EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Drug-device combination products under the MDR

EMA 1-year experience

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Outline

MDR implementation

- What have we observed?
  - Experiences and challenges
- What is ongoing and what is next?

What have we observed?

- **Changes and inconsistencies in the qualification and classification** (e.g. some medical devices/medical device parts with impact on evidence provided, 'add-on' smart device (to integral device) and of connected App as MD software, accessory to MD vs not MD)
- Need for **adjustment of economic operator roles** (medicinal product applicant vs medical device manufacturer)
- MAHs seeking **advice to EMA on lifecycle management of integral device changes**
- Proposals from applicant/MAH to address **device labelling requirement of co-packaged devices**

Article 117: Experiences and challenges

1. Device classification issues and impact on NB Opinion requirement

Example of single-use prefilled syringe (PFS) without needle

- ❑ Similar intended use but classified as I, Is, IIa or III by manufacturers / MAA applicants
- ❑ A Notified Body issued an Opinion for a PFS they considered as Class I ➔ remit?
- ❑ Co-packaged or separately-obtained CE-marked needle outside the scope of the PFS NB Opinion
- ❑ Any benefit for patients and healthcare professionals to provide a PFS without needle?
  - ➢ Attaching a suitable needle before administration represents additional risks
- ❑ **Article 117 matters should be discussed and agreed during pre-submission**

Article 117: Experiences and challenges

2. Partial compliance with relevant GSPRs

The NB Opinion is binding to CHMP

- **Lack of full compliance with the relevant GSPRs impacts the approvability of the MAA, line extension and variation**
  - CHMP cannot bypass the NB Opinion
  - CHMP cannot follow-up on deficiencies identified in the NB Opinion
- In case of partial compliance, the applicant should liaise with the Notified Body to address the deficiencies and provide a revised NB Opinion before CHMP Opinion
  - **Recommendation to have the final NB Opinion ready at submission to avoid delays**

    But in practice many applicants file the MAA/line extension and NB Opinion applications in parallel to save time

Article 117: Experiences and challenges

3. Lifecycle management: what is a "substantial" change?

- ❑ Change affecting design, performance, safety characteristics, intended purpose of the medical device
- ❑ Impact on QTPP, DDC CQAs, DDC overall control strategy, delivery, IFUs

BUT:

- ❑ No legal definition of a substantial/significant change to a medical device
  ➔ Applicability of MDCG 2020-3, ISO 20069 or TeamNB guidance?
- ❑ Different perspectives on the importance/relevance of a change
- ❑ Does a change in intended use (e.g. new paediatric indication) always qualify as a substantial change? ➔ It depends!

Article 117: Experiences and challenges

4. Lifecycle management: challenges

- **Advising on the need for new or revised NB Opinion for device changes falls outside EMA remit**
- **But industry cannot consult a NB if they did not previously assess the device (due to their legal mandate)**
- New or revised NB Opinion, if required for device changes, expected in the line extension/variation based on MAH risk assessment. If not provided, a justification is expected in the dossier
- Classification guideline on variations lacks granularity for device changes
  - ➔ "Substantial" device-related changes not defined
  - ➔ 4 scenarios for devices changes: variation (yes/no); new/revised NBOp (yes/no)
- ICH Q12 example to define Established Conditions for a PFS: work in progress
  - ➢ Should inform the **revision of the Classification guideline (Pharma Strategy)**

Art 117: Experiences and challenges

5. Qualification and proof of compliance with MDR

- **Numerous variations to remove declaration of conformity and CE-mark for some device components** (part of existing integral drug-device combinations or co-packaged device)
- Device manufacturers no longer classifying a number of previous class Inm, ns, nu, devices as medical devices and removing declaration of conformity and CE-mark (e.g., for syringe system components; dosing cup for water for reconstitution)
- **What evidence to show compliance with GSPR?**
- For MD or accessories to MD, evidence needed. Hence **if to be issued after 26 May 2021 even for an existing integral device, either a DoC, EU-certificate or a NB opinion in accordance with MDR is required** (but not a kind of conformance statement by the MAH)

What is ongoing and what is next?

EMA/CMDh exchanges on MDR implementation to share cases/industry requests and develop harmonised way forward

Ongoing review of Industry comments
(post-publication of Q&A update, final Quality guideline and current experience)

Plan for an **update of the Q&A on MDR/IVDR implementation** in 2022

Plan to enhance **training on MDR**

Thank you for your attention

Further information

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MDR implementation – Recap on state of play

Medicinal products used in combination with a medical device (Art 117)

- MDR entered into application on 26th May 2021
- Almost 1-year experience with the transitioning from MDD to MDR