DRUG-DEVICE COMBINATION PRODUCTS

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The EU Medical Devices Regulation (MDR) 2017/745, which replaces the existing medical devices Directives 93/42/EEC and 90/385/EEC and amends the medicinal products Directive 2001/83/EEC, will apply from 26 May 2020.

The MDR, amending Directive 2001/83/EEC, clarifies the definitions of products with a medical purpose to determine whether the products are regulated as medicinal products or medical devices depending on their principal intended mode of action. The mode of action for medicinal products is primarily pharmacological, immunological or metabolic, while the mode of action for medical devices is primarily physical or mechanical.

If the principal intended action of the drug-device combination products is achieved by the medicine, the entire product is regulated as a medicinal product under Directive 2001/83/EC and Regulation (EC) No 726/2004 (for centrally authorized products).

Since the beginning of 2019, the EMA has published two documents in relation to this new regulation and the expectations for manufacturers of drug-device combination products:

> A Q&A guide on implementing the MDR published in February 2019

> A guideline for public consultation on the quality requirements for drug-device combinations published in June 2019

Two types of drug-device combination products are defined in the MDR:

> Integral drug-device combinations: The medicinal product and the medical device form a single integrated product. Two types of integral drug-device combination products are defined:

- Any device that incorporates, as an integral part, a medicinal product where the action of that substance is principal and not ancillary; e.g. a drug eluting intra-uterine device
- Any device that is intended to administer a medicinal product, in such a way they form a single integral product intended exclusively for use in the given combination and which is not reusable; e.g. a pre-filled syringe

> Non-integral drug-device combinations: The medicinal product and the medical device are separate items, but they are combined for administration of the medicine. They can be co-packaged or obtained separately. These devices should be CE marked.

In case of integral drug-device combinations, there is a new requirement described in article 117 of the MDR that amends Annex 1 of the medicinal products Directive 2001/83/EEC. The marketing authorisation application for medicinal products that incorporate a device component as a single integral final product will need to:

> Include, where available, the **results of the assessment of the conformity of the device part** with the relevant general safety and performance requirements […] contained in the manufacturer's EU declaration of conformity or the relevant certificate issued by a notified body

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> **If the application dossier does not include the results of the conformity assessment** […] and where for the conformity assessment of the device, if used separately, the involvement of a notified body is required […], **the authority shall require the applicant to provide an opinion on the conformity of the device part** […] issued by a notified body […]

For integral drug-device combinations already authorized or those submitted before the date of application of the MDR (26 May 2020), the requirement of article 117 is not applicable, except if manufacturers make substantial changes to the design or intended purpose of the device component or introduce a new device.

EMA published on June 3, 2019, a draft guideline on the quality requirements for drug-device combinations including the manufacturing and control methods. This draft guideline:

> Covers integral drug-device combinations and non-integral drug-device combinations

> Applies to drug-device combinations where the medicinal product constituent is a chemical, biological or radiopharmaceutical

> Clarifies what is expected in the quality part of the dossier for a marketing authorisation application or a variation application

> Contains a template for the notified body opinion on the conformity of the device to the relevant general safety and performance requirements described in Annex I of the EU medical device regulation

A marketing authorisation application for a drug-device combination should include:

> A demonstration of compliance with any relevant European Pharmacopeia chapters or monographs

> Structured information on the device:
  - Relevant to the quality, safety and efficacy on the medicinal product
  - Demonstrating compliance of the device with MDR Annex I
  - Related to manufacture, control and usability of the device drug combination as defined for the intended patient population

> A discussion and justification for the use of platform technology/technologies

The specific requirements for what should be included in marketing authorisation applications (with reference to the modules of the eCTD) for integral drug-device combinations and non-integral drug-device combinations are provided in chapters 5 and 6 of the draft guidance. Chapter 6 differentiates a non-integral drug-device combination with co-packed medical devices and a non-integral drug-device combination with separately obtained devices.

EMA specifies that this guideline will increase transparency and consistency of information in regulatory submissions, reducing work for all stakeholders and ultimately improving patient safety.

Contact us at **healthsciences@nsf.org** or visit **www.nsfhealthsciences.org** if you have any questions on the article.

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