NEW IMPLICATIONS FOR DRUG-DEVICE COMBINATION PRODUCTS

Although a short Article, Article 117 has significant impact to the manufacturers of integral drug-device combination products (for example pre-filled syringes, pre-filled injector pens or novel pre-filled devices) and device manufacturers that supply their products to be sold with pharmaceutical or biopharmaceutical products (for example an empty syringe). Currently, combination products with device components are required to fulfill certain aspects of the Medical Device Directive 93/42/EC however the information may or may not be included in the regulatory dossier for the medicinal product and no specific medical device body is directly involved. With this amendment of the Medicinal Product Directive (MPD), Marketing Authorization Applications (MAA) must include either:

1) CE certificate issued by a Notified Body for the medical device component OR
2) Notified Body Opinion (NBO) on the conformity of the device

In option 1, the manufacturer of the medical device would obtain CE marking using the appropriate conformity assessment process applicable to the device. The CE Certificate would be submitted in the MAA. In option 2, where the device component on its own has not been issued a CE mark, the manufacturer must seek the opinion on the conformity of the device from a Notified Body and provide the NBO report in the MAA.

To provide an NBO, Notified Bodies will require Technical Documentation that provides evidence/scientific data to support product claims. Technical Documentation expectations are detailed in Annex II of the MDR. Although not a comprehensive list, information that is typically required by Notified Bodies to support a conformity assessment for medical devices includes:

- Risk Management Documentation
- Safety and Performance Data including clinical data
- Functionality Testing (accuracy of dosage, performance of device)
- Instructions for Use/Training for Users
- Usability/Human Factor Testing
- Compatibility Testing
- Sterilization Validation, Sterility Test Data
- Packaging Validation Testing

WHAT DOES IT SAY?

**Article 117** of the new European Union Medical Device Regulations (EU MDR) amends Annex I of the Medicinal Product Directive (MPD) 2001/83/EC.

**IT STATES:**

Where...a product is governed by this Directive, the marketing authorization dossier shall include, where available, the results of the assessment of the conformity of the device part with the relevant general safety and performance requirements set out in Annex I to that Regulation contained in the manufacturer’s EU declaration of conformity or the relevant certificate issued by a notified body allowing the manufacturer to affix a CE marking to the medical device. If the dossier does not include the results of the conformity assessment referred to in the first subparagraph and where for the conformity assessment 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.
NEXT STEPS FOR MANUFACTURERS

The scientific data submitted must demonstrate conformance to the applicable General Safety and Performance Requirements (GSPRs) found in Annex I of the EU MDR. Based on the data provided, Notified Bodies will assemble an NBO Report that concludes whether the device meets or does not meet all the applicable requirements. If the NBO concludes that requirements are not met, the manufacturer should work with the Notified Body to obtain a positive opinion. The NBO Report is expected to be submitted in full to the European Medicines Agency (EMA) in the MAA by the manufacturer. Final approval of the product will remain with the EMA. A guidance document outlining quality requirements for medicinal products containing a device component for delivery or use of the medicinal product is expected to be released for comment by the EMA in Q2/2019.

To obtain an NBO, manufacturers should engage with Notified Bodies as soon as possible. The Notified Body must be designated to assess the specific medical device technology under the EU MDR. Since there is a sizable reduction in the overall number of Notified Bodies certified to the EU MDR, the number of Notified Bodies designated and thus available to assess specific medical device technology will be limited.

Although there are many questions that remain about implementation of Article 117, the following are current thoughts – they are subject to change as further information becomes available:

- Article 117 will apply to all MAAs containing a medicinal product with an integral medical device as of 26 May 2020.
- Article 117 will not apply retrospectively to medicinal products with an integral medical device already authorized or to MAAs filed prior to 26 May 2020.
- Article 117 and NBO requirements will be applicable to authorized products that undergo a significant change after 26 May 2020.
- Notified Body Opinions will not include quality management certification.
- Not all GSPR’s will be applicable to integral drug-device combination products.

In preparation for implementation of Article 117 of the EU MDR, manufacturers should:

1) Identify a Notified Body intending to be EU MDR designated for their specific technology;
2) Assess which GSPR’s are applicable to their products;
3) Obtain scientific data that demonstrates conformance to the applicable GSPRs;
4) Assemble Technical Documents to support the medical device components.

LET US HELP YOU PREPARE FOR IMPLEMENTATION OF ARTICLE 117 OF THE EU MDR.

Do you have more EU MDR questions?
Reach out to us. We can help you navigate the new regulations!