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# Stricter 'Equivalency' Requirements On The Cards For EU Device Clinical Evaluations

► By Vibha Sharma, 5 May 2016

A key working group at the European Commission has approved major changes to the current guideline on clinical evaluation of medical devices (MEDDEV 2.7/1, Rev 3)<sup>1</sup>, including stricter requirements for demonstrating equivalency between a device under evaluation and an approved product, says Françoise Schlemmer, director of the EU association of medtech notified bodies (TEAM-NB).

The changes aim to minimize –but does not eliminate – the use of the “equivalency route” (also called the “literature route”) by device sponsors, under which they are currently able to rely on clinical data from other similar products to show that the new product for which a CE-mark is being sought is at least as safe and performs as well as the approved device. The revised guideline (MEDDEV 2.7/1, Rev 4), when in effect, would force more companies to generate fresh clinical data to support the approval, and also the renewal, of their devices.

The changes to the MEDDEV appear to be a prelude to the forthcoming EU Medical Device Regulation, which contains even stricter requirements on clinical evaluation of devices, says Gert Bos, executive director and partner at consultancy company Qserve Group. The revised MEDDEV, however, cannot go as far as the MDR as it needs to stay in line with the current EU Medical Devices Directive, and “therefore there are limits to the push [in the revised MEDDEV] for demanding a company to have its own data derived from its own clinical studies,” Bos said.

Specifically, the revised MEDDEV states that sponsors may use only a single device against which to demonstrate equivalency and that when demonstrating equivalency, all three characteristics of a device – ie, clinical, technical and biological – should be critically discussed. Also, it clarifies that devices being compared

should have “the same material and [should be] for the same intended use and medical indication. The differences between the device under evaluation and the device presumed to be equivalent need to be identified, fully disclosed, and evaluated,” Schlemmer told *Scrip Regulatory Affairs*.

This is in sharp contrast to the current practice, wherein device sponsors typically refer to “several equivalent products”, and are mostly able to make a case that the new device (for which a CE-mark is being sought) raises no new safety or performance concerns and that there is, therefore, no need to undertake fresh clinical evaluation with the new product, and that they can rely on post-market surveillance and/or post-market clinical follow-up, Bos told SRA.

In complex cases, device sponsors “bring together a matrix of equivalent devices” and claim that each device is equivalent to some degree, e.g., in relation to physical aspects, biocompatibility, clinical use, etc, with the new product. So, in essence, various devices contribute additional elements in the equivalence equation, similar to the substantial equivalence claims that one can have under the US regime, explained Bos.

The revised MEDDEV requires notified bodies to “challenge the ability of a device sponsor to access information relevant for demonstrating equivalence,” Schlemmer added. With the introduction of these changes, demonstration of equivalence might be difficult or impossible for some devices, especially in cases where sponsors have limited access to technical documentation of the comparator device, she explained.

As a result of these changes, Schlemmer said that device manufacturers would have to update the clinical evaluation reports (CERs) for their respective products,

and might therefore have to employ additional resources. Also, they would have to decide which devices in their portfolio can follow the literature route.

The revised MEDDEV was adopted by the EU working group on Clinical Investigation and Evaluation (CIE) on April 13. It was then submitted to the Medical Devices Expert Group (MDEG) for approval via a written procedure, and this process is still ongoing. After finalization, the revised guideline will be published on the commission's website.

If things go as planned, the revised MEDDEV would likely be published on the commission's website later this month, Schlemmer said, adding: "There is a high pressure to finalize this document as fast as possible."

### Strict Enforcement Likely

Bos pointed out that some notified bodies have already started to slowly push device sponsors, whose files are currently under active review, to start adjusting to the principles outlined in the revised MEDDEV as these principles also form the basis of the joint assessments of notified bodies that are carried out by the commission and national competent authorities.

As the basis for equivalence will change under the new MEDDEV, and given the urgency with which authorities want to finalize the document, "it is clearly envisaged that once published it will be heavily enforced by the joint authorities and the joint inspection teams," Bos said.

However, some of the crucial questions that need answering are: when will notified bodies start enforcing the new MEDDEV? Will they apply it for new certificates and renewals only or also for reviewing change requests, or for all products currently on the market that have their CER based on equivalence?

For each of these scenarios, the real impact of the revised MEDDEV will be determined by how much time manufacturers would be allowed to re-work their data set. Also – and most importantly – it remains to be seen whether there would be any cases where the underlying certificates will be put under suspension until the revised CERs have been reviewed and approved, Bos said.

Given the huge implications of the revised MEDDEV for device sponsors, Bos recommended that

if a group of very similar devices has been used to demonstrate equivalence, the company could pick the product most resembling its own device. "But for matrix-based equivalence, it might be impossible to just select one and claim equivalence, as the matrix approach was needed due to the fact that there is no equivalence to a single product alone," he said.

In such cases, manufacturers will need to start with the "best fit" equivalent product, and then fill the gap in equivalence with additional data, probably from post-market clinical follow-up if they have such data, or otherwise by undertaking clinical trials to obtain data to fill the gap. "For some products this might be feasible, for others it might ultimately result in market withdrawal for the products," he said.

Some of the other changes made to the MEDDEV include:

- clarifying that the clinical evaluation requirement applies to all classes of medical devices and that it is the responsibility of the device manufacturer;
- clarifying that the clinical evaluation process is mandatory for obtaining the initial CE mark and that it must be updated thereafter;
- improvements to the various stages of the clinical evaluation process to reflect a clearer picture;
- new examples of the types of studies deemed inadequate to demonstrate clinical performance and/or clinical safety of a device;
- the introduction of a special interpretation for devices for unmet medical needs;
- the introduction of specific requirements regarding the clinical evaluation team at the manufacturer and the clinical assessment team at the notified body site; and
- specifying minimum expectations regarding the clinical evaluation assessment report (CEAR) of the notified body's assessment of the manufacturer's application.

### References

1. *Clinical evaluation: Guide for manufacturers and notified bodies (MEDDEV 2.7/1 Rev.3)*, Dec. 2009, <http://ec.europa.eu/DocsRoom/documents/10324/attachments/1/translations/en/renditions/native>