MDR's Art. 61(10)
Facts and Fiction

Is a Clinical Evaluation possible without Clinical Data?

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Clinical evaluation is mandatory for all medical devices under MDR

Clinical evaluation is defined in Art. 2(44) of the MDR as 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 […]

A clinical evaluation shall be performed for all devices under the MDR.

Acc. to Art. 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****, including where applicable relevant data as referred to in Annex III.*

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Is the use of clinical data the only appropriate pathway to demonstrate conformity with GSPRs?

No, in some cases ONLY and under specific conditions, the use of clinical data may not be deemed appropriate/relevant Art. 61(10) may be used in these cases.

Important!
The clinical evaluation of implantable and class III medical devices shall always be based on clinical data.

Acc. to Art. 61 (1),

*The manufacturer **shall 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 shall plan, conduct and document a clinical evaluation in accordance with this Article and Part A of Annex XIV.

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What is the Article 61(10) talking about?

10. Without prejudice to paragraph 4, where the demonstration of conformity with general safety and performance requirements based on clinical data is not deemed appropriate, adequate justification for any such exception shall be given 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. In such a case, the manufacturer shall duly substantiate in the technical documentation referred to in Annex II why it considers a demonstration of conformity with general safety and performance requirements that is based on the results of non-clinical testing methods alone, including performance evaluation, bench testing and pre-clinical evaluation, to be adequate.

Art. 61(10) describes the instances in which the use of clinical data may not be appropriate to demonstrate conformity with these GSPRs.

CAUTION!
Art. 61(10) is NOT a derogation that waives the need for clinical data but rather a potential evaluation strategy for specific, low-risk devices with low level of novelty for which a clinical data-based evaluation is deemed irrelevant and/or inappropriate.

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In which cases is Article 61(10) potentially applicable?

Leveraging Art. 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.

Ideal candidate: A device that

- ✓ does not have a direct measurable clinical benefit, such as an accessory,
- ✓ is not making any clinical claims of its own
- ✓ does not have direct influence on the clinical performance of the device with which it is intended to be used.

A thorough justification why the use of Art. 61(10) is applicable, i.e., why clinical data are not necessary to prove conformity with GSPRs is mandatory and should be part of the clinical evaluation report.

CAUTION!

Art. 61(10) is NOT a pathway for the evaluation of devices that are lacking clinical data, but a pathway for the evaluation of devices for which the clinical data is deemed inappropriate or irrelevant.

If there are appropriate clinical endpoints for the assessment of the device's clinical safety, performance, and benefit and at the same time there is insufficient clinical data available on the device in question or its equivalent devices, then a clinical investigation is required.

Within this context, if there are similar and/or equivalent devices for which relevant clinical data are available, applicability of Art. 61(10) for the device in question should be questioned, as the availability of clinical data for similar and/or equivalent devices suggests it is indeed possible to obtain relevant clinical data for the generic device group.

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In which cases is Article 61(10) potentially applicable?

- **Sterilizing equipment**

It would be possible to conduct a clinical investigation on sterilizers, where patients undergo a surgical procedure with instruments sterilized with the sterilizer under evaluation.
However, it will be very difficult to extract meaningful, quantifiable clinical outcomes on the sterilizer itself as there would be no way to link potential adverse events, e.g. a peri-operational infection to the sterilizer.
In such a case, validation of the sterilization method would be more meaningful in terms of performance demonstration.

- **Accessories to medical devices**

In case where an accessory is intended to assist another medical device to achieve its intended purpose, without having a direct therapeutic or diagnostic function itself, e.g., a guidewire, and without making clinical claim of its own and has no influence on the clinical outcomes of the patient, then validation of its performance with technical testing and conformity with applicable standards is more meaningful and more easily quantifiable. Other such examples include data transfer and image processing devices.

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In which cases is Article 61(10) potentially applicable?

- **Devices with indirect clinical benefit**

According to MDCG 2020-6

[…] **while direct clinical benefits should be supported by clinical data, indirect clinical benefits may be demonstrable by other evidence** such as:

- ✓ pre-clinical and bench test data (e.g., compliance to product standards or common specifications)
- ✓ real world data such as registries, information deriving from insurance database records, etc.
- ✓ data from another device that is used with the subject device which does have direct clinical data (e.g. data from a stent used to justify safety and performance of a guidewire) […]

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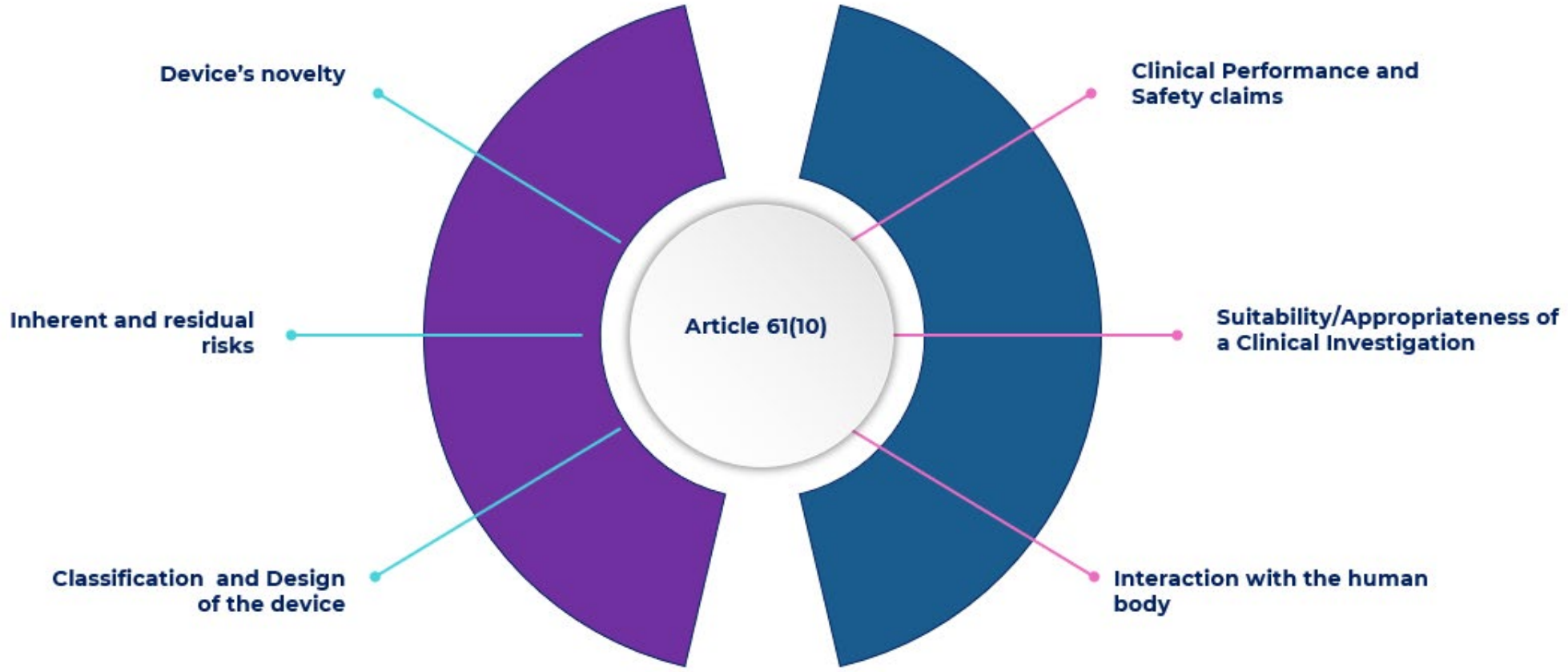
What aspects to consider when determining the applicability of Article 61(10)



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What aspects to consider when determining the applicability of Article 61(10)

Novelty
Eligible devices generally have a low degree of novelty, also demonstrated by lack of clinical data for similar devices.

Inherent and residual risks
Eligible devices have low inherent and residual risks and would normally belong to a generic device group with a well-established safety profile.

Classification and design of the device
Eligible devices generally have low classification.

Clinical performance and safety claims
Eligible devices make no direct clinical claims and generally have no direct clinical benefit.

Interaction with the human body
The invasiveness, duration of use and interaction with the human body of the eligible devices are generally low and are not introducing new risks. Typically, eligible devices will not have direct interaction with the human body, but the Article does not explicitly exclude the ones that do. For example, a basic surgical instrument such as scissors, forceps etc. may be applicable for Art. 61(10) but an instrument used to implant another medical device may not be.

If my device is eligible for Article 61(10) do I still have to present the State of the Art and PMS data?

YES!

The fact that clinical data is not considered appropriate/necessary to demonstrate the safety and performance of a device does not mean that any available clinical datasets should be excluded.

The review of the State of the Art remains mandatory and the relevant conclusions should be used as an argument for eligibility with Art. 61(10) on top of identifying emergent risks.

In the case of legacy devices, i.e., devices marketed under the Directives, PMS data are an extremely useful source of real-world data, which is mandatory for the clinical evaluation report and should be used to support the non-clinical data available for the device.

CAUTION!

Devices eligible for Art. 61(10) are **NOT excluded** from

- ✓ The obligation to submit a Clinical Evaluation Report
- ✓ The Clinical Evaluation Assessment acc. to MDCG 2020-13

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If there are no device-specific clinical data for my device, what type of data should the clinical evaluation report include?

For potential sources of data, the suggested hierarchy from MDCG 2020-6 should be taken into account.

All sources from rank 6-12 are eligible and should be leveraged depending on their availability.

Focus should be on :

- The exhaustive discussion of the State of the Art
- Demonstration of compliance with harmonized standards
- High quality pre-clinical testing
- PMS data including both manufacturer-held and vigilance data

1. Results of high quality clinical investigations covering all device variants, indications, patient populations, duration of treatment effect, etc.
2. Results of high quality clinical investigations with some gaps
3. Outcomes from high quality clinical data collection systems such as registries
4. Outcomes from studies with potential methodological flaws but where data can still be quantified and acceptability justified, e.g. literature sources
5. Equivalence data (reliable / quantifiable) BUT equivalence must be established as per EU-MDR criteria
6. Evaluation of state of the art, including evaluation of clinical data from similar devices as defined in Section 1.2 of MDCG 2020-06
7. Complaints and vigilance data; curated data **Note: not generally considered a high-quality source of data due to limitations in reporting. It may be useful for identifying safety trends or performance issues.**
8. Proactive PMS data, such as that derived from surveys
9. Individual case reports on the subject device
10. Compliance to non-clinical elements of common specifications considered relevant to device safety and performance
11. Simulated use / animal / cadaveric testing involving healthcare professionals or other end users **Note: particularly in terms of usability, such as for accessories or instruments.**
12. Pre-clinical and bench testing / compliance to standards

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If there are no device-specific clinical data for my device, what type of data should the clinical evaluation report include?

CAUTION!

The analysis of the available non-clinical data should be thorough and clearly presented, along with **a justification/explanation of how it contributes to the (non-clinical) performance and safety claims of the device in question**.

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If a device was complying with Annex X, section 1.1D of Directive 93/42/EEC, is it automatically eligible for Article 61(10)?

NO!

Although the wording is similar, the updated regulatory requirements for clinical evaluation under the MDR are quite more stringent.

It is possible that a device was eligible under the Directives but no longer under MDR.

If a device is eligible for Article 61(10), does it still have to plan PMCF activities?

YES!

Applicability of Art. 61(10) is in no way an exemption from the PMCF requirements of the MDR.

Normally, a device eligible for Art. 61(10) is not applicable for a PMCF clinical investigation for the same reasons it is not eligible for a clinical evaluation based on clinical data.
However, general PMCF activities are still required and should be deployed (e.g., literature review, feedback from HCPs and/or patients etc.

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How can Evnia help?

Headquartered in Denmark, the company current has offices in the UK, Greece, Switzerland and Italy and is servicing life-science clients globally.

It has been certified under ISO 9001:2015 as a Clinical and regulatory affairs consulting agency within the life science industry.

Evnia offers a cluster of interconnected services from the early stages of a medical device's lifecycle until its post-market adulthood.

We support healthcare innovation and promotion of patient safety by providing services in the fields of:

- 📌 Due Diligence
- 📌 Regulatory Strategy
- 📌 Clinical Development Strategy
- 📌 Post-Market Surveillance
- 📌 Real World Evidence
- 📌 Market Access and Reimbursement
- 📌 EU and UK Representation Services (Authorised Representative & UKCA UKRP)

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