SUBSTANCE-BASED MEDICAL DEVICES: A CHALLENGING REGULATORY FRAMEWORK

I. Giovanetto; A. Iavello; E. Costanzo; A. Conto
ChemSafe Srl, Colleretto Giacosa (TO), Italy

N° poster:31

One of the challenges highlighted by the medical device regulation 2017/745 is its application for substance-based products. Based on the form in which these products are developed (drops, ointments, gels, ...) they could be associated with other regulatory fields.

DEFINITIONS

In accordance with the first indent of Article 2(1) of the MDR, **medical devices** may be intended to treat and prevent disease, along with other specific medical purposes (specified by the manufacturer).
Devices that are composed of substances or of combinations of substances may fall within the scope of the MDR.

MEDICAL DEVICE	DRUG (PIM)
Treat and prevent disease	
does not achieve its principal intended action by Pharmacological, Immunological or Metabolic means, in or on the human body, but which may be assisted in its function by such means.	by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis

decisive criterion for the demarcation between the two categories is the «**principal mode of action**».

MDR

Typically, the medical device's principal intended action is achieved by physical means (including **mechanical action**, **physical barrier** such as a film, lubrication, heat transfer, radiation, ultrasound, replacement of or support to organs or body functions). Furthermore, hydration or dehydration and pH modification may also be means by which a medical device achieves its principal intended action.

*The **principal intended action** of a **medical device** is described in manufacturer's labelling and claims and must be based on state of the art scientific data regarding the principal mode of action, on a case-by-case basis.*

Although the manufacturer's claims are important, it is not possible to place the product in one or other regulatory category in contradiction with current scientific data. Manufacturers will be required to justify scientifically in the technical file their rationale for the qualification of their product.

The pharmacological mode of action includes two following steps:

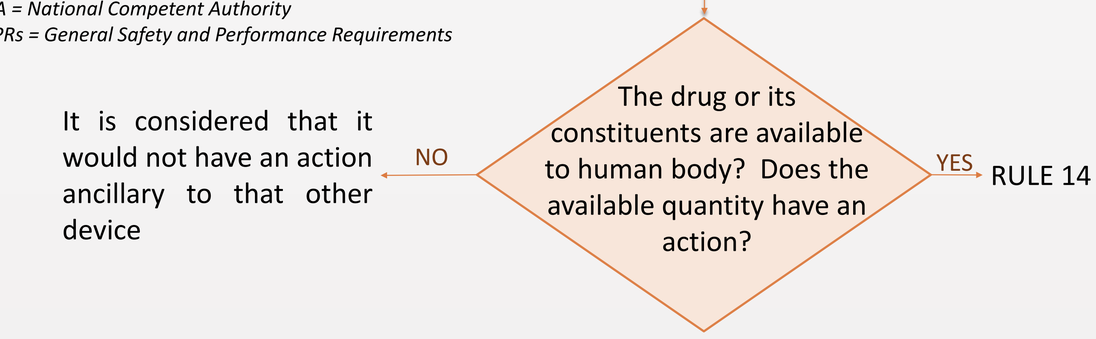
1. **interaction** ("Pharmacological means' is understood as an interaction between a substance or its metabolites and a constituent of the human body),
2. **event triggered by the interaction** ("which results in initiation, enhancement, reduction or blockade of physiological or pathological functions").

MEDICAL DEVICE (MD) OR MEDICINAL PRODUCT (MP)

When a substance-based device incorporates a substance which, if used separately, would be considered to be a medicinal product there may be different regulatory frameworks:

	MPD (Medicinal Product Directive)	MDR (Medical Device Regulation)
MD intended to administer medicinal product	MD + DRUG = single integral product which is intended exclusively for use in the given combination, and which is not reusable (GSPRs apply to the device part)	All other cases
MD + DRUG = single entity MD incorporating, as an integral part, a medicinal product.	DRUG → principal intended action (The notified body must seek a scientific opinion from either a NCA* or EMA. GSPRs* apply to the device part)	DRUG → action ancillary to that of the device (Consultation of EMA or NCA is required. For some examples, see the MDCG 2021-24)

*NCA = National Competent Authority
*GSPRs = General Safety and Performance Requirements



PRODUCT OF ANNEX XVI

Actually, annex XVI of MDR, is a list of six groups of products without an intended medical purpose, which fall within the scope of the medical device regulation.
One of these groups is represented by "*substances, combinations of substances, or items intended to be used for facial or other dermal or mucous membrane filling by subcutaneous, submucous or intradermal injection or other introduction, excluding those for tattooing*".
The application of the MDR is subject to several transitional provisions, symmetrically, these amendments apply to the products of Annex XVI. On the right is a schematic view of the applying regulations:

The MDR shall apply to the products listed in Annex XVI from 22 June 2023, the date of application of the CS.

APPLICATION of the MDR products of Annex XVI

two implementing regulations

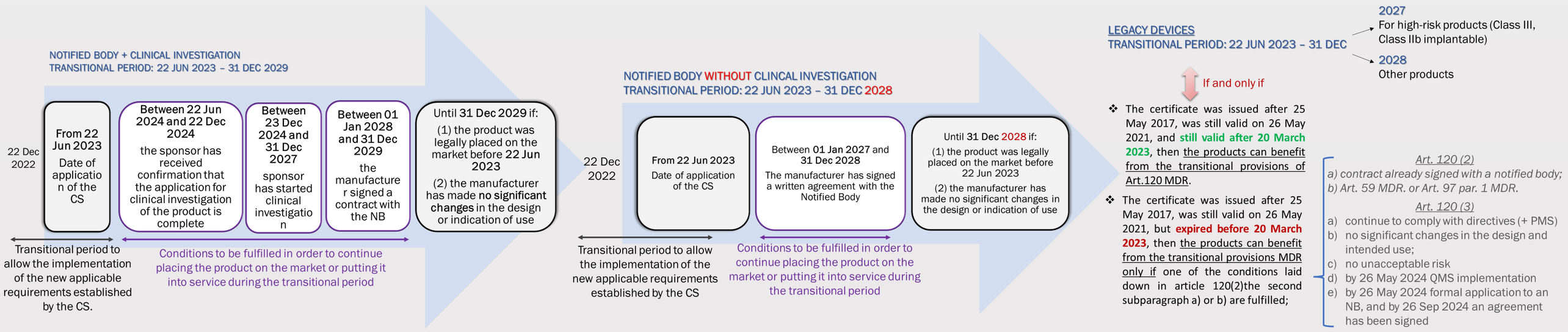
Implementing Regulation (EU) **2022/2346** defines common specifications (**CS**) and provides for derogations for the application of the MDR where:

- a notified body has to be involved in the conformity assessment;
- a clinical investigation is planned;
- the prouct was certified according to the Directive 93/42/CEE.

Implementing Regulation (EU) 2023/1194 amending Implementing Regulation (EU) 2022/2346 as regards the transitional provisions.

Implementing Regulation (EU) **2022/2347** lays down the detailed rules for the application of the MDR with regard to the reclassification of groups of certain active products not intended for medical use.

Below are the timelines for products requiring the intervention of a notified body, with and without a clinical investigation and for legacy devices:



References

- Medical device Regulation 2017/745
- Regulation (EU) 2022/2346
- Regulation (EU) 2022/2347
- Regulation (EU) 2023/1194
- MDCG 2022-5
- 3 May 2024 Rev.4 EMA/37991/2019 Human Medicines Division

ChemSafe srl
www.chemsafe-consulting.com
e-mail: chemsafe@chemsafe-consulting.com