EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EU: Regulatory issues involving an integrated therapeutic with a device or computerized training

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- No conflict of interests.

Outline

- **MEDICAL DEVICE**
  - DEFINITIONS, EXAMPLES, REGULATORY FRAMEWORK
  - MEDICAL DEVICE SOFTWARE
- **DIGITAL HEALTH TECHNOLOGY**
  - DEFINITIONS, EXAMPLES, REGULATORY FRAMEWORK
  - EMA EXPERIENCE
  - QUALIFICATION PATH

Medical device (1)- Definition

"Any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:

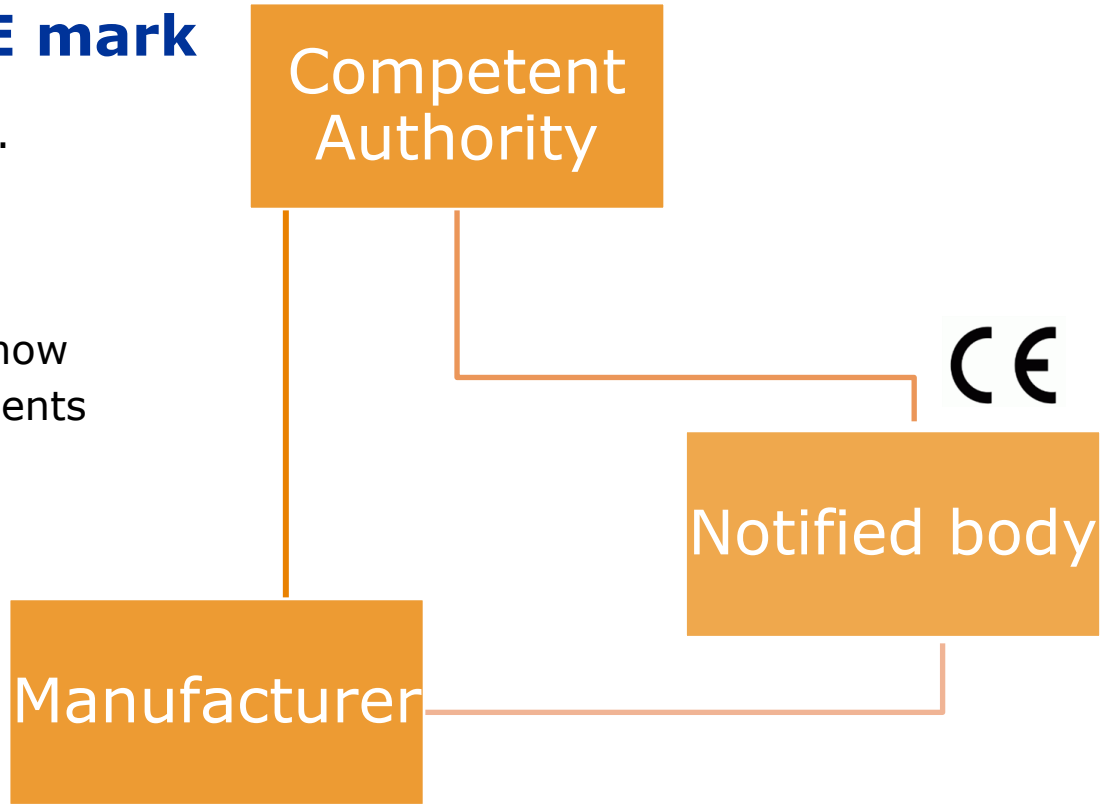
- diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease
- diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability
- investigation, replacement or modification of the anatomy or of a physiological or pathological process or state
- providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations" (In vitro diagnostic medical device)

Medical device (2)-EU Regulation

- Regulation (EU) 2017/745 on Medical Devices (MDR) and Regulation (EU) 2017/746 on In-Vitro Diagnostic Devices (IVDR) changed the European legal framework for medical devices, introducing new responsibilities for EMA and for national competent authorities.
- **Transitional period** of the Medical Devices Regulation - until 26 May 2021.

Medical device (3) – CE mark

- Regulated at **Member State** level.
- **Not EMA competence** to confirm classification of medical devices
- Device must bear a **CE mark** to show that it conforms with the requirements of the directives (and regulations)
- **"Conformité Européenne"**
- = "European Conformity"



Medical device (4) -Medicinal products that include a medical device

- **Traditional Examples** : pre-filled syringes, pre-filled pens, nebulizers pre-charged with a specific medicinal product, patches for transdermal drug delivery and pre-filled inhalers without digital component
- **Digital examples** : with sensor attached to pre-filled pen/inhaler collecting and sending data on the patient use to a mobile application for tracking of dose administered, reminders for the patient to take the treatment..

Medical device (5)- Medical Device Software

- **Software** : a set of instructions that processes input data and creates output data.
- ***Is your software a medical device?***
  - https://ec.europa.eu/health/sites/health/files/md_sector/docs/md_mdcg_2021_mdsw_en.pdf
  - **Medical Device Software (MDSW)** : Software that is intended to be used, alone or in combination, for a purpose as specified in the definition of a "medical device" in the Medical Devices Regulation (MDR) or In Vitro Diagnostic Medical Devices Regulation (IVDR)
    - imaging assistance for diagnosis
    - treatment monitoring, adherence
    - …

Digital Health Technologies (1) – a various entity

- **Sensors** (e.g. ingestibles, implantables),
- **Mobile health (mHealth) tools, e.g. wearable device** to measure certain health related parameters, remote patient monitoring
- **Digital Biomarker/endpoint** to measure patient activities, to monitor disease as well as its progression and response to treatment.
- **Tele-healthcare in clinical trials** (e.g. video consultations)
- **Digital record systems** (e.g. digital applications, also referred to as "apps")
- **Health data analytics** (e.g. data processing systems that support bioinformatics modelling)
- **AI/ML :** collection of technologies that combine data, algorithms and computing power

Digital Health Technologies (2)- Regulatory framework

- **EMA's remit : specific to DHT in the development, use or monitoring of medicinal products pre- or post-authorisation**
  - Need to ensure safe & effective use and appropriate labelling
  - assessment focuses on B/R and its use in the intended patient population
- DHTs development plan should comply with the general standards, guidelines and legal framework set **for any medicine's development**
- DHTs must be verified and validated to ensure their functionality in accordance with **any relevant additional legislation** on the digital technology of interest (eg:medical device)

Digital Health Technologies (3) – Fast evolving field

- **In the future**, medical care and diagnostics are likely to rely more and more on **data-driven technologies**
- DHT are likely to produce a large volume of data, both raw and algorithm-processed data, which poses many questions (statistical, clinical..)
- How efficiently integrate data analysis into our assessment processes and decision-making?

Digital Health Technologies (4) - Data protection framework in the EU

- The **General Data Protection Regulation (EU) 2016/679** (GDPR) is a regulation in EU law on data protection and privacy in the European Union (EU) and the European Economic Area (EEA) into force in May 2018.
- The assessment of data protection **compliance** falls outside of the scope of EMA.
  - **remit of the national data protection authorities of Member States.**

Digital Health Technologies (5) EMA Experience

- ✓ **MAA applications** (eg inhaler with sensor to be used with separate mobile app, tablet with sensor to be connected to a mobile app
- ✓ **Variations** (eg new presentation of a blister that can be connected to a mobile app)
- ✓ **printed QR Code/URL** on Package Leaflets & Outer cartons allowing the patients/users/health care professionals to access dedicated websites containing the Instructions for Use in electronic format.
- ✓ **Participation to IMI initiatives** (e.g. SPRINT-T, PROactive)
- ✓ **Qualifications/ITF meetings**

Digital Health Technologies (6) EMA qualification procedure

- Applicants can submit a qualification request **at any time** during the development
- **Early dialogue, step-wise approach** is key as the use of DHTs in clinical trials poses multiple challenges that require identification and input from different types of experts.
- Qualification **Advice**/Qualification **Opinion**
- Specific **EMA Q&A document** for DHTs

https://www.ema.europa.eu/en/documents/other/questions-answers-qualification-digital-technology-based-methodologies-support-approval-medicinal_en.pdf

Digital Health Technologies (7) EMA experience - qualification procedure

- ***Digital endpoint***
- ***Digital Biomarker***
- ***Digital measures***
- ***Electronic Clinical Outcome Assessment (eCOA)***

- **eSource qualification**
- **Adherence/Compliance (Ingestible sensor qualification)**
- **qualification opinion on stride velocity** measured by an ankle wearable device, as a secondary end point in Duchenne muscular dystrophy (DMD)

Any questions?

Further information

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