CLINICAL EVALUATIONS OF MEDICAL DEVICES IN THE EU

After reading this Fact Sheet you should:

- Have a basic understanding of what clinical evaluations entail and why they are needed.
- Know which regulations apply (specifically to medical devices and in vitro diagnostics).
- Have links to related resources.

Clinical evaluation of medical devices verifies safety and performance for its intended use so that the device can be approved, and CE marked. It is an integral part of the medical device development process, applicable to all medical device manufacturers, and as an innovator you need some basic understanding of this area. Clinical evaluation is a specialist area and as an innovator you should involve experts to assist, since a poorly planned or executed process can be costly and risk a new medical device opportunity.

What regulations and guidelines apply?

- The requirements for medical device clinical evaluations are part of Articles 62 through 82 and Annex XV of the **EU MDR 2017/745 (Medical Devices)**. Useful updates and publications can be found **HERE**.
- Additional to the above regulations, good clinical practice (GCP), according to **ISO 14155:2020** "Clinical investigation of medical devices for human subjects", must be adhered to.
- Useful Guideline Documents: **MEDDEV 2.7/1 Rev. 4 (2016)**, **MDCG 2020-5** and **MDCG 2020-6**.

Why are clinical evaluations necessary?

Satisfying regulatory requirements is the main reason for undertaking clinical evaluations, to demonstrate the device is safe and effective before placing it on the market, but if existing clinical data are insufficient new data must be generated via a clinical investigation or trial. There are however various are other legitimate reasons for clinical evaluations:

- Market: Healthcare providers, payers and patients all want evidence that a new device provides clinical and health economic benefits before adopting it.
- Venture finance: Investors seek ongoing affirmation that product development is on the right track and that their investment is protected.
- Independent verification: Experts in the field that can verify that a product works in accordance with its intended use and indications provides objectivity and confidence for providers, payers and investors.
- Insight: Clinical tests may reveal issues or even opportunities that may necessitate a design revision.
- Intellectual Property (IP): Clinical investigations are the best way to support IP claims.

Is a clinical investigation/trial always necessary?

Broadly, two approaches exist for a manufacturer to prove safety and efficacy, depending on the nature of the device: (i) Proving equivalence to an existing device, or (ii) presenting data specific to a new device via a clinical investigation.

With the 'proving equivalence' route, clinical data of an equivalent or 'predicate' device can be used to prove safety and performance of your device under evaluation, and the clinical data can be obtained through literature search and post-market surveillance. But for this route all the following characteristics must be fulfilled regarding your device:

- Clinical: The device is indicated for use for the same clinical condition or purpose, and
- Biological: The device uses the same materials or substances that will be in contact with the same human tissues or body fluids, and
- Technical: The device is of similar design, is used under similar conditions of use, and has similar specifications and properties.

For the clinical investigation route, the generation of clinical data for the new device under investigation is necessary, and such data can be obtained from clinical investigations/trials and literature search. As a rule a clinical investigation is required for implantable devices and class III devices. The EU MDR 2017/745 does allow for exemptions under certain conditions (refer **MDCG 2020-5**), but for active implantable medical devices there are no exceptions and a clinical investigation cannot be avoided. For existing, established medical devices in continued use refer to **MDCG 2020-6** for the data requirements.

Importantly, the generation of data does not end once a device has been placed on the market; The clinical evaluation data must be updated through continuous monitoring of clinical performance and safety. In particular, the product needs to be re-evaluated in the case of technical adaptations and optimisations and data from post-market surveillance of the product (e.g., observational studies) must be considered.

What types of clinical investigations are there?

The **EU MDR 2017/745** legislation (MDR) specifically describes the following types of clinical investigations:

- Pre-market clinical investigations: Clinical investigations of devices without a CE mark (Art. 62 of **MDR**).
- Post-market clinical investigations: Post-market clinical follow-up (PMCF) investigations (Art. 74 of **MDR**).
- Clinical Investigations undertaken for purposes other than those listed in Art. 62 of the MDR: Refer Art. 82 of the **MDR**. And for investigations conducted in Ireland you should refer to the additional requirements laid out in Irish national legislation (**S.I. No. 261 of 2021**).
- Clinical investigations of medical devices without an intended medical purpose: Refer Annex XVI of **MDR** for further information.

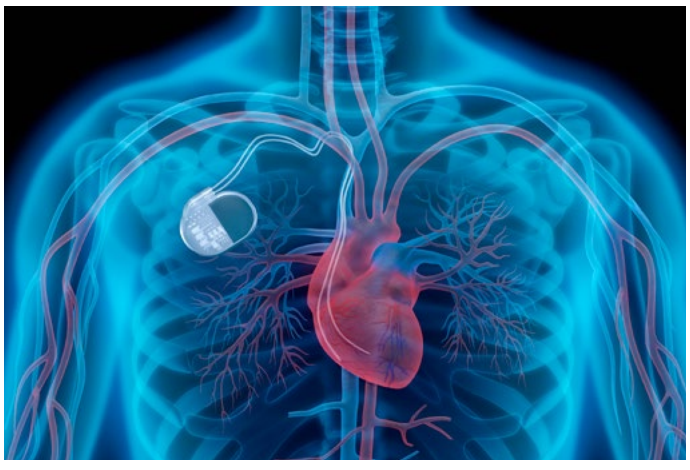
Ireland's HPRA presents useful information and links on **Clinical Investigations**.

What about preclinical trials?

As an innovator you will almost certainly consider pre-clinical studies, where a prototype can be tested prior to production and testing in humans. Preclinical testing may include bench testing, technical testing and animal studies to assess feasibility and biocompatibility, toxicology and other safety concerns. Note that animal research in the EU is regulated under **Directive 2010/63/EU** on the protection of animals used for scientific purposes. The human studies for new devices - pre-market clinical investigations Art. 62 of **MDR** - are broadly of two types: (i) Feasibility or pilot study: A small study to test the feasibility of the device by collecting preliminary safety and performance data, guide any necessary device modifications and guide pivotal study design; (ii) Pivotal study: A large, statistically driven study to confirm clinical efficacy, safety and risks. Post market studies: Monitor the long-term effectiveness, safety and usage in the general population.

Where do I learn about trial design?

The design of the medical device clinical investigation must generally follow two principles: The well-being of subjects (minimal risks and minimal impairments), and the generation of scientifically valid, reliable, and robust clinical data. The basis of the medical device clinical trial is the clinical investigation plan (CIP) including information about type, structure, and parameters. The structure of the CIP is defined in Annex XV Chapter II of the **MDR**. The clinical trial must reflect "latest scientific and technical knowledge" (**MDR** Annex XV I 2.1). The clinical methods must be appropriate to the investigational device (**MDR** Annex XV I 2.2) and consider technical and functional features of the investigational device regarding safety and performance (**MDR** Annex XV I 2.5). Finally, to obtain scientifically valid results, a sufficient number of subjects must be included. Thus, the sponsor must calculate the sample size based on plausible success criteria. Moreover, the clinical environment must be representative for normal conditions of use (**MDR** Annex XV Chapter I 2.1 and 2.4). Medical device clinical trials must be in line with the CIP as referred to in **MDR** Annex XIV Part A. A document called a Clinical Evaluation Report (CER) is where the results of the Clinical Evaluation Plan (CEP) process is defined which leads to the analysis and conclusions which is then recorded and documented in the report. It is required for every EU medical device class.



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