GMED LNE GROUP Newsletter

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ARTICLE 61(10) OF REGULATION (EU) 2017/745: INSTRUCTIONS FOR USE AND FAQ

According to Article 2(44) of the Medical Devices Regulation (EU) 2017/745 (MDR), clinical evaluation is defined as a "systematic and planned process to generate, collect, analyze and evaluate clinical data relating to a device on an ongoing basis in order to verify the safety and performance, including clinical benefits, of the device when used in accordance with the manufacturer's intended purpose." Clinical evaluation is therefore the analysis of clinical data required to demonstrate compliance with the General Safety and Performance Requirements (GSPR) of Annex I. However, in some cases, the use of clinical data may not be appropriate to demonstrate compliance with these general safety and performance requirements: the clinical evaluation may then be based on the Article 61(10) route.
In what cases can Article 61(10) be used? What is the rationale for using this pathway to demonstrate compliance? How do you conduct a clinical evaluation using the Article 61(10) pathway?
The purpose of this newsletter is to answer these questions in order to help you better understand the expectations of Notified Bodies (NBs) in the context of the Article 61(10) clinical evaluation.

A WHAT DOES ARTICLE 61(10) MEAN? DECODING

Article 61(10) begins with "Without prejudice to paragraph 4". Far from being a detail, this introduction means that **implantable and Class III devices are not eligible** for clinical evaluation under the Article 61(10) route.

For other devices, Article 61(10) is potentially applicable "where compliance with the general safety and performance requirements is considered not to have been satisfactorily demonstrated by clinical data", i.e., where demonstration of compliance based on clinical data is considered inappropriate. In other words, recourse to Article 61(10) is possible when the performance and safety of the device can be demonstrated by non-clinical data **and** there are no relevant or meaningful measurable clinical criteria.

This is the case for a device that does not provide a direct measurable clinical benefit, such as a medical device accessory, without its own clinical claim or direct influence on the clinical performance of the device with which it is intended to be used.

In this case, an "appropriate justification" must be provided explaining why the manufacturer "considers adequate a demonstration of compliance with general safety and performance

requirements that is based solely on the results of non-clinical test methods, such as performance evaluation, bench testing, and pre-clinical evaluation."

The justification for the use of Article 61(10) is therefore a regulatory requirement.

B HOW TO JUSTIFY THE USE OF ARTICLE 61(10)?

According to the MDR, manufacturers who wish to opt for the Article 61(10) pathway must provide a detailed justification for this choice, based on the following:

- **Risk management**: For potentially eligible devices, risk management plays a major role in justifying the reliance upon Article 61(10). If the risk assessment indicates that there are relatively high residual risks, this calls into question the 61(10) pathway as additional clinical data may be required. The elements of risk management should be sufficiently detailed in the clinical evaluation report to determine whether these elements support the use of non-clinical test methods. Recall that the Clinical Evaluation Report (CER) is intended to be a self-supporting document and therefore a simple reference to the risk management report is insufficient. Potential device-related harm must therefore be described, the hazards and hazardous situations that caused it must be listed, and it must be demonstrated that the non-clinical test methods are appropriate considering the identified risks.

- **Detailed data on the interaction between the device and the human body**: Most devices for which Article 61(10) is applicable do not have a direct interaction with the human body. However, Article 61(10) may also be applicable for some devices that have a direct interaction with the human body, for example for basic surgical instruments such as scissors or forceps. On the other hand, if it is a specific surgical instrument that is essential to the success of the surgical procedure and the clinical performance of the implant, the 61(10) pathway is not applicable.
  Elements to consider here are the duration of contact with the human body, the type of contact and mode of action, and the type of tissue in contact with the device. If the interaction between the device and the human body has novel characteristics (different from those described in the current state of the art for this type of device), additional clinical data may be required.

- **Expected clinical performance and manufacturer's claims**: In general, performance and safety claims are purely technical in a clinical evaluation according to Article 61(10). If the manufacturer claims a clinical performance, clinical data is required to demonstrate this, and Article 61(10) cannot be applied. This does not mean, however, that devices evaluated under Article 61(10) have no clinical benefit: most of those devices have an **indirect clinical benefit** derived from their technical performance. The fact that the indirect clinical benefit is not measurable by clinical data is part of the justification for the reliance upon Article 61(10). In this case, it is therefore acceptable for this indirect clinical benefit to be demonstrated by non-clinical data.

Other parameters to be considered for the justification of the choice of track 61(10) are:

- **The degree of novelty of the device**: Devices eligible for pathway 61(10) generally have a low degree of novelty. Otherwise, there would be little data available on similar devices, and the clinical effects of this type of device would not be well documented in the scientific literature. This would call into question the choice of Article 61(10).

- **Appropriateness and/or feasibility of a clinical investigation**: For some types of devices, clinical investigations may not be feasible, ethical, or relevant. In such cases, it may be more appropriate to use non-clinical tests to demonstrate the safety and performance of the device. This should be part of the justification for relying upon Article 61(10).

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C DOES THIS MEAN THAT THERE IS NO CLINICAL DATA IN THE CLINICAL ASSESSMENT REPORT?

No. The fact that clinical data is not considered appropriate to demonstrate the safety and performance of the device does not mean that such data (if it exists) should be excluded. Article 61(10) **allows for** the demonstration of compliance with the GSPR without clinical data. However, in accordance with Annex III of the MDR, a review of the scientific literature must always be conducted to identify risks or data that is not known to the manufacturer.

In addition, **legacy devices** will have **post-market surveillance data** that will be required to be provided in the clinical evaluation report (see MDCG 2020-6).

D IS ARTICLE 61(10) APPLICABLE TO A DEVICE FOR WHICH THERE IS INSUFFICIENT CLINICAL DATA?

No. Article 61(10) is not a pathway for evaluating devices for which there is a lack of clinical data, but a pathway for evaluating devices for which the clinical data is deemed inappropriate or

irrelevant. If there are appropriate clinical endpoints to assess the safety, performance, and benefit of the device, and there is insufficient clinical data available on the device (or equivalent devices), then a clinical investigation is required.

This also means that if there are similar (not necessarily equivalent) devices for which relevant clinical data are available, the reliance upon Article 61(10) should be questioned, as this suggests that it is indeed possible to obtain relevant clinical data for such devices.

E WHAT SHOULD THE CLINICAL EVALUATION REPORT INCLUDE IF THERE IS NO CLINICAL DATA?

Even if a demonstration of compliance with the GSPRs without clinical data is conducted, a **clinical evaluation report must be written** and the report must be evaluated by the Notified Body. But which information should be included in a clinical evaluation report in the absence of clinical data?

As noted above, a detailed rationale must be provided to support the reliance upon Article 61(10).

In the case of a legacy device, a **search of the scientific literature on the device** in question must be conducted. This search must be done on the one hand to show that there is no clinical data available (which is part of the justification for the use of Article 61(10)) and on the other hand to identify possible clinical data of which the manufacturer was not aware. It must be documented in the clinical evaluation report.

In all cases, a literature review should be performed to **determine the state of the art** in medicine in the field, alternatives to the device under evaluation, and available data on similar devices.

A summary of the non-clinical data should then be presented, including:

- Demonstration of compliance with harmonized standards through non-clinical evidence, such as mechanical testing, evidence of biocompatibility, usability testing, etc. It is acceptable to summarize test results and refer to test reports for detailed results.
- Where applicable, the results of pre-clinical testing on animals, phantoms, or cadavers, ideally involving healthcare professionals or other end users. These are not clinical data but can be used to demonstrate compliance with GSPRs, particularly in terms of usability.

Vigilance database search results for the legacy device and similar devices should be included. The search strategy and databases used should be described.

For legacy devices, **post-market surviellance data** held by the manufacturer should be provided.

Finally, an analysis of the available data should be presented, with a clear indication of how **each performance and safety claim is supported by these data**.

F IF A DEVICE PREVIOUSLY COMPLIED WITH ANNEX X §1.1D OF DIRECTIVE 93/42/EEC, IS IT AUTOMATICALLY ELIGIBLE FOR ARTICLE 61(10)?

Not systematically. The wording of Annex X 1.1.(d) is very similar to Article 61(10) but the regulatory requirements for clinical evaluation are not identical under the Directive and the MDR. It is possible that a legacy device for which this pathway has been used to demonstrate compliance under the Directive may not be eligible for the Article 61(10) pathway.

G HOW TO ORGANIZE POST-MARKET CLINICAL FOLLOW-UP?

A post-marketing surveillance (PMS) plan is systematically required for devices for which Article 61(10) is applicable. But what about post-market clinical follow-up (PMCF)? If clinical data are not considered relevant to demonstrate compliance with the pre-market GSPRs, does this mean that no post-market clinical follow-up is required?

The applicability of Article 61(10) does not constitute an exemption from the PMCF obligations. As shown in Annex XIV Part B of the MDR, the concept of PMCF includes specific methods (including post-market clinical studies) and general methods, including for example user feedback on the device and review of the scientific literature.

Where the Article 61(10) pathway has been used for the clinical evaluation of the device, it is unlikely that a post-market clinical investigation is feasible. This investigation would otherwise have been feasible and even necessary before the device was placed on the market. However, general post-market follow-up methods can and should be applied. For example, a literature review will determine whether the device still corresponds to the state of the art in the medical field in question. Feedback from users of the device may identify new risks or more accurately estimate the frequency of known risks.
Therefore, a PMCF plan should be written and incorporated into the post-market surveillance plan.

If post-market clinical follow-up is not deemed necessary, this should be justified and duly argued in the PMS plan.

Conclusion

The choice of the 61(10) pathway requires a detailed justification as to why a demonstration of compliance with the GSPR based exclusively on non-clinical data is relevant and sufficient. Those non-clinical data should then be summarized in the clinical evaluation report. For legacy devices, it is essential to include all available data on the device, including post-market surveillance data.

Article 61(10) is therefore not a derogation clause allowing the need for clinical data to be waived, but a possible evaluation pathway for certain devices, generally low-risk and with a low degree of novelty, for which an evaluation based on clinical data is deemed inappropriate or irrelevant.

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

→ CHECK OUT THE PROGRAM

Post Market Surveillance and Vigilance New Requirements under the European Medical Device Regulations
8-hour training session | June 28 | November 1-2 | Virtual classroom

→ 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

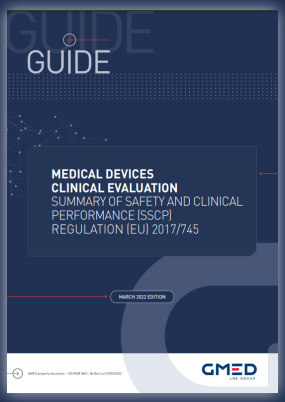
Apply the requirements of the European Regulation 2017/745 on medical devices
SA56 | 2-day training session | On demand

→ 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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