MDR Clinical Data Mandate Threatening Device Access in Europe

A single requirement of the Medical Device Regulation (MDR; 2017/745) is playing a disproportionate role in the failure of medical device companies, especially SMEs, to comply with the MDR, often resulting in excessive expenditure to accomplish the objective. This requirement is also linked to some companies abandoning the European CE marking process altogether with a recognized negative effect on patient health in Europe. The requirement in question concerns the blanket MDR requirement for clinical data for all devices regardless of device classification. This article discusses this issue and proposes a solution for resolving this critical problem.

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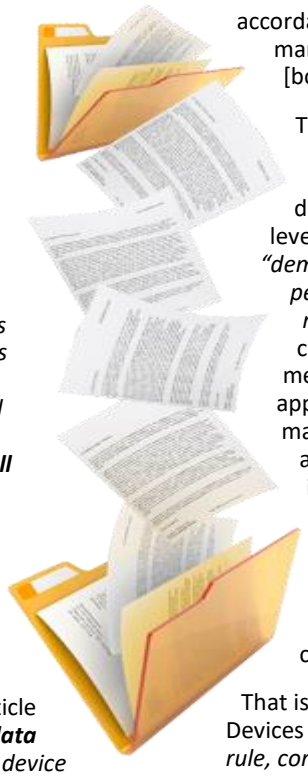
MDR's blanket requirement for clinical data

The MDR requires clinical data for all devices. That is, the MDR states that clinical data are required to confirm conformity with relevant general safety and performance requirements (GSPRs) set out in Annex I. Specifically, Article 61, Clinical evaluation, paragraph 1 states:

"Confirmation of conformity with relevant general safety and performance requirements set out in Annex I under the normal conditions of the intended use of the device, and the evaluation of the undesirable side-effects and of the acceptability of the benefit-risk ratio referred to in Sections 1 and 8 of Annex I, ***shall be based on clinical data*** *providing sufficient clinical evidence, including where applicable relevant data as referred to in Annex III."* [bold text for emphasis]



In addition, Article 61(1) requires that manufacturers specify and justify the level of clinical evidence necessary to demonstrate conformity with the relevant GSPRs. MDR Article 2(51) defines "clinical evidence" as *"**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."* [bold text for emphasis]

Annex XIV, Part A, Clinical Evaluation, in Section 1, requires manufacturers to identify available clinical data, appraise all relevant clinical data, generate any new or additional clinical data necessary to address outstanding issues, and analyze all relevant clinical data.

Specifically regarding the post-market period, Article 61(11) states: "The clinical evaluation and its documentation shall be updated throughout the life cycle of the device concerned with clinical data obtained from the implementation of the manufacturer's PMCF plan in accordance with Part B of Annex XIV and the post-market surveillance plan referred to in Article 84." [bold text for emphasis]

The sole exception to the blanket requirement for clinical data is provided by Article 61(10), which understandably does not apply to implantable devices or class III devices, due to their higher risk levels. That is, if the manufacturer can justify that the *"demonstration of conformity with general safety and performance requirements based on clinical data is not deemed appropriate,"* the demonstration of conformity can be based on non-clinical testing methods alone. The justification for using this approach must be based on the results of risk management, the interaction between the device and the human body, the clinical performance intended, and the claims of the manufacturer.

Slightly more flexible clinical data requirement under the Directives

In comparison with the blanket clinical data of the MDR, the Medical Devices Directives required clinical data "as a general rule."

That is, Annex X, Clinical Evaluation, of the Medical Devices Directive (MDD; 93/42/EEC) stated: *"As a general rule, confirmation of conformity with the requirements concerning the characteristics and performances referred to in Sections 1 and 3 of Annex I, under the normal conditions of use of the device, and the evaluation of the side-effects and of the acceptability of the benefit/risk ratio referred to in Section 6 of Annex I, must be based on clinical data."* [bold text for emphasis]

Annex 7 of the Active Medical Devices Directive (AIMD; 90/385/EEC) included an analogous requirement on clinical data, which was also required *"as a general rule."* Similar to the MDR, the Directives also included a provision allowing the demonstration of conformity with safety and performance-related essential requirements based on non-clinical data where the demonstration of conformity with essential requirements based on clinical data was not deemed appropriate.

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Thus, the simple addition of *"as a general rule,"* although still arguably excessive, allowed a degree of flexibility that the MDR does not offer. As discussed later, returning to the previous language of the MDD does not provide an ideal solution to the problem being faced in Europe regarding the blanket requirement for clinical data.

Role of harmonized standards in flexibility of the Directives' clinical data requirements

Additional flexibility regarding the clinical data requirements of the Directives was provided by MEDDEV 2.7/1 Rev 4, the 2016 European guidance on clinical evaluation. That is, MDD Annex X, Section 1.1 and AIMDD Annex 7 stated: *"The evaluation of this data, hereinafter referred to as 'clinical evaluation', where appropriate taking account of any relevant harmonised standards, must follow a defined and methodologically sound procedure…"* [Bold text for emphasis]

The ability to take account of any relevant harmonized standards was addressed in MEDDEV 2.7/1 Rev 4, Section 7, Definition of the scope of the clinical evaluation (Stage 0), which stated: *"Similarly, it may be possible to use compliance with harmonised standards to satisfy the clinical evidence requirements for devices based on technologies with well established safety and performance characteristics."*

In this manner, the guidance acknowledges that the safety and clinical performance characteristics of some medical devices are well known and adequately addressed in European harmonized standards, when they specify technical requirements directly related to safety and clinical performance. Thus, under the Directives and following the guidance, while exercising sufficient care, it was possible to evaluate whether demonstrating compliance with harmonized standards fulfilled the essential requirements concerning safety and clinical performance.

Unfortunately, the current blanket clinical data requirement of the MDR and regulatory pushback on the use of Article 61(10) are severely hindering the use of harmonized standards and other non-clinical data, even when based on sound regulatory principles, to demonstrate conformity with MDR safety and clinical performance requirements.

Proposed solution for resolving MDR's blanket requirement for clinical data

The following text is suggested for replacing the current text of Article 61(1):

Confirmation of conformity with relevant general safety and performance requirements set out in Annex I under the normal conditions of the intended use of the device, and the evaluation of the undesirable side-effects and of the acceptability of the benefit-risk ratio referred to in Sections 1 and 8 of Annex I, shall be based on clinical data providing sufficient clinical evidence, where necessary, including where applicable relevant data as referred to in Annex III.

Where clinical evidence is necessary, the manufacturer shall specify and justify the level of clinical evidence to demonstrate conformity with the relevant general safety and performance requirements. This level shall be appropriate considering the device's characteristics and intended purpose.

This proposed text is based on the fundamental prerequisite that the general safety and performance requirements (GSPRs) of the MDR must be met. Clinical data may or may not be needed to demonstrate compliance with the GSPRs. Other means may suffice, such as animal data, bench testing or standards compliance. For example, compliance with clinical performance requirements may need to be demonstrated by conducting clinical studies but may also be able to be demonstrated by other means that do not require the generation of clinical data. Compliance with safety-related requirements should be based on compliance with the harmonized standard for risk management. Critically, risk analysis documentation should clearly indicate whether clinical data are needed to verify the effectiveness of risk control measures or whether other means are sufficient.

That is, clinical data should be required only when these data are needed to demonstrate conformity with the GSPRs related to safety and clinical performance, the acceptability of side effects, and an acceptable benefit-risk ratio. Furthermore, where clinical data are needed to demonstrate conformity, manufacturers should be prepared to generate such data characterized by methodological quality and scientific validity.

European Parliamentary resolution and European Commission launch of public consultation

The problem of impending device shortages in Europe and the urgent need to revise the MDR and In Vitro Medical Devices Regulation (IVDR) has been addressed in the European Parliament Resolution of 2024/2849 (RSP) adopted on 23 October 2024. A summary document points out that many stakeholders have reported difficulties in navigating the complex regulatory procedures under the current MDR and IVDR framework, with potential risks posed to the continuous availability of life-saving medical devices and critical in vitro diagnostic tests in the EU.

To address these and other problems the Parliament has called on the European Commission to propose by the end of Q1 2025 *"delegated and implementing acts to the MDR and the IVDR to address the most pressing challenges and bottlenecks in the implementation of the legislative frameworks and to propose the systematic revision of all relevant articles of these regulations, accompanied by an impact assessment, to be conducted as soon as possible."* This has led to the launch by the European Commission of a public consultation, which ends on 21 March 2025 (midnight Brussels time) requesting the public and stakeholders to provide views and possible solutions on the problem.

The views expressed in this article regarding the elimination of the blanket requirement for clinical data by the MDR have been submitted for consideration in the European Commission's public consultation on the effectiveness and efficiency of the MDR and IVDR.

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