

Clinical Evaluation of Innovative Products: A Revised Requirement of CE Marking

This issue contains two perspectives, that of an expert in helping companies develop clinical studies and that of our insight as a notify body providing certification to CE Marking requirements under the Medical Device Directives.

Part I: How Manufacturers Benefit from a Robust Clinical Assessment

by **Stephanie Malakpour**, Business Development Manager,
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Recent amendments made to the European Medical Device Directive (MDD 93/42/EEC) state that every medical device (MD) sold in Europe, regardless of its classification, must have a clinical evaluation report in its technical file. This is meant to reinforce safety and performance of Innovative Health Technologies (IHT).

The Directive's specific focus on implantable or class III medical devices gives the false impression that clinical investigation does not apply to other MD.¹ This has led to the current situation where clinical trials are rarely done in the pre-market steps of MD development.

Clinical investigation should embody the end of an innovative MD's development, yet is also rarely conducted because of the investment in time, human resources and costs. In addition, clinical investigation is sometimes perceived as risky or harmful.

Benefits of Early Clinical Evaluation

In this paper, I explain why these fears are without basis and describe the many benefits and advantages of performing early clinical assessment of IHTs,

LNE/G-MED View

Part II: Start Early with Notified Body for Better Speed and Results

by **Marc-Henri Winter**, Technical Director,
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With the implementation of Directive 2007/47/EC, clinical evaluation has become a central element of regulatory compliance under the Medical Device Directive and Active Implantable Medical Device Directive.

Manufacturers of innovative technologies face the greatest impact, as they must present complete and sufficient clinical evaluation files to ensure timely assessment and favorable review of their products.

Working Early with Notified Body Pays Off

As early as 1999, LNE/G-MED recognized the benefit of evaluating a manufacturer's clinical investigation plan before its implementation. Our project managers worked with clients to ensure a clinical investigation was adequate to generate relevant data, prior to engaging patients in such a study.

Today, LNE/GMED has taken additional

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About Our Guest Expert

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provided that the clinical assessment is performed with rigor and a robust methodology.

What is Clinical Evaluation?

Definition: Assessment and analysis of clinical data pertaining to a MD to verify the clinical safety and performance of the device when used as intended by the manufacturer.

- Regulatory conformance: Conforming to the regulatory framework is necessary and should be done to your advantage. Choosing to perform a clinical investigation is the best answer to conform to the new requirements of MDD 93/42/EEC. Thanks to an adapted design and a well-researched methodology, it is possible to provide an accurate performance and safety demonstration.
- Price and insurance coverage: When the manufacturer has an innovative MD that he believes will result in a tangible benefit for patients, a clinical investigation should be performed at an early stage. Demonstrating the benefit, thanks to a well-designed clinical investigation, allows for a higher sales price and/or insurance coverage. Conversely, relying on existing data related to older devices, conveys the explicit message that the device is no more innovative than the bulk of existing similar devices.
- Early detection and resolution of safety issues: Over 25% of safety alerts are due to manufacturing defects. This high proportion demonstrates the importance of an early detection of potential safety issues.

Should the MD raise a safety issue, early assessment gives the manufacturer time to take corrective action; it will avoid potential damages to the company's reputation consequently to a publication in a medical journal or worse, in the news, and lawsuits that may altogether be fatal to business. On the other hand, if the clinical study demonstrates that the MD is safe, documenting this safety allows the manufacturer to counter unwarranted claims of harm.

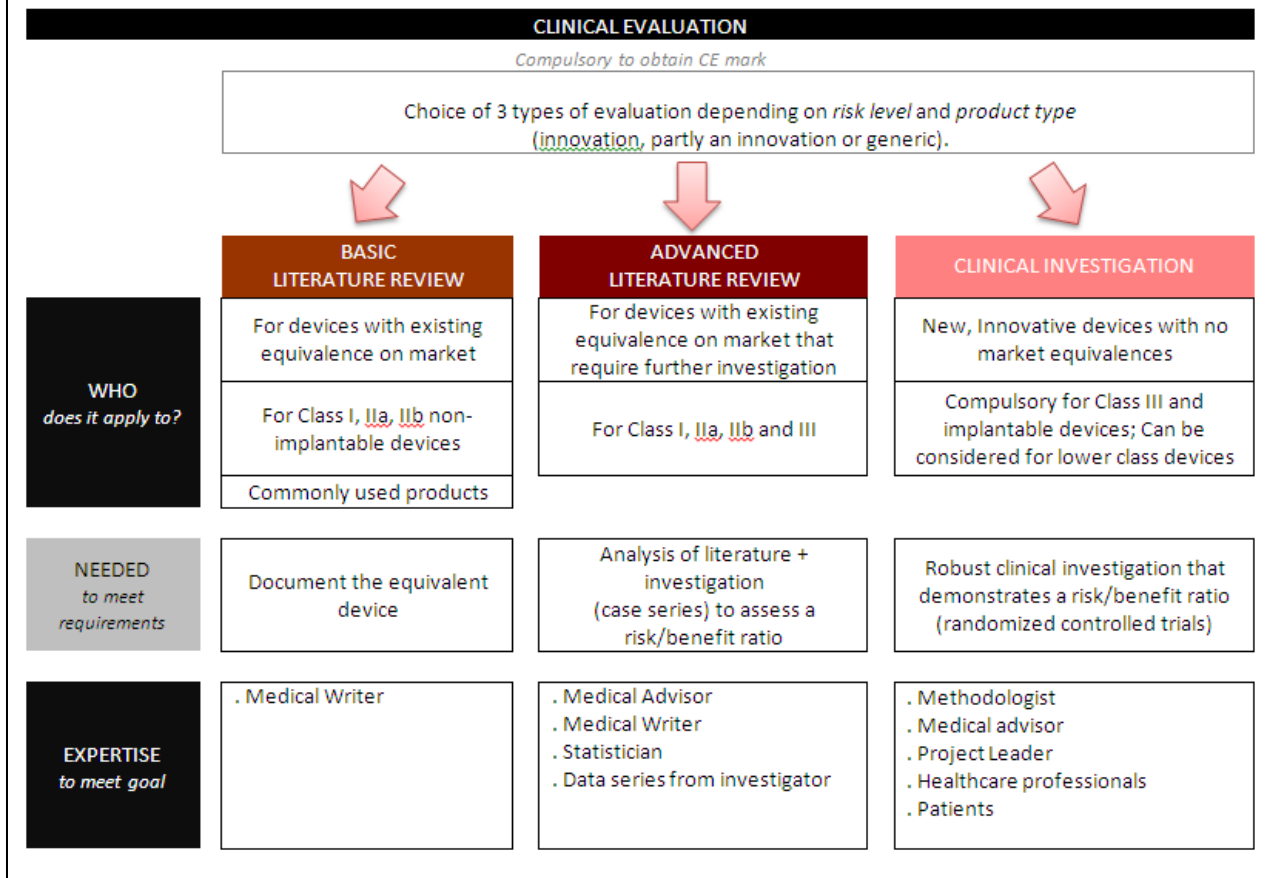
- Manufacturer image: An early clinical investigation most often results in a positive image and greater usage of the product throughout the healthcare system. A well-designed clinical investigation based on a robust methodology gives a chance to publish a scientific article in a peer-reviewed journal. Satisfied healthcare professionals contribute to the success of a device when assessing it in the clinical protocol framework. The positive image will be transmitted to readers of the generated publication and the clinical investigation which is carried out in accordance with the declaration of Helsinki will contribute to establish a confident relationship with physicians as well as with patients.

Avoiding the Pitfalls of Clinical Evaluation

Clinical evaluation is a true opportunity for manufacturers to give added value to their device. In order to bring forward the health benefits, conform to regulatory requirements and reach the best sales price and higher insurance coverage, the clinical evaluation must be conducted in a strict and efficient manner.

There are three types of clinical evaluation: 1) basic literature review, 2) advanced literature review, and 3) clinical evaluation. The route you take will be based on your product classification and product type. (See chart on page 3.)

Clinical Evaluation: Guidelines for Selecting from Among Three Types



Methodology and Guidelines when Performing an Investigation

Many aspects must be taken into consideration when setting up a clinical investigation. The MEDDEV Guidelines on clinical investigation for MD published by the European Commission² classifies different factors that must be taken into consideration according to the type of MD. In addition, MD specificities must be taken into account in the clinical investigation plan.

The most important part lies in the methodology used. Any evaluation must be conducted following a strict design as the choice of the study design and methodology conditions the success of the clinical study.

For each field of study, a specific methodology must be developed and adapted. The assistance of methodological experts is necessary to ensure that the right clinical evaluation is performed. A team of specialized doctors, experienced medical researchers with access to top hospitals, research sites and clinical experts is your best asset for a successful trial. Choosing a trusted partner to perform your evaluation is crucial.

Notes

¹Section 1.2 of Annex 7 of directive 90/385/EEC and section 1.1a of Annex X of directive 93/42/EEC

²Guidelines on clinical investigation: a guide for manufacturers and notified bodies, MEDDEV 2.7/4, December 2010

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LNE/G-MED View: Start Early with Notified Body for Better Speed and Results

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steps to provide early feedback and strengthen communication with clients. Our systematic approach includes evaluation tools to use prior to new product submissions to facilitate estimation of the:

- Level of innovation
- Relevance of the clinical evaluation strategy
- Specific expertise needed to accurately analyze the technical documentation

The above estimates are based on a general description of the device, its indication and intended use, and its technical features. This approach has proven effective, with both new and existing clients of innovative products, to build confidence in the capability and the reliability of the overall assessment process.

Communication and Organizational Tools

LNE/G-MED also provides clients with a detailed checklist of required information for submission for an EC type or design examination. Along with being a helpful tool for clients, we find this step facilitates the assessment of these data, with the added benefit of shortening the overall review time.

Other internal process improvements have increased the consistency of our assessments. Along with reinforcing our partnership with our clients, this process allows for better predictability of the outcome of the eventual EC type or design examination per Annex II.4 or III of the MDD and AIMD.

Beyond that systematic approach, LNE/G-MED also offers to assess, on a voluntary basis, the clinical evaluation strategy prepared by the manufacturer, including the substantiation of the decision on whether a clinical investigation is necessary and the outline of the clinical investigation plan, as deemed necessary.

Overall, our ultimate goal is for the patients to have access to new and innovative devices and technologies in an optimal timeframe without jeopardizing the expected level of public health safety.

Marc-Henri Winter is the technical director of LNE/G-MED North America. For questions, feedback or information on assessment to CE Marking, ISO 13485 and other certifications, please contact him at (301) 495-0477 or at certification@lne-gmed.com.

Additional Documents Related to Clinical Evaluation

The European commission issued two new MEDDEV guidance documents in December 2010 related to Clinical Investigations, while a new version of a related ISO standard was released in February 2011:

- **MEDDEV 2.7/4 – Guidelines on Clinical investigations: a guide for manufacturers and notified bodies.** Based on the GHTF guidance document GHTF/SG5/N3:2010 on the same topic, this document addresses when a clinical investigation should be considered and considerations for the design of the clinical investigation.
- **MEDDEV 2.7/3 – Clinical investigations: serious adverse event reporting.** This document clarifies the criteria for the reporting of adverse events experienced during a clinical investigation, and the modalities for this reporting.
- **ISO 14155:2011 - Clinical investigation of medical devices for human subjects – Good Clinical Practices.** The new version supersedes both parts of the previous version of ISO 14155 from 2003. It is expected to become the new harmonized standard under the directives MDD and AIMD.

MEDDEV documents are available for download at <http://ec.europa.eu/consumers/sectors/medical-devices/documents/guidelines/>. Additional information on ISO 14155 is available at: http://www.iso.org/iso/catalogue_detail?csnumber=45557

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