

Progress Report January 2010

LNE/G-MED: Sharing a Passion for Progress

CE Marking of Medical Devices: Prepare for Enhanced Role of “Clinical Evaluation” as an Essential Requirement

Manufacturers selling products in Europe face new requirements under the Medical Device Directive (MDD) and the Active Implantable Medical Device (AIMD), specifically in relation to clinical evaluation of these devices. The new requirements, introduced in December 2009 by Directive 2007/47/EC, become enforceable on March 21, 2010.

That leaves manufactures only a couple of months to ensure they meet clinical evaluation enhanced requirements, which concern both the development phase of products as well as the post market phase. This impacts:

- The Essential Requirements
- The design validation activities
- The post market surveillance phase
- The assessment by the Notified Bodies

The definition for clinical evaluation is introduced in the Annex X of the MDD (7 of the AIMD). It may be summarized as the critical analysis of all relevant data allowing assessment of the level of safety and effectiveness when used clinically (i.e., on humans).

Essential Requirements (E.R.)

The new E.R. 6a, replacing the previous E.R. 14, is clear on that the demonstration of the safety and performance must be based, whenever the concept is relevant, on clinical data. This requirement applies to any medical device, regardless of its class and regardless of the modality of assessment by the Notified Body.

Note: The Annex X of the directive still includes specific provisions for cases where a clinical evaluation is not deemed the appropriate method for demonstrating the compliance with the E.R.

Design validation activities

The clinical evaluation is clearly an essential element of the design validation for a device. It is now specified that it must be performed according to a “sound procedure”. The quality management system may therefore need to be updated in order to demonstrate the implementation of a systematic approach assuring the credibility of the conclusion of the clinical evaluation report. The clinical evaluation must be understood as a demonstration effort, not only as a documentation requirement.

Additionally, the clinical evaluation aims at confirming the acceptability of the potential hazards; there is an explicit link with the Risk Management process. The EN ISO 14971:2009 standard, whose transition period also ends this coming Spring, should therefore interconnect with the clinical evaluation activities. In particular when the quality system is a requirement, it should clarify this interaction.

The methodology to implement is briefly explained in annex X of the MDD (annex 7 of the AIMD). It clarifies that clinical data from different sources might be considered appropriate. Typically, they may be issued from published articles and/or from clinical investigation (clinical trials). These data must be critically analyzed.

The just issued guidance document MEDDEV 2.7.1 rev.3 (Clinical evaluation: Guide for manufacturers and notified bodies - December 2009) elaborates on the methodology to implement. It suggests the following steps:

- Definition of the objectives of the clinical evaluation
- Establishment of the method
- Assignment of the evaluation team and allocation of resources
- Identification of the sources of data/documentation relevant to the device and its intended use:
 - o Data/documents from the literature
 - o Data generated through clinical experience (outside the framework of clinical investigation)
 - o Clinical investigation
- Appraisal of the clinical data (assessment of their credibility)
- Analysis of the clinical data (assessment of demonstration character)
- Establishment of the clinical evaluation report

The expected thoroughness of clinical evaluation may vary based on the risks, the degree of innovation, the pre-clinical evaluation, etc. Nevertheless, it should always be objective and its conclusion must be credible and reflect the generally recognized scientific and medical knowledge. The revised annex X of the MDD clarifies that in case of implantable or class III medical devices, the clinical evaluation must be based on clinical investigation unless duly justified.

Post market surveillance phase (PMS)

The PMS is defined as the range of activities intended to collect information relative to the safety and effectiveness of the device once it has been commercially launched. The extent of the PMS should be adjusted as well based on the risks, the actual knowledge of the clinical behaviour of the device during a representative period of its lifetime, etc. It is an essential element to actively update the clinical evaluation.

The concept of Post Market Clinical Follow-up (PMCF) was introduced by the MEDDEV 2.12.2 in 2004. It is now added to the regulation as the recognition itself to take into account the recognized limitations inherent to pre-market clinical evaluations and the possible extent of the data that can be gathered in the pre-market phase does not enable the manufacturer to

detect infrequent complications or problems only apparent after widespread use, or /long term performance issues. It is especially true when it is a long-term device (such as implants). Such PMCF must be implemented unless duly justified.

As a consequence, it is now expected that the PMS plan be established at the time of the commercial launch, based on the conclusion of the pre-market clinical evaluation and the risk management file. It will be updated as necessary whenever new data might suggest the rise of new concerns.

Assessment by Notified Bodies

In parallel to the enhanced expectation on the manufacturer's side, the Notified Body is invited to clarify their method of assessment of the clinical evaluation reports. The MEDDEV 2.7.1 rev.3 guidance document includes explicit tools for this assessment, including a turnkey analytical checklist.

For more information on this topic:

- See the complete Guidelines:
 - MEDDEV. 2.7.1 Rev.3 at: http://ec.europa.eu/enterprise/sectors/medical-devices/files/meddev/2_7_1rev_3_en.pdf
 - MEDDEV 2.12.2 Rev.1 at http://ec.europa.eu/enterprise/sectors/medical-devices/files/meddev/2_12-2_05-2004_en.pdf
- Learn about upcoming training sessions by emailing: gmedna@lne-gmed.com. Please put "Clinical Evaluation Training" in the subject line.

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