clinical evaluation plan , manufacturer's claim, common specifications and harmonized standards applied, equivalence and state of the art*	**10. State of the art:** a) Clinical context: • Identification of medical fields concerned/relevant medical conditions • Description, natural course and consequences of the medical conditions concerned. Whether there are different clinical forms, stages and severities of the conditions. Frequency in the general population, by age group, gender, ethnicity, familiar predispositions, genetic aspects b) Literature search: • A Brief summary and justification of the literature search strategy applied for retrieval of information on current knowledge/the state of the art, including sources used, search questions, search terms, selection criteria applied to the output of the search, quality control measures, results, number and type of literature found to be pertinent • Literature search documentation to provide: – Literature search protocol – Literature search report – Full list of retrieved articles – Full list of excluded articles provided, with reasons for exclusion – Full text copies of relevant documents available c) Benchmark devices, state of the art and other available treatment options: • Description of available therapeutic/ management/ diagnostic options, historical context and developments, summary of advantages and disadvantages of the different options, benefit/risk profiles and limitations in relation to the different clinical forms, stages, and severities of the medical conditions and in relation to different target populations. Description of the benefits and risks (nature, extent, probability, duration, frequency), acceptability of undesirable side-effects and other risks (including the nature, severity, probability and duration of acceptable harm) d) Safety, performance and risk-benefit claims - requirements in terms of the state of the art: • Performance and safety endpoints identified by the manufacturer • Outcomes achievable with benchmark products and other treatment options • Safety and performance references identified by the manufacturer in terms of the state of the art • Description of 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 device intended purpose(s) **11. Novelty:** • Identification of the degree of novelty for the device according to the ANSM degree of novelty for a medical device (see Annex 1 of this guide) • Explanation of any novel features of the device and/or the related clinical procedures and their purpose • Detail on possible clinical or health impact in terms of benefit-risk

4. → Clinical evaluation report (CER) (afterparts)

TABLE OF CONTENTS	EXAMPLE OF CONTENTS
Section C : *Clinical literature review*	**12. Brief summary and justification of the literature search strategy applied for retrieval of clinical data on the device under evaluation or on a device demonstrated to be equivalent:** • Detail search terms, databases used, inclusion and exclusion criteria, quality control measures, results, number and type of literature found to be pertinent **13. Literature search documentation to provide:** • Literature search protocol • Literature search report • Full list of retrieved articles • Full list of excluded articles provided, with reasons for exclusion • Full text copies of relevant documents available **14. Data appraisal:** • Summary of the data appraisal methods applied to evaluate their methodological quality, scientific validity, relevance to the clinical evaluation, weighting attributed to the data
Section D : *Clinical investigations and related documentation*	**15. Pre-market or post-market clinical investigations:** – If pre-market or post-market clinical investigations were conducted, provide the following elements: • Clinical investigation plan (CIP) • Copy of all clinical investigation reports • Information on publicly registration of clinical investigations • Information on publicly registration on EUDAMED of clinical investigations conducted with respect to Regulation (EU) 2017/745, including EUDAMED single registration number where available • All Competent/Regulatory Authority correspondence (from all countries, including outside of EU) • A rational if clinical investigations not performed under Regulation (EU) 2017/745 were not publicly registered or published – If any pre-market or post-market clinical investigations were not conducted, provide a rationale

4. → Clinical evaluation report (CER) (afterparts)

TABLE OF CONTENTS	EXAMPLE OF CONTENTS
Section E : *PMS and PMCF*	**16. Post-Market Surveillance and a Post-Market Clinical Follow up:** – If PMS and PMCF are conducted, provide the following documents: • PMS Plan • PMS Report (where relevant) • PMCF Plan, PMCF Report (where relevant) • PSUR (if available) ***Please, note that the MDCG 2020-7 "Post-market clinical follow-up (PMCF) Plan template – A guide for manufacturers and notified bodies" provides a PMCF plan template to meet the requirement of the Regulation (EU) 2017/745. GMED advises the manufacturer to use this template to build the PMCF plan.*** ***Please, note that the MDCG 2020-8 "Post-market clinical follow-up (PMCF) Evaluation Report Template - A guide for manufacturers and notified bodies" provides a PMCF evaluation report template to meet the requirement of the Regulation (EU) 2017/745. GMED advises the manufacturer to use this template to build the PMCF evaluation report.*** • If no PMCF is planned, provide a justification for not conducting a PMCF **17. Demonstration of equivalence and link to post-market clinical follow-up:** Description of the means implemented to verify that there are no clinically significant difference in the safety and clinical performance of the device under evaluation compared with the equivalent device which appears during post-market surveillance or post-market clinical follow-up
Section F : *IFU, SSCP, labelling and other information supplied with the device*	**18. Information as provided in IFU and all information materials supplied with the device:** • Intended purpose as claimed • Intended patient population • Intended users • Indications • Contraindications • Limitations • Undesirable effects • Warnings and precautions **19. Identification of consistency or differences between the clinical data, the information materials supplied by the manufacturer, the risk management file for the device under evaluation**

4. → Clinical evaluation report (CER) (afterparts)

TABLE OF CONTENTS	EXAMPLE OF CONTENTS
Section G : *Summary of all available data and conclusions*	**20. Summary of safety data:** • Summary of safety data (with reference to the relevant section of the CER and the PMCF Evaluation Report). The qualitative and quantitative aspects of clinical safety should be addressed 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 of Regulation (EU) 2017/745. • Summary of clinical data regarding safety, and also residual risks and any undesirable side-effects. The methods to be used for examination of qualitative and quantitative aspects of clinical safety should be specified with clear reference to the determination of residual risks and undesirable side-effects. • If relevant, summary of any significant complaint, trends or vigilance issues associated with earlier device iterations, which may be equivalent or similar devices, and an explanation whether or not they have any impact on the clinical evaluation assessment. **21. Summary of performance data:** • Summary of performance data (with reference to the relevant section of the CER and the PMCF Evaluation Report). • Summary of 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. **22. Justify that the clinical data provide sufficient clinical evidence:** • To demonstrate of compliance with the relevant general safety and performance requirements • To support the intended use, the claims and the information in the IFU and SSCP **23. Identification of unanswered questions regarding the device under evaluation and description of means put in place during the PMS and PMCF; follow-up on these questions**

4. → Clinical evaluation report (CER) (afterparts)

TABLE OF CONTENTS	EXAMPLE OF CONTENTS
Overall conclusions	**24. Summary of clinical benefits:** • Describe the clinical benefits 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 **25. Summary and short description of risks with clinical relevance:** • Information on uncertainties or limitations of clinical data, undesirable side-effects, potential for misuse, etc. • Information on incidence, severity, duration, vulnerable patient subgroups, dose-response relationship where relevant, etc. **26. Discussion on the impact of risks (as described above) in relation to the clinical benefits taking into account the factors and in particular the uncertainties in relation to available clinical data** **27. Information on consistency or discrepancies between the clinical data, the information materials supplied by the manufacturer, the risk management documentation for the device** **28. Conclusion on the ratio benefits/risks related to clinical also considering the current state of the art**
Specific Considerations	
Section H : *Where demonstration of conformity based on clinical data is not deemed appropriate (Article 61(10) of Regulation (EU) 2017/745)*	If the demonstration of conformity with general safety and performance requirements based on clinical data is not deemed appropriate, adequate justification based on proof should be given in accordance with Article 61(10) of Regulation (EU) 2017/745. ***It should be noted that in this case, a clinical evaluation is still required and the evidence-based justification shall be presented in the clinical evaluation report.*** **The justification that the demonstration of conformity with general safety and performance requirements based on clinical data is not deemed appropriate should be based on:** • The results of the manufacturer's risk management and on consideration of the specifics of the interaction between the device and the human body • The clinical performance intended and • The claims of the manufacturer • Any clinical data available on the device or an equivalent device • Clinical data available for similar devices if these provide information relevant to the safety and performance of the device being evaluated **After this justification, the demonstration of conformity with general safety and performance requirements should be documented. This demonstration should be based on:** • The results of non-clinical test methods, such as performance evaluation • Test benches and • Preclinical evaluation
Section I : *The voluntary clinical consultation on the clinical development strategy (Article 61(2) of Regulation (EU) 2017/745)*	• Expert panel consultation reference • Expert panel recommendation • Expert panel recommendation in the clinical evaluation report

IV PART B: SUMMARY OF SAFETY AND CLINICAL PERFORMANCE

Article 32 of Regulation (EU) 2017/745 requires manufacturers to establish a summary of the safety and clinical performances for implantable devices and class III devices other than custom-made devices or devices subject to an investigation.

The minimum content of the summary of safety and clinical performances is defined in Article 32(2) of Regulation (EU) 2017/745.

The MDCG has published a guide for manufacturers and notified bodies on the summary of safety and clinical performances: MDCG 2019-9 "Summary of safety and clinical performance A guide for manufacturers and notified bodies". (https://ec.europa.eu/growth/sectors/medical-devices/new-regulations/guidance_en).

This guide provides recommendations for the structure and content of the summary of safety and clinical performances. GMED recommends that the manufacturer follow the recommendations of the MDCG 2019-9 guide for the establishment of the summary of safety and clinical performances.

The MDCG 2019-9 guide will be used by GMED as a reference document when validating the summary of safety and clinical performances.

ANNEX 1

ANSM Degrees of novelty for a medical device

DEGRÉ DE NOUVEAUTÉ *DEGREE OF NOVELTY*	TYPE DE NOUVEAUTÉ *TYPE OF NOVELTY*	NOUVEAUTÉ À DOMINANTE *INNOVATION WHERE THE DOMINANT IS :*		
		TECHNOLOGIQUE *TECHNOLOGICAL*		CLINIQUE *CLINICAL*
5	**Innovation majeure** *Major innovation*	**Rupture technologique** *Breaking technology*	**et** *and*	**Impact clinique fort** *Strong clinical impact*
4	**Innovation (dispositif innovant)** *(innovative device)*	**Rupture technologique** *Breaking technology*	**ou** *or*	**Impact clinique fort** *Strong clinical impact*
3	**Nouveauté substantielle** *Substantial novelty*	**Incrémentation technique** *Incremental technology*	**et** *and*	**Impact clinique modéré** *Moderate clinical impact*
2	**Nouveauté modérée** *Modarate novelty*	**Incrémentation technique** *Incremental technology*	**ou** *or*	**Impact clinique modéré** *Moderate clinical impact*
1	**Nouveauté inexistante ou mineure** *Lacking or minor novelty*	**Technologie connue** *Known technology*	*et*	**Impact clinique inchangé** *Unchanged clinical impact*

Breaking technology: Device that disrupts technologies in healthcare and could replace it definitely.

Incremental technology: Device including a technological breakthrough in comparison to another device.

Strong clinical impact: Device which presents a major interest for healthcare especially by improving very statistically the clinical practice, and/or the patient's condition, and/or providing a new diagnostic strategy in a clinical field.

Moderate clinical impact: Device which presents a new interest for healthcare especially by improving the clinical practice, and/or the patient's condition, and/or providing a diagnostic alternative.

Lacking or minor novelty: Device with no or negligible modification compared to a similar device already on the market (like aesthetic modification).

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