EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Lifecycle management of combination products at post-authorisation.

13th Meeting of the industry stakeholder platform on the operation of the centralised procedure for human medicines

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Connected combined products

Variation classification for Connected Combined Products

- The current variation guidance and its revision do not state specific requirements per device type (including CCP). A risk-based approach is applied to the classification and it is based on potential impact on the device combination with the medicinal product.
- Once enough experience is gathered, specific requirements per type of device could be covered in guidance (e.g. Q&A), if needed.
- The revision of the guidance, which is done within the context of the current pharmaceutical legislation, aimed at keeping the principles broad, so that the text does not become obsolete if/when new technologies are developed and may present new peculiarities.

Variation classification for Connected Combined Products

The choice of variation category is always based on the potential impact on quality, safety, efficacy and performance of the combined product from the medicinal product perspective.

Current classification guidance

Type II – Introduction or major changes to a CCP
Type IB – Minor changes to a CCP

New draft classification guideline

Type II – Introduction or major changes to a CCP
Type IB – Minor changes to a CCP
Type IA – Only if all conditions are met (If assessment is needed to determine the impact, a IA is not appropriate)

General data requirements for non-integral CCPs

- Impact assessment of CCP on quality, safety and efficacy of the medicinal product and mitigation measures (including data)
- Usability study for the CCP, unless absence justified by use-related risk analysis
- Compatibility with medicinal product
- Risk management plan review (if needed)

Additional requirements may be needed on a case-by-case basis, the current guidance on quality documentation for medicinal products when used with a medical device does not cover specific requirements per device type.

EMA support on variation classification for CCPs

For type II variations, MAHs are invited to contact the Product Lead (PL) for any query related to pre-submission aspects, such as variation classification; for **quality** type II variations, the PL is the quality specialist assigned to the product.

For type I variations, queries should be submitted through the portal (link below).

Once adequate experience has been gained through formal and informal interactions with stakeholders on a specific topic where a more detailed description of the regulatory requirements would be beneficial to stakeholders, such as requirements for CPPs, the possibility of publishing a guidance document, such as a Q&A, will be considered by EMA.

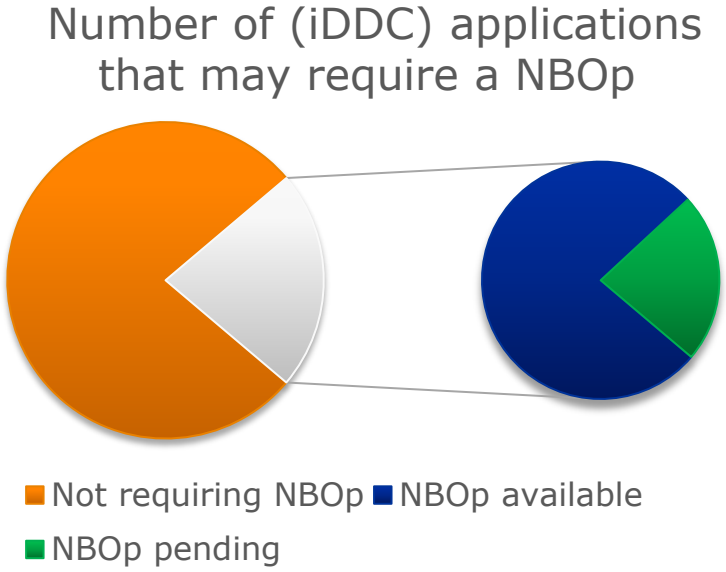
https://www.ema.europa.eu/en/human-regulatory-overview/post-authorisation/contacting-ema-post-authorisation

Analysis of Art 117 Notified Body Opinions for Integral Drug-Device Combinations through the centralised procedure

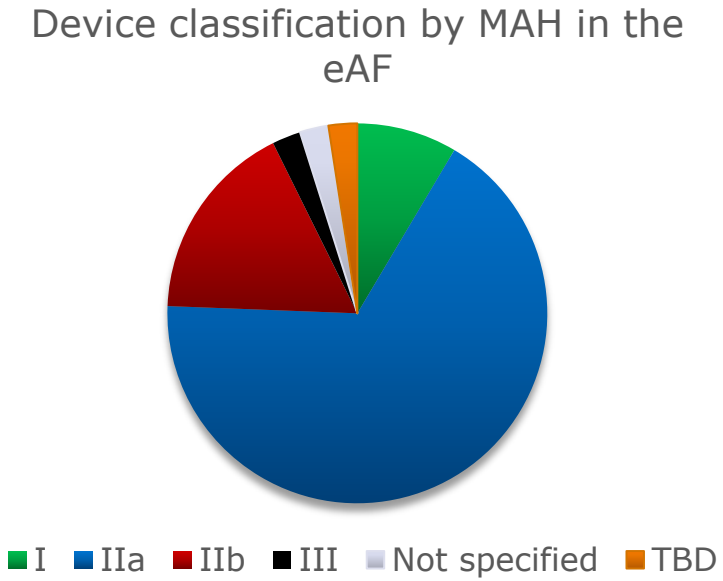
May 2021-Mar 2024 analysis

Preliminary findings

- Analysis of submitted **MAA and extensions** between **26 May 2021 to 31 Mar 2024**
- About **25% of all (68) procedures concerns integral drug-device combinations** falling under MDR Art 117
- Out of 68 procedures, **75% had one or more NBOps currently available**. The others were still to be provided prior to CHMP opinion.
- **Only 2 dossiers provided a DoC**



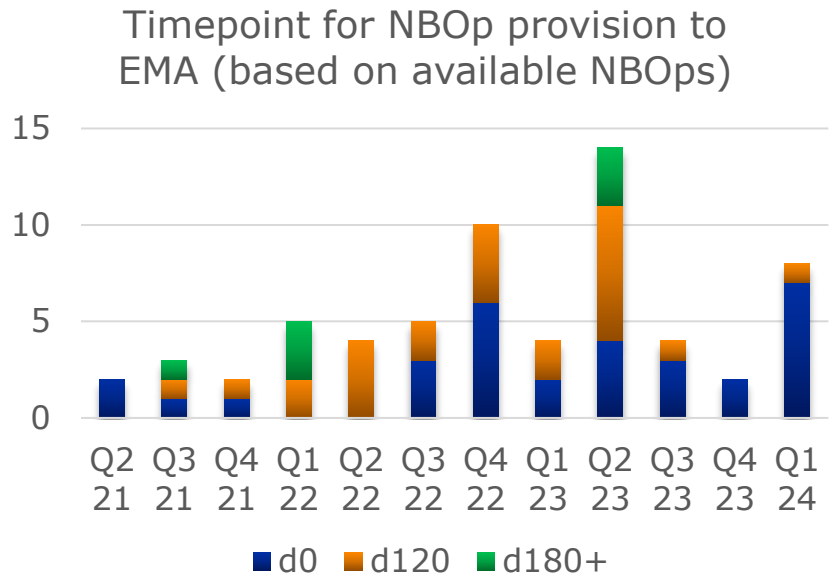
Preliminary findings – classification and type of device



- **Majority** of device-components identified in eAF by MAH are **class IIa**
- Almost exclusively PFSs and PFPs/Autoinjectors
  - Classified by the MAH mainly as class IIa but also class I, Is, IIb, III
  - Other forms : (1) inhaler and (1) applicator for implant
- Of note **NBOps were provided for class I devices** (in comparison to 2 cases where DoC provided)

Preliminary findings – Timepoint for NBOp provision

- At the time of entry into force of the Art 117, NBOps were mostly provided at time of submission of the MA application
- Then a trend showing provision of the NBOp during the MA evaluation procedure
- From Q4 22, seems to evolve towards provision of the NBOp at time of submission



Findings – Variations and NBOp

- To determine the number of **(14) NBOps submitted in the context of a variation** (type II or potentially IB) – same time period, the analysis focuses on variation scopes most likely to prompt the need for new/updated NBOp which are the ones listed below:

Scope	N° of variations	Art 117 documentation
Type II B.IV.1.c *Addition or replacement of a device which is an integrated part of the primary packaging*	14 (inc. 1 withdrawn)	12 NBOp, 1 DoC
Type IB B.II.g.5.b *Implementation of changes foreseen in an approved change management protocol*	9	1 NBOp
Type IB B.II.g.5.c *Implementation of a change for a biological/immunological medicinal product*	63	None

- Findings aligned with MA/LE findings in terms of concerned NB, class, types of devices (PFP/PFS, 2 inhalers and 1 spray)

Preliminary findings – NBOps content

NBOps provided in the concerned CP procedures were issued by 7 different NBs (but mainly 2 NBs issuing together approx. 75% of NBOps)

- Contents are relatively aligned between NBs in terms of aspects covered:
  - High-level description of the device component
  - Description of the integral DDC (intended purpose, therapeutic context, etc.)
  - Technical description of the device
  - GSPR (check)list and solutions implemented
  - Compliance conclusion

But some inconsistencies have also been noted such as:

- The extent of the report on the findings and assessment for the GSPR
- The GSPR labeling: either the medicinal product labeling for the outer packaging and instructions for use with the PL are provided or just a reference to the PI of the finsihed product is made

Of note: for the MAA/extension/variation, need for a **NBOp concluding on full compliance with relevant GSPRs**

Any questions?

Further information

[Insert relevant information sources or contact details as applicable.]

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