MEDTECH INSIGHT
CITELINE COMMERCIAL

25 Nov 2022 | **Interviews**

Define, Identify And Protect: How EU Regulators Can Prevent Device Shortages

by Eliza Slawther

There are growing fears that the new EU medtech regulations could result in products used for children or rare diseases vanishing from the market. In an interview with *Medtech Insight*, regulatory expert Tom Melvin explains how these devices can be protected.

“Define, identify and provide solutions” would be the mission statement of Tom Melvin, associate professor of Medical Device Regulatory Affairs at Trinity College, Dublin, Ireland, if he were tasked with preventing vulnerable medical devices from disappearing from the market in the EU.

While capacity bottlenecks, high costs for manufacturers and lengthy assessment times as a result of the EU Medical Device Regulation are set to *impact a wide range of medical devices*, Melvin’s focus is on products that are most at risk of becoming unavailable: those used in smaller numbers of patients.

While pediatric devices are more easily definable because age is a distinct metric, medtech companies need a “clear definition” of what an “orphan device” is, he said.

“But I would suggest that we don't require companies to have an intended use for that orphan indication,” Melvin contended.

“I think what we really need in a policy sense is to allow or accommodate devices that are not just intended by the manufacturer to be used for whatever we define as orphan device use, but simply ones that are used in this way by clinicians.”

Policy must, Melvin said, “allow or accommodate” for devices to be used not just as the manufacturer intended, where reasonable. For instance, off-label use of products is common practice in the EU where no alternative is available, but the MDR could change this (more below).

The creation of—or amendment to existing—policy would fall under the third and final stage of Melvin's three-pronged proposal to prevent device withdrawals and shortages. But for policy changes to be effective, regulators must also "identify" those at-risk devices to tailor their efforts.

"Once you define and identify, then you have to support. You have to decide what support is available under current legislation, and whether new legislation is needed."

Other changes, such as the reduction of costs and increasing the predictability of conformity assessments, would also be needed to create a more sustainable system for device manufacturers in the long-term. However, this is "no easy task," he said, so the "define, identify and protect" approach could be a strong starting point.

Melvin has previously authored an *academic paper* that sets out why the MDR could see medtech products used in *pediatric or orphan indications withdrawn* or never even placed on the EU market.

Off-Label Rules

In the *first part of this interview*, Melvin told *Medtech Insight* how the MDR's stricter clinical evidence requirements in particular are proving problematic for manufacturers. He also proposed the use of common specifications and policy change to make conformity assessments more predictable.

But clinical evidence requirements are not the only element of the MDR that could result in patients and health care professionals no longer having access to certain products.

A lack of support for companies around off-label use of devices under the new regulations, combined with requirements around gathering post-market data on off-label practices, also may have a negative impact on children or people with rare conditions.

"It's important to remember that when you're thinking about products for use in children or for rare diseases, typically, the majority are used in an off-label fashion," Melvin said. This means that the manufacturer will market it for one intended purpose, but it's actually used "in an entirely different population or organ system or an entirely different use."

Under the former medical device directives, off-label use of devices was "not really mentioned," which means that using products outside of their approved indication has become a "standard practice" for health care professionals if they have few alternative options, Melvin said.

"From my perspective, this is a very reasonable practice when you have limited intervention options," he said. For instance, surgeons may need to use a stent designed and CE-marked for an

adult renal artery on a baby's right ventricular outflow tract during heart operations.

"Under the MDR, something that's changed is manufacturers now have a responsibility to look at how their device is being used in the post-market stage and detect whether or not there is systemic off-label use," Melvin said. Indeed, if there is consistent or regular off-label use of a product, companies should control this or ideally add this indication to the product label.

Although this change is not in itself problematic, Melvin explained that it is an example of the MDR asking manufacturers to "be more particular", giving companies more defined responsibility for how their device is used after it is CE-marked.

"Hopefully, [the MDR] doesn't hinder the use of devices off-label where necessary," he said, but it does demonstrate the need for regulators to support companies in gaining on-label indications for devices—particularly given the difficult market dynamics for products used in less common patient groups or for rare conditions.

"For regulators, this will be a challenge because they would in a sense be allowing that off-label use, but it's a necessary allowance they would have to give here in the public health interest."

The EU notified body association, TEAM-NB, issued a *position paper* on the off-label use of products in October.

While using products off-label is not technically legal, it would be unethical for a physician to deny a patient care and therefore if no suitable alternative device is available, using a device outside of its labeled indication is acceptable.

Incentive Schemes Not The Answer

As outlined in the paper authored by Melvin and his research colleagues, incentive schemes are in place for pharmaceutical companies who develop medicines to treat pediatric and rare diseases.

For instance, the European Medicines Agency (EMA) offers '*orphan designation*' to investigational therapies that meet certain criteria around addressing an unmet need within the rare disease space. This is because by nature, drugs and medical devices used to treat people with rare conditions do not generate much profit as the number of patients they can be used for is small.

Could such incentives be translated into the medical device sector to encourage the development of products that are less profitable? Melvin is not so sure.

While drug companies who qualify for the EMA orphan designation scheme can benefit from

scientific advice, which would be helpful for medtech firms, the main advantage to this designation is extended market exclusivity.

“Regulation, reimbursement and the world of intellectual property are entirely separate [for medical devices] in Europe, which makes a definitive policy that brings those things together impossible without an enormous legislative push that I don’t think would happen.”

Patent exclusivity rules are also very different in medtech. While pharmaceutical companies may develop a specific chemical product under a brand name that other companies can reproduce exactly to product a generic or biosimilar, medical devices may have the same purpose but be designed and developed in different ways.

In the US, *priority review vouchers* are offered to companies who develop medicines for rare pediatric diseases. These vouchers can then be used for another product in the company’s portfolio to speed up the review process, or even sold to another firm.

Once again, this type of incentive is unlikely to work in Europe’s decentralized medical device regulatory system.

> *“Regulation, reimbursement and the world of intellectual property are entirely separate in Europe”*

“We have more of a free market dynamic in medtech,” Melvin said. “You're free to select a notified body with competencies for your device, so something like [priority review vouchers] probably wouldn't be much of a runner.”

Funding Initiatives

Rather than offer incentives to companies in the form of vouchers and exclusivity, public-private partnerships that provide funding and support to manufacturers of these niche devices would be more suitable in Europe, Melvin suggested.

“Europe is great at doing that through program such as the *Horizon health initiative*,” he said. “The EU is really good at getting those things organized across disciplines and specialists and stakeholder types and groups.“

Horizon Europe is a funding program for innovation in the EU that will run until 2027 with a

budget of €95.5bn ($99.5bn). Its aim is to boost scientific innovative research across numerous sectors, including in health.

> *"We need a way to allow companies to continue marketing under the old rules until we get the necessary support."*

Meanwhile, the EU4Health 2023 work program, *announced this week*, includes a *call for action grants that will orphan medical devices*, particularly those used for rare childhood conditions.

While it "would be nice to see something in this area," Melvin said, this is "not going to help in the next six months or year."

"What we need is basically a triage step and we need a way to allow companies to continue marketing under the old rules until we get the necessary support."