ASPHALION
MedTech

Regulation (EU) 2017/745: Understanding its impact on Drug-Device Combinations in Directive 2001/83/EC

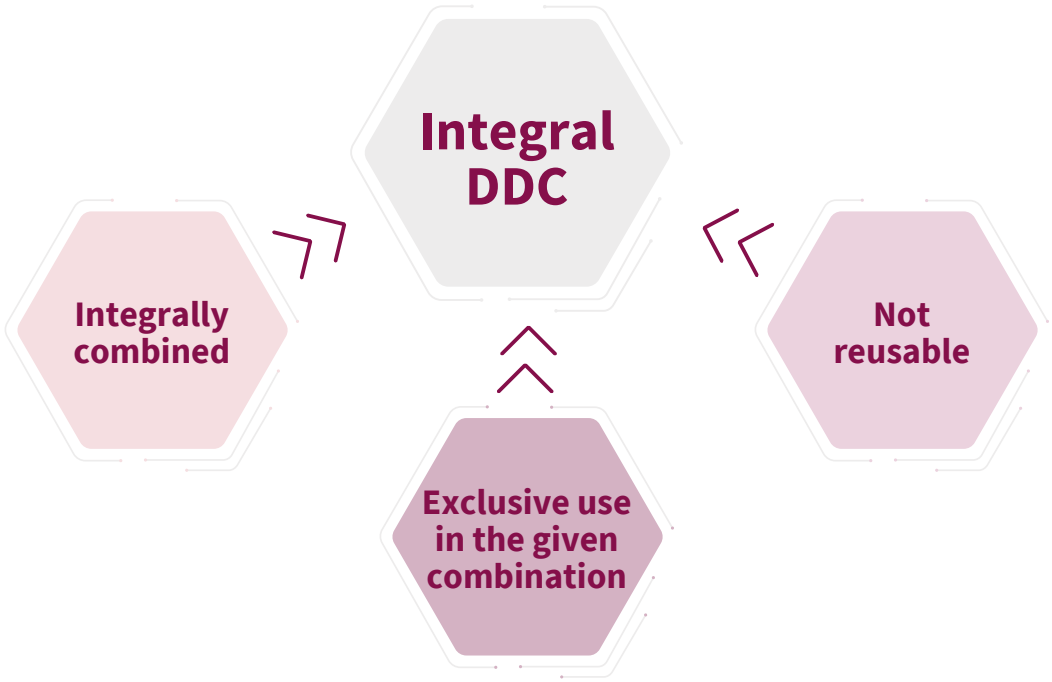
ASPHALION MedTech

What are drug–device combination products (DDCs) and how are they classified in Europe?

DDCs incorporate a medical device component and a medicinal product component, under EU frameworks: Regulation (EU) 2017/745 (MDR) and Directive 2001/83/EC (MPD).
DDCs are considered "integral" only if ALL of the following apply. Otherwise, they are "non-integral".

Article 177 of MDR

Article 177 - Integral drug device combinations



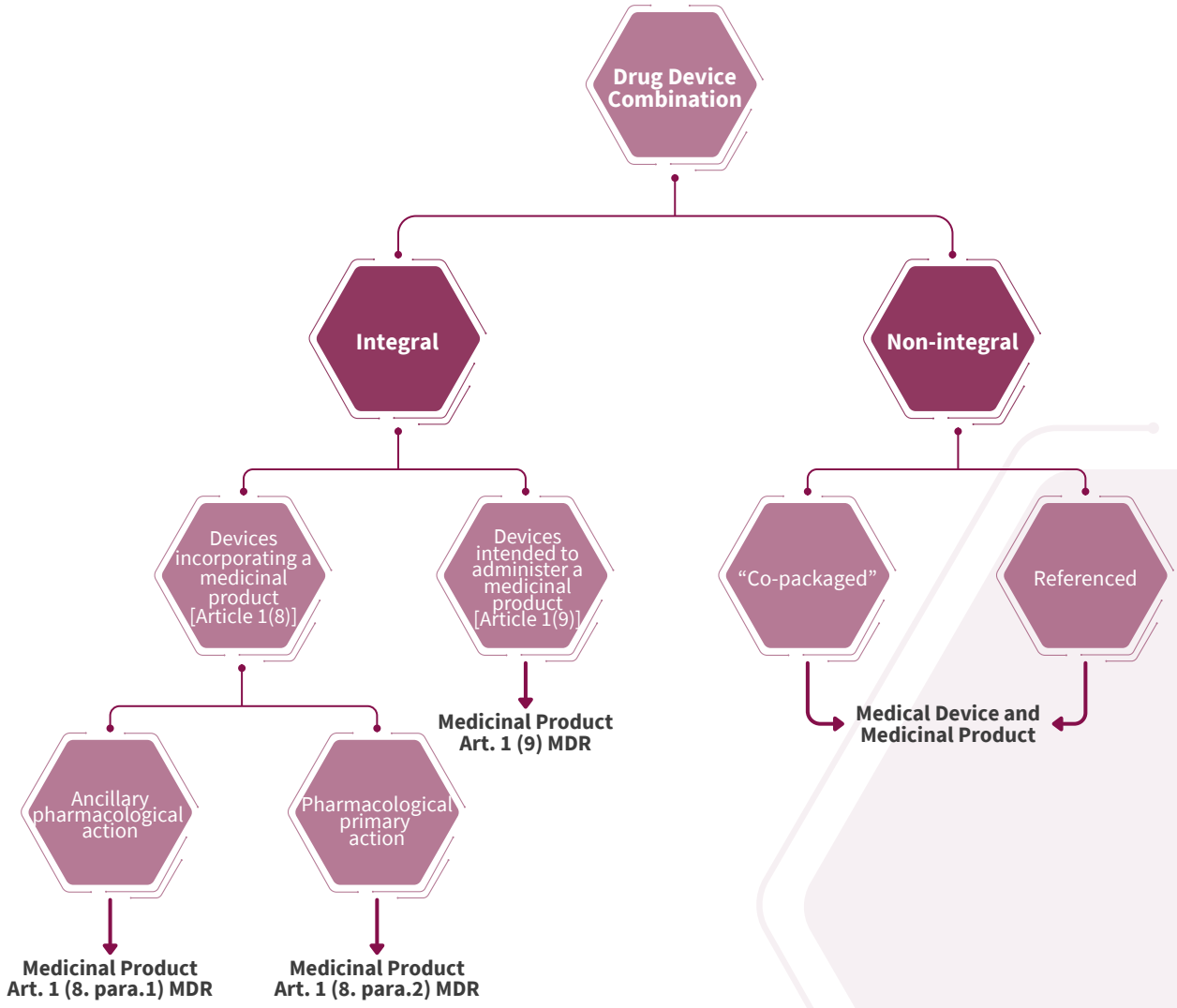
www.asphalion.com
medtech@asphalion.com | +34 93 238 59 45

ASPHALION MedTech

What types of DDCs exist?

- **Integral DDCs:** can be regulated as a medicinal product or a medical device, depending on the component responsible for the principal mode of action.

- **Non-integral DDCs:** each component retains its own regulatory pathway. They are subdivided into:
  - **Co-packaged:** combination established at the secondary packaging level.
  - **Referenced:** combination established at the medicinal product leaflet or SmPC level, identifying the specific model or brand of the required medical device.



www.asphalion.com
medtech@asphalion.com | +34 93 238 59 45

ASPHALION MedTech

How is the authorisation procedure for these products?

- **Non-integral DDCs:** Each component follows its own authorisation (medicine) or CE certification (device). Compatibility must be demonstrated before approval.

- **Integral DDCs:**
  - If the device provides the principal mode of action: CE certification under MDR as a Class III device with a Notified Body; a medicines authority evaluates the pharmaceutical substance (Annex I, MPD).

  - If the medicine provides the principal mode of action: medicinal product authorisation applies, but Article 117 of the MDR amends MPD to require evidence of device compliance with the requirements of the MDR.

Notified Body Device

- Article 117: "[…] the conformity of the **device part with the relevant General Safety and Performance Requirements (GSPRs) set out in Annex I** of MDR."

Competent Authority DDC

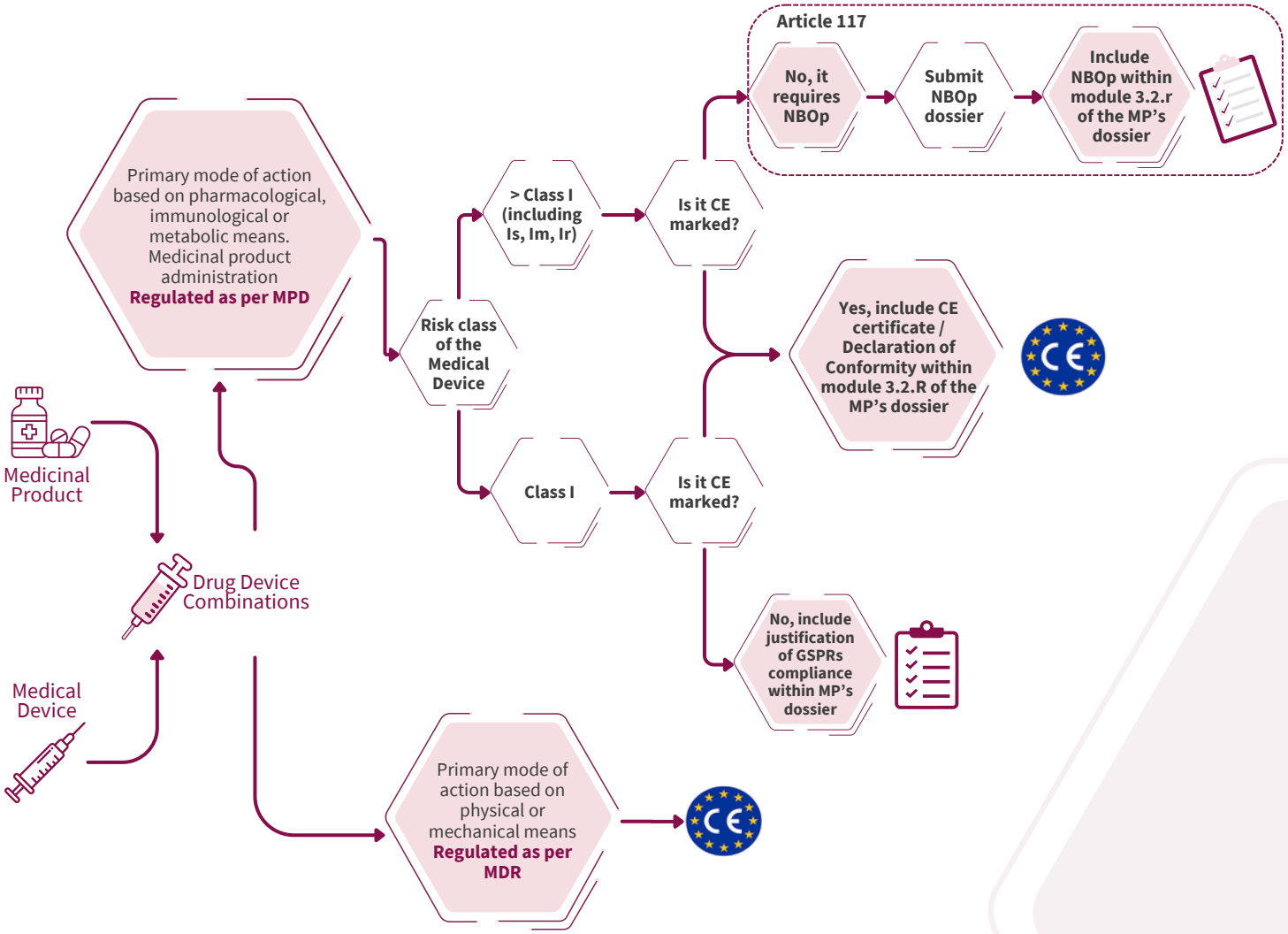
- CA will evaluate the **device specific aspects of safety and performance relevant to the quality, safety and efficacy of the MP** (Medicinal Product).
- Assessment of the suitability of a device for its intended purpose.

www.asphalion.com
medtech@asphalion.com | +34 93 238 59 45

ASPHALION
MedTech

How to demonstrate MDR compliance for the device component in DDCs regulated as medicines?

- **MDR compliance depends on the device's risk class** and may require a Notified Body.
- **Evidence of MDR compliance is included in Module 3.2.R of the medical product dossier.** Health authorities advise including this from the start of the MAA (Marketing Authorization Application) process, although in practice it may be accepted by Day 120 clock-stop of the CHMP evaluation.



www.asphalion.com
medtech@asphalion.com | +34 93 238 59 45

ASPHALION MedTech

Differences between NBOp and CE certification

	CE Certification	NBOp
Responsibilities	✓ MAH: marketing authorization holder ✓ Legal Medical device manufacturer	✓ MAH
CE Certification	CE Mark	Without CE Marking
QMS	QMS as per MDR (Article 10) ✓ EN ISO 13485:2016	QMS as per MPD (Article 46) ✓ ICH Q7
Clinical Data	'Complete' Clinical Investigation	Clinical data based on the performance of the device constituent part provided no additional claims apart from delivery action are included for the device part
Audit	Remote / on-site audit	No audits
Labelling	Assign to the device a UDI which will allow identification and traceability	Labelling requirements following MPD requirements (Title V)

www.asphalion.com
medtech@asphalion.com | +34 93 238 59 45

ASPHALION MedTech

Life-Cycle Management

Article 117 of the MDR applies from 26 May 2021:

- **For DDCs authorised before 26 May 2021**, Article 117 does not apply unless a variation to the medicinal or device part could significantly impact the device's safety or performance.
- **For DDCs authorised after 26 May 2021**, Article 117 of the MDR applies.

Reference guidelines

- Guideline on quality documentation for medicinal products when used with a medical device (EMA/CHMP/QWP/BWP/259165/2019).
- Commission Delegated Regulation (EU) 2024/1701 of 11 March 2024 amending Regulation (EC) No 1234/2008 as regards the examination of variations to the terms of marketing authorisations for medicinal products for human use.
- Proposal for a REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL laying down Union procedures for the authorisation and supervision of medicinal products for human use.
- Team-NB Position Paper on Documentation Requirements for Drug Device Combination Products Falling in the Scope of Article 117 of MDR 2017/745.
- Position paper for the interpretation of device related changes in relation to a Notified Body Opinion as required under Article 117 of Medical Device Regulation (EU)2017/745.
- Questions & Answers for applicants, marketing authorisation holders of medicinal products and notified bodies with respect to the implementation of the Regulations on medical devices and in vitro diagnostic medical devices (Regulations (EU) 2017/745 and (EU) 2017/746) (Click to visit)
- Asphalion Whitepaper: Impact of MDR on Directive 2001/83/EC: What you need to know.

ASPHALION
MedTech

Need help? Contact us!

www.asphalion.com

medtech@asphalion.com

+34 93 238 59 45

Author

Francisco Rodríguez
Medical Device Manager
Co-coordinator of the DDC Working Group of the RA Section of AEFI