MEDTECH INSIGHT
CITELINE COMMERCIAL

17 Feb 2023 | **Interviews**

How Can The EU Get Clinical Evaluations For High-Risk Devices Right?

by Eliza Slawther

The new EU medtech regulations were developed as a reaction to unsafe products reaching patients; yet implementing new rules on clinical evidence has been anything but smooth. An expert from the BioMed Alliance tells *Medtech Insight* how this challenge can be addressed.

Manufacturers of high-risk medical devices often face the unknown when it comes to generating clinical evidence for EU regulatory conformity assessments. Dialogue between notified bodies and manufacturers is prohibited under the EU Medical Device and In Vitro Diagnostic Regulations, which can result in a misalignment between the data a company submits to a notified body, and the expectations that the notified body has.

More specifically, companies are not allowed to seek prior advice about what clinical investigations would be expected for a particular high-risk device before they select a notified body and submit their documentation.

This in-built feature of medtech regulation in the EU is "one of the major deficiencies in the system," according to Alan Fraser, chair of the BioMed Alliance in Europe's medical devices task force, as it means that companies are unable to identify in advance what evidence they will need to present to notified bodies during conformity assessments.

"We're told currently that one of the reasons for delays in renewal of certificates is that manufacturers are frequently asked by notified bodies for more evidence and more information, and that cycle can go backwards and forwards an average of three times," Fraser, who is also Professor of Cardiology at Cardiff University, told *Medtech Insight* during a recent video interview.

If manufacturers knew in advance what evidence they were going to be asked for at this stage, then it would shorten the review process, he noted. This is "probably even more true," Fraser

said, for new devices where "there aren't clear specific standards on methodologies for evaluation."

Indeed, the fact there is no option for manufacturers to enter early dialogues with notified bodies is just one contributor to clinical evidence generation challenges under the new regulations. More generally speaking, Fraser explained, there are still too few documents such as joint clinical standards, common technical specifications and Medical Device Coordination Group (MDCG) guidance for use in interpreting the MDR/IVDR rules.

"Notified bodies, in some circumstances, don't know how clinical standards should be judged. And we still do not know as a clinical community what standards they are applying."

Despite much criticism from industry, the European Commission is not likely to budge on its ban of consultation between notified bodies and manufacturers, as it stems back to the historic decision to use notified bodies in the regulatory approval system, which are independent commercial organizations.

Fraser acknowledged that the reason for banning early dialogue between notified bodies and manufacturers is structural, but argued that it is "illogical" and "not part of an ideally designed system."

Data suggests that manufacturers, and in particular those with innovative products, are venturing to non-EU markets and in particular the US to launch their products. "The European Union does need to do something," he said.

> *"Notified bodies, in some circumstances, don't know how clinical standards should be judged"*

Better Utilizing Expert Panels

Expert panels are one already established means of supporting manufacturers in generating suitable clinical evidence in the context of the MDR/IVDR, but their full potential is yet to be seen, according to Fraser.

While the main role of expert panels is to provide an opinion on the notified bodies' assessments of clinical evaluation of certain high-risk products under the new medtech regulations as part of a pre-market "scrutiny" process that reinforces MDR and IVDR clinical evidence rules, these

panels can also provide advice to manufacturers in some situations.

Ad hoc advice to companies should be made in line with *Articles 106* and *61(2) of the MDR*. There are 10 expert panels for products regulated under the MDR and one for IVDs.

"We support that they should be doing more work," Fraser said. "They have been appointed, but they're not being used as much as they might be at the moment."

This could be set to change, however. In January, the European Medicines Agency (EMA) announced a pilot scheme in which 10 successful medtech companies will receive fee-free advice on their clinical development strategies, with the aim of supporting them in generating the evidence required for successful conformity assessments from EU notified bodies.

The outcomes of the pilot project expert panel assessments will not be made public, however. Fraser has urged the EMA to ensure that after the pilot phase is completed, the scientific advice provided to companies is made available to other notified bodies, organizations and industry. If this information is not published, those in favor of more transparency argue, it could impact the ability of medical professionals to select the devices that they deem suitable for certain patients.

With a drug product, for instance, clinicians would be able to assess the clinical evidence generated in trials themselves to determine if the product is suitable. For medical devices, there is no guarantee of public access to documents submitted by companies during conformity assessments, which some health professionals believe impacts their ability to make fully informed treatment decisions.

"It should be transparent," Fraser said of clinical evidence evaluated during conformity assessments. "There is no clinically logical reason why the evidence that is available publicly should be so different from the evidence available for a new drug."

CORE-MD Project

Expert panel advice may help to improve the number of successful conformity assessment outcomes for innovative companies, but it will not solve greater problems with the implementation of MDR clinical evaluation rules.

CORE-MD, an EU Horizon 2020 project in which the BioMed Alliance is a partner, aims to improve the way in which high-risk medical devices are evaluated to promote innovation while maintaining safety provisions for patients.

The three-year long project, which began in April 2021, will review the methods used in clinical evaluations for high-risk medical devices and produce new trial design recommendations that are more suitable for these products.

For instance, data from randomized registry trials and the use of artificial intelligence (AI) are just some of the innovative evaluation methods on the CORE-MD radar.

As part of the first work package, CORE-MD is reviewing publicly available evidence for certain medical devices. During one such review, Fraser explained, researchers analyzed a random sample of high-risk implantable orthopedic devices.

“They found that for those they had reviewed, none had published clinical evidence at the time of CE-marking,” he said. Meanwhile, it takes an average of nine years on average for the first paper about a device to appear, which may be evidence from registries.

“This means decisions about choosing new devices for orthopedic implants are being made without proper scrutiny of the clinical evidence,” he said, something that is inappropriate.

In 2018, Fraser was the lead *author on a scientific paper*, published in *The Lancet*, which stressed the need for transparency of clinical evidence for medical devices in Europe. It seems that now, five years on, this sentiment is still highly relevant.