Roundtable Session – Table 8 – The MDR Regulation Including the Latest Updates

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Abstract:

This roundtable will bring together experts to discuss real-word experiences and implementation challenges since the MDR entered into force and how the European Commission's latest MDR proposal updates could address (or fail to address) those challenges—both for CE marked devices but particularly for integral drug-device combination products (iDDCs).

Discussion Questions:

1. Since MDR implementation, which areas have been improved and which 2-3 areas have created the biggest friction for stakeholders? If you could change one specific thing in the MDR or how it is applied what would that be - and what outcome would you expect?

2. From your experience with iDDCs, what are the most significant practical challenges across the framework - specifically: a) pre-submission/NB engagement (what is unclear, when and why?), b) evidence/documentation expectations for Notified Body (NB) involvement, c) post-market obligations and lifecycle management (how coordination actually happens in practice) Where have you most often seen duplicate effort, misalignment or gaps?

3. The current framework does not enable early, coordinated scientific advice for iDDCs? What is your preferred model to achieve it? (e.g. a single integrated scientific advice mechanism, who should provide it, what should be covered, should structured dialogue exist alongside dedicated scientific advice for iDDCs)

4. Looking at the MDR proposals/updates, which elements do you believe are the most relevant steps toward a better and more competitive European device framework and why? Conversely, what crucial aspects are not being changed (or are being changed in a way that still leaves uncertainty) that you believe must be addressed to improve predictability and patient access.

Notes from roundtable discussion:

Some areas from the MDR have been approved and some parts are more challenging. For the purpose of this roundtable discussion, EMA is the term used here and can also be considered to be interchangeable with EU national regulatory agencies.

The Challenges and Opportunities

Since the introduction of the MDR, the Notified Body is responsible for assessing the device part of the integral drug device combination product whereas the EU national agency/EMA (hereafter referred to as EMA) is responsible for assessing the drug product.
Challenges are experienced on both sides. where there is a fragmented process with regards to the responsibility split between the EMA and the Notified Body. There is a need for clear expectations as to what needs to be communicated to both EMA and the Notified Body by the company, as it is often the company who has to mediate between the two. There is duplication of assessments by the Notified Body and EMA, which is compounded by the different timelines of the assessments by the Notified Body and EMA, and lack of standardisation of the Notified Body opinion itself, and sometimes with notes for EMA. In some cases, it is difficult to understand the outcomes of the Notified Body. There is need for harmonization for the drug-device combination products, and it was encouraging to hear from the authorities that they face the same problems as industry and are discussing drafting a guidance to address this. To this end it could be an idea to go through the Notified opinions of similar DDCs for similar dosage forms to see where there are overlaps and where there are gaps.

In Europe there are 50 NBs accredited to assess medical devices, but to-date only 5 to 10 have the expertise for integral DDCs. Hence a selection of a Notified Body needs careful planning, as it may take some time to find a suitable NB, potentially resulting in a cost on timeline for submission if the Notified Body needs to be changed.

Scientific advice

There is lack of scientific advice from the NB as it is a private company and not an authorized regulatory body. Scientific advice can be obtained for the drug product part from EMA, but not from the Notified Body for the device part of the iDDC. The criticality of the combined product (iDDC) can be important for the device platform, and difficult to connect both device and product. One solution could be to have a joint scientific advice between EMA and the Notified Body.

Lifecycle management

Although EMA provides Q/A guidance, it is not always clear on how to handle LCM changes, eg when there are changes to a iDDC, or an additional indication is needed, or introduction of a new strength, where the specifications may be different for the product. A clear guidance for both the Notified Body and EMA is needed for handling changes. Furthermore, there are challenges with legacy products, which previously were not subject to the MDR Art.117 and where only an EMA assessment was required at the time of approval, and where a Notified Body opinion is now required.

Clinical trials

A disharmonisation in the requirements for devices used in the clinical trials where there appears to be different requirements or acceptability of devices used within the national agencies in the EU. Some companies may choose not to run a clinical study in a given country, if they anticipate that their device may not be accepted and needs prior approval, thus potentially delaying a clinical trial.

The future and proposals for moving forward

To address some of the challenges the Combination Products Operational Group (COMBO) with experts from competent authorities responsible for medicines and medical devices, notified bodies, EMA and the European Commission and members from the MDCG (Medical Device Coordination group), EMA and notified bodies –was set up last year in the autumn. This group is currently setting up their mandate and a position paper and will consult later with industry (more information to be provided on EMA's website)

Proposal from roundtable group: could have a platform approach for devices used for iDDCs that could facilitate a baseline for a type of integral iDDC to establish a foundation for approvals and postapproval changes.

Proposal from roundtable group: to have one entry point with EMA reaching out to the NB for the device expertise, ie a closer relationship between EMA and the Notified Body. Proposal is for the company to choose the Notified Body and maybe have a Letter of access for EMA to directly contact the Notified Body. In addition, a joint scientific advice between EMA and the Notified Body is proposed.

The MDR is currently open for targeted revisions