Major Regulatory Change for Combination Products in the EU – Are you prepared?

anteris medical GmbH
Dr. Michael Gschwandtner

Aug 31st 2018

With the release of the Medical Device Regulation (MDR) 2017/745 the Medicinal Product Directive in the EU has been amended and significant changes for medicinal products that include a device constituent part (e.g. pre-filled syringes, autoinjectors and inhalers) were introduced.
This article outlines the changes and the expected impact for your combination product.

CURRENT STATUS

If a product comprised of a drug and a device constituent part and is governed by the Medicinal Product Directive 2001/83/EC, the device constituent part needs to fulfill certain aspects of the Medical Device Directive 93/42/EC (i.e. Annex I of the directive). This is typically including device development activities such as requirements engineering, design verification, human factors engineering, and others. Like all medical device development activities, such activities need to be documented in specific device files which may or may not become referenced or included in the regulatory dossier for the medicinal product. As part of the review by the health authority (e.g. the European Medicinal Agency, EMA) the device part can be expected to be examined by the regulators. Ergo, no specific medical device body is directly involved.

CHANGES UNDER THE MDR

With the implementation of the MDR the situation has now fundamentally changed.
The key concept is that the Medicinal Product Directive continues to be the governing regulatory framework for the combination product as described above. However, Article 117 of the MDR has amended the Medicinal Product Directive 2001/83/EC in the following way:
"...the involvement of a notified body is required in accordance with Regulation (EU) 2017/745, the authority shall require the applicant to provide an opinion on the conformity of the device part with the relevant general safety and performance requirements set out in Annex I to that Regulation issued by a notified body designated in accordance with that Regulation for the type of device in question."

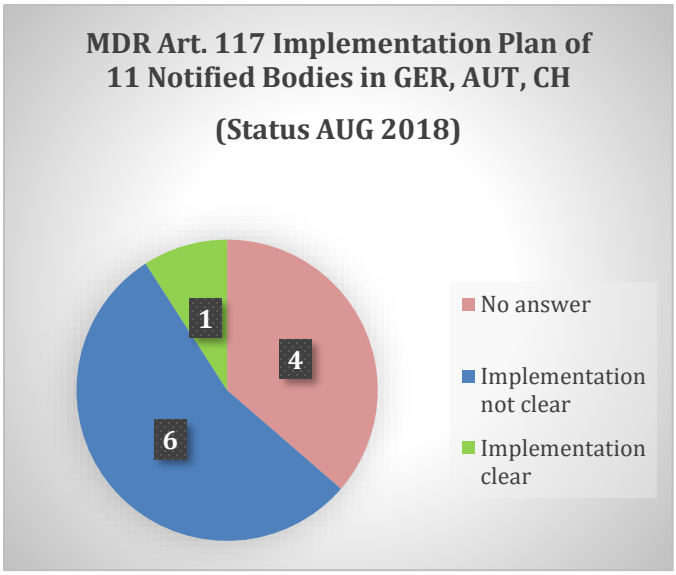
The key question, therefore, is the necessity of the involvement of a device regulatory body, i.e. a specific Notified Body. It has to be involved by reviewing the device part of the regulatory dossier and by providing an opinion whether this part fulfills Annex I of the MDR, or not. Considering that combination products which are regulated as medical devices under the MDD and having a drug constituent part (e.g. coronary stents coated with a drug) need to obtain an opinion from a medicinal authority in order to achieve approval, the change described above is only consequent, however, the impact for all stakeholders can be expected to be huge.

ISSUES

One major issue is that the medical device industry, including the Notified Bodies, are under immense time pressure implementing the changed and additional MDR requirements for all medical devices. Due to the increasing regulatory requirements for the Notified Bodies, some are closing doors or go into acquisitions to form larger organizations . It should be emphasized that for Notified Bodies the described combination

products are considered just one out of dozens of product types and don't have particular priority over other MDR implementation aspects they need to address during a dwindling remaining time window.

We asked 11 Notified Bodies from Germany, Austria and Switzerland how they interpret this MDR Article 117 and how this process of obtaining an opinion would work.
Only 1 out of 11 had a plan in place how this process might be implemented. This Notified Body seemed to be very pragmatic as here the lack of guidance from the regulators is interpreted as freedom to define it in the best way for their organization.
4 Notified Bodies did not answer at all and 6 did answer, but either asked us to come back at a later point in time, or they already indicated that they will not offer such kind of support.



The issue for pharmaceutical companies who are planning to submit a drug product with device constituent part to e.g. the EMA will need this Notified Body opinion very soon (especially once the transition of the MDD to the MDR in 2020 is over) and before they submit their regulatory dossier. If there is no Notified Body offering this in time, this might put the complete submission at risk.

WHAT TO DO

Therefore, we can only encourage manufacturers falling under this requirement to make sure all device requirements are fulfilled for their product and then get in touch with a Notified Body as soon as possible to reserve a time slot very soon to get this essential opinion. The more companies asking for this opinion the more pressure is on them.

If you need any advice or assistance e.g. for your pre-filled syringe, autoinjector, or on-body device project please do not hesitate to reach us at info@anteris-medical.com.
We are very happy to provide a first opinion quickly and free of charge and to help you with your specific project challenge.