GMED LNE GROUP Newsletter

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CLINICAL EVALUATION: FEEDBACK AND GOOD PRACTICES

Regulation (EU) 2017/745 (MDR) puts the patient at the center of its scope. This is an important development to strengthen the medical devices' safety for the patients' benefit. The clinical evaluation is therefore the central document of the technical documentation. The purpose of the clinical evaluation is to verify the safety and performance of the device, including clinical benefits. The clinical evaluation is the focus of all attentions, particularly the regulatory organizations: European Commission, Competent Authorities, Expert Panels, or Notified Bodies.

In addition, when the manufacturer should prepare a Summary of Safety and Clinical Performance (SSCP) per MDR Article 32, the clinical data will no longer be the manufacturer's confidential data, but data accessible to all via EUDAMED. The clinical evaluation thus becomes a central step in the products conformity assessment under MDR.

In this newsletter, the GMED teams share their experience of the last two years on clinical evaluation. You will then be able to learn about the findings and good practices to be implemented for your clinical evaluation report(s).

The MDR requirements are not comparable to those of the directives (93/42/EEC and 90/385/EEC) concerning clinical evaluation.

It should be noted that a significant effort to upgrade the Clinical Evaluation Reports (CER) has been made by manufacturers to bring them to compliance. However, GMED's teams have identified points of vigilance relating to the CER. These can facilitate reviews, limit questions, allow a positive opinion to be issued from the first round of evaluation, and thus allow the certification of your products as soon as possible.

The identified areas of improvement include the following:

- CER format;
- Device description;
- Equivalence route.

A CER FORMAT

For the first time, the regulation lists the provisions to be followed regarding the technical documentation form. This shall be clear, organized, unambiguous, and in a readily searchable form (see Regulation (EU) 2017/745, Annex II, Introductory Part). These requirements are applicable to all the technical documentation elements and are therefore also applicable to the CER.

1 - Our findings

GMED's teams have observed the following situations:

- The CER is not easily searchable;
- Information is not readily available;
- The document is not in the appropriate language;
- The CER includes several products that do not have the same indications, are not intended to be combined and/or interconnected, and do not have the same clinical data.

These defects can impact the evaluation time and consequently the duration of the conformity assessment process.

2 - The proposed tools

The *Technical Memo: Technical Documentation - Information to be provided for assessment - Regulation (EU) 2017/745*[1] edited by GMED, is not specific to the CER but should nevertheless be considered. This technical memo reflects for example how an electronic document can meet the basis of Annex II of the MDR: it shall be clear, organized, unambiguous, and in an easily searchable form to allow product reviewers to fluidly navigate the document.

For example, an electronic document shall be in searchable PDF format. It shall have an interactive summary, especially when it includes several hundred pages. The use of tree structure bookmarks is also highly recommended, particularly when the document is large. It is important to consider that these keys should not only be applied to the master document body text, but also to the annexes. For instance, the state of the art report is appended to the CER and does not follow the provisions required by Annex II of the MDR. The state of the art report is often several thousand pages long and is a critical part of the evaluation.

Like all Notified Bodies, GMED has built its Clinical Evaluation Assessment Report (CEAR) based on the MDCG 2020-13 guidance. This gives you a way to access the different topics that are discussed in the CER, as well as the questions that GMED reviewers will need to answer. You will therefore need to construct a report that addresses all of the items listed in this guidance.

Furthermore, when the clinical evaluation concerns a MD for which the consultation procedure is applicable, namely class III implantable devices and class IIb active devices intended to administer into the body and/or to remove from the body a medicinal product (Regulation (EU) 2017/745 article 54), the clinical evaluation documents shall be submitted in English. Indeed, the Clinical Evaluation Assessment Report (CEAR) and all documents reviewed in connection with it are transmitted to the European Commission and then to the dedicated expert panels. The CER and the CEAR shall be understandable to all and therefore in the universal language of English.

Finally, in 99% of cases, one CER shall cover one medical device and all its variants. There are few cases where the CER can cover several medical devices. If you think that this strategy is necessary, we invite you to discuss the subject with GMED.

B DEVICE DESCRIPTION

The device description is one of the foundations of the CER; it is the device identity and its function. If GMED does not have a complete description at the beginning of the CER evaluation, the teams cannot make a decision on the device clinical evidence demonstration because they are confronted with shortcomings.

1 - Our findings

Here are a few cases encountered during the CER review that raised questions:

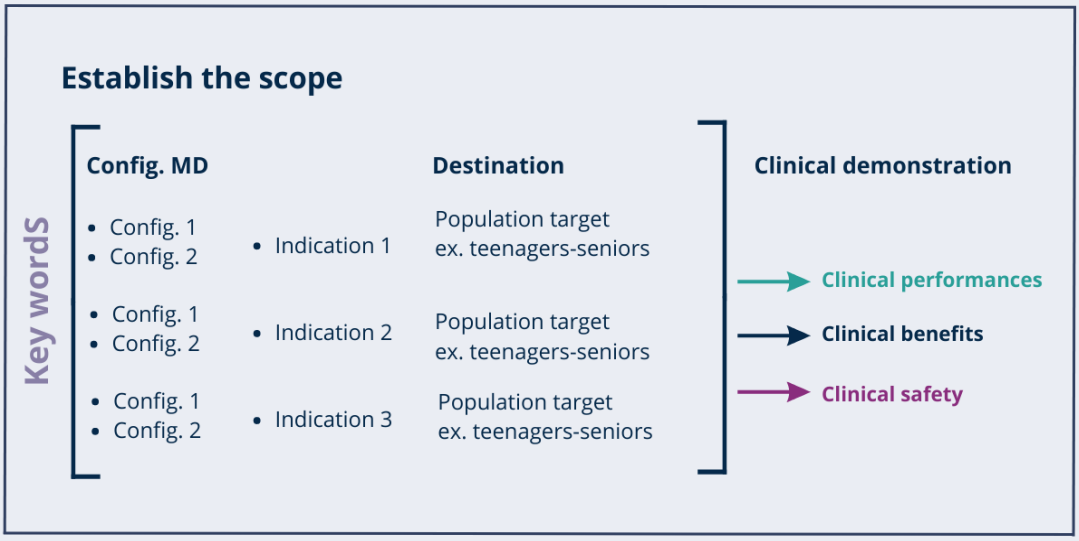
- The device description is not detailed;
- The device description is incomplete;
- The description is inconsistent with the rest of the technical documentation;
- The description is not present in the CER because a reference is made to a general part of the technical documentation.

These deficiencies result in a partial description of the product. In this case, the clinical data often supports only part of the claimed use of the device or will cover without distinction, all variants and all indications.

[1] The GMED Technical memos are for the exclusive use of GMED customers.

2 - GMED's recommendations

It is important that you detail the CER scope, i.e., the device description and what its actions/functions are with regard to patients. Without an accurate description of the device, a part of the scope is missing. The clinical demonstration may therefore be partial.



To avoid omitting essential elements in the description of the medical device, you can draw up a checklist based on Annex A3 of MEDDEV 2.7/1 rev. 4.

A particular attention should be given to ensure that the output of the clinical evaluation matches the input data. All indications, variants, and configurations of the device that have been described shall be supported by the clinical data. The link between the input data and the output data of the clinical evaluation shall be visible and accessible within the generated and collected clinical data. At the end of the clinical evaluation, you shall conclude about the demonstration of the clinical benefit for each indication for all variants and configurations.

Also keep in mind that the CER is a self-supporting document, which shall be readable and understandable by a third party who does not have access to the entire technical documentation. Therefore, you can not reference a generalized part of the technical documentation for the description.

C THE EQUIVALENCE ROUTE

Equivalency is a route through which you can collect data that are applicable to the assessed device. It shall, however, meet the regulatory criteria. Going down this pathway requires mastering the scope of its possibilities, or you risk finding yourself in a dead-end street.

1 - Our findings

Here are a few instances where this strategy has been misused:

- The equivalence is claimed with a previous generation, while the components have similar but not identical materials;
- Equivalence is claimed for a class III or implantable MD with a device from another manufacturer not CE marked under MDR;
- Equivalence is carried out with the same product having a drug status;
- The manufacturer claims equivalence without demonstrating it through a comparison and analysis;
- Equivalence is claimed with a product that has no or no longer regulatory status;
- The demonstration of equivalence does not include the accessories marketed with the MD.

2 - GMED's recommendations

When engaging in this strategy, it is essential that you know the possibilities of this pathway but also its limitations. This requires understanding that new limitations have been incorporated under Regulation (EU) 2017/745 as compared to the equivalence described in MEDDEV 2.7/1 rev. 4. The regulatory text should not be subject to interpretation and should be applied as written. It should be read in conjunction with MDCG 2020-5 guide.

The demonstration of equivalence already existed under Directives 93/42/EEC and 90/385/EEC and shall be carried out on the three characteristics: technical, biological, and clinical.

According to the MDR, technically, the characteristics between the device under evaluation and the equivalent device can be similar. Biologically, they shall be the same, only the release characteristics of the substances may be similar, including degradation products and leachables. Clinically, the characteristics shall be the same for a similar population. When the term "same" is used, it cannot be replaced by the term "similar", as this implies that the characteristics are identical.

In addition, when equivalence is claimed for a class III or implantable MD with another device, the so-called equivalent device must be CE marked under the MDR. This is how the following statement in paragraph 5, Article 61, of Regulation (EU) 2017/745 should be understood: "*the original clinical evaluation has been performed in compliance with the requirements of this Regulation*". The explanation of this statement is given in paragraph 4(d) second paragraph of the MDCG 2020-5 guide: "*This implies that the presumed equivalent device is certified under the MDR. As such, it will not be possible to claim equivalence to a device certified with respect to the Directives 93/42/EEC or 90/385/EEC.*"

Furthermore, equivalence is only possible with a product that has MD status, regardless of whether the equivalent product is identical. For example, if the equivalent product has drug status because it is marketed in another country, which by its regulations considers it to be a drug, then equivalence is not allowed.

Finally, MDCG 2020-5 guide provides a table to present the demonstration of equivalence. If this route is applicable to your product, use that table as it provides a framework and exhaustively identifies all the aspects in which you should demonstrate equivalence.

Conclusion

In conclusion, the keys to smoothly obtain a favorable opinion on the clinical evidence demonstration are:

- Know all the available guidances;
- Understand the purpose of the assessment and how it is conducted by the Notified Body;
- Do not risk an interpretation of the regulatory texts when they do not lend to do so.

In your CER, tell a compelling and argued story, be transparent.

See the next page to go further

To go further

TRAININGS FOR AMERICA REGION

The Clinical Evaluation Report (CER) Requirements under the EU MDR 2017/745
8-hour training session | June 19-20 | October 30-31 | Virtual classroom

- Identify the key changes for Clinical data under the Regulation (EU) 2017/745 (MDR)
- Determine what is considered "sufficient" clinical data for clinical evaluations
- Understand the Clinical Investigation Requirements
- Identify the Post-Market Surveillance Requirements (PMS), the Post-Market Clinical Follow-Up (PMCF), and the Periodic Safety Update Report (PSUR)

→ CHECK OUT THE PROGRAM

TRAININGS FOR OTHER REGIONS

Understand the regulatory requirements for clinical evaluation to choose the right route
SA65 | 1-day training session | On demand

Conduct clinical evaluation of medical devices using the literature route
SA09 | 1-day training session | On demand

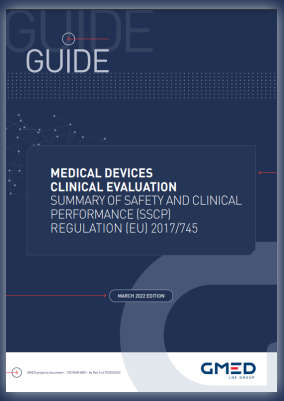
Conduct clinical evaluation of medical devices using the clinical investigation route
SA26 | 1-day training session | On demand

→ CONTACT GMED TRAINING CENTER

GUIDE

Medical Devices Clinical Evaluation – Summary of Safety and Clinical Performance (SSCP) – Regulation (EU) 2017/745

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 under Regulation (EU) 2017/745.



This guide recalls the principles of clinical evaluation and describes 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, within the framework of CE marking procedures for medical devices, regardless of the medical device class.

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