Are Pharmaco- and Medical Device Vigilance the same?
And the new Medical Device Regulation (MDR)

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230

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AGENDA

- Scope
  - Medical Device Vigilance and how does it compare to Pharmacovigilance
  - From a manufacturer/Vigilance team perspective;
  - Activities and responsibilities of authorities are out of scope
  - MDD -> MDR
- Medical devices: Definitions
- Procedures and Methods
The MDD Transposition to the MDR

- the Medical Device Directive 93/42/EEC (MDD)
- the Medical Device Regulation EU 2017/745 (MDR)
A medical device

• ‘medical device’ means 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 (IVDR),

• and which 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.
A medical device

• Combination products
  - Medical device with pharmaceutical
    • E.g. Drug eluting stents
  - A pharmaceutical with a medical device
    • E.g. Dry powder Inhaler
Process according to MDR

• CHAPTER VII: POST-MARKET SURVEILLANCE, VIGILANCE AND MARKET SURVEILLANCE
  • SECTION 1: Post-market surveillance
    - Article 83: Post-market surveillance system of the manufacturer
    - Article 84: Post-market surveillance plan
    - Article 85: Post-market surveillance report
    - Article 86: Periodic safety update report (PSUR)
  • SECTION 2: Vigilance
    - Article 87: Reporting of serious incidents and field safety corrective actions
    - Article 88: Trend reporting
    - Article 89: Analysis of serious incidents and field safety corrective actions
Process and deliverables

Starts during the design phase of the medical device and continues during life cycle of the device.

- Clinical Evaluation (report)
- Update CER, Risk Management Report and Instructions For Use
- PMS plan
- Trending, analysis and PSUR
- PMCF (active) Vigilance (passive)
## Stages and Comparison

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<tr>
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<th>Medical Device</th>
<th>Pharmaceutical compound</th>
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| **Under investigation Studies** | Investigational Medical Device  
Serious Adverse Events and device deficiencies | Investigational Medicinal Product  
(Serious) Adverse event |
| **Commercially available PMS**    | CE marked  
Passive Vigilance  
Active Post Marketing Clinical follow up studies (PMCF)  
Serious Incident | Market authorization  
Passive Spontaneous reports  
Active Phase IV studies: e.g. safety studies  
(Serious) Adverse Event |
In comparison: SAE

**MEDICAL DEVICE (INVESTIGATION ONLY)**

- Death
- Serious deterioration in the health of the subject, that resulted in any of the following:
  - Life-threatening illness or injury
  - Permanent impairment of a body structure or a body function
  - Hospitalisation or prolongation of patient hospitalisation
  - Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function
  - Chronic disease
- Foetal distress, foetal death or a congenital physical or mental impairment or birth defect;

**PHARMACEUTICAL**

- Results in death,
- is life-threatening,
- requires inpatient hospitalization or prolongation of existing hospitalization,
- results in persistent or significant disability/incapacity,
- is a congenital anomaly/birth defect
- & Important Medical Events
Medical device: Serious Incident

- Any incident that directly or indirectly led, might have led or might lead to any of the following:
  - the death of a **patient**, **user** or **other person**,  
  - the temporary or permanent serious deterioration of a **patient’s**, **user’s** or **other person’s** state of health,  
  - a serious public health threat;  
  - ‘serious public health threat’ means an event which could result in imminent risk of death, serious deterioration in a person’s state of health, or serious illness, that may require prompt remedial action, and that may cause significant morbidity or mortality in humans, or that is unusual or unexpected for the given place and time;
And then, an incident or SAE is observed and reported by the user

- Device related?
- Serious?
- Expected?
- Applied according to intended use?
- Root cause
- All data received?
### What to report: Serious events

<table>
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<tr>
<th>Medical Device</th>
<th>Pharmaceutical compound</th>
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<tbody>
<tr>
<td>Serious Incident</td>
<td>Serious Adverse Event</td>
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<tr>
<td>Suspected Related</td>
<td>Suspected Related</td>
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<tr>
<td>Unexpected</td>
<td></td>
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<tr>
<td>Field Safety Corrective Actions</td>
<td></td>
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<tr>
<td>SAE (studies)</td>
<td>SUSAR (studies)</td>
</tr>
<tr>
<td>Suspected Related</td>
<td></td>
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<tr>
<td>Unexpected</td>
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</table>

Event is expected: When documented in the product information and quantified in the technical documentation (e.g. risk management report & IFU), and is subject to trend reporting.
Assessment of the event

• To be analysed and confirmed by the vigilance team
  • Related
  • Unexpected
  • …..

• Medical device
  - > 600,000 different medical devices

• Pharmaceutical
  - Several hundred classes

• Manufacturer needs to perform a root cause analysis
  • Specific medical device knowledge required
    • Manufacturer will have the specific medical device and application knowledge
    • When not the manufacturer: Vigilance team needs training on medical device and application: IT IS NOT EASY!
How to report: Serious events

- Manufacturer’s Incident Report (MIR)
- CIOMS form
When to report

MEDICAL DEVICE

• Immediately after established causal relationship but not later than
  - 15 days after awareness
  - 10 days in the event of death or an unanticipated serious deterioration in a person's state of health
  - 2 days if serious public health threat

PHARMACEUTICALS

• SAE < 15 days
• SUSAR
  - < 7 days (F/LT)
  - <15 days (other)
Where to report

MEDICAL DEVICE
- Competent Authority of the Member State in which that serious incident occurred
- 28 different addresses for the EU
  http://ec.europa.eu/health/medical-devices/links/vigilance_contact_points_en.htm
- Future: Eudamed database

PHARMACEUTICALS
- To the national competent authorities, cc Eudra-Vigilance
- Eudra-Vigilance database (22 November)
Post marketing surveillance data and Clinical Evaluation Report

MEDICAL DEVICE

- PSUR
  - depending on the risk class of the product:
    • Class I: Not required
    • Class IIa: every 2 years
    • Class IIb&III: yearly

- Update of the Clinical Evaluation Report

PHARMACEUTICAL

- PBRER and PSUR
  - New product: yearly
  - Different period depending on life cycle of the drug
    - every 6 months, and then yearly

- DSUR: every year
Quality Management System

- Manufacturer
  - ISO 13485 certified QMS
- Vigilance Service provider
  - ISO 13485 or
  - ISO 9001 or
  - Following QMS manufacturer
  - Supplier audit necessary
- Medical Device Regulation
- MEDDEV 2.12/1 rev.8 (Guidelines on a Medical Devices Vigilance System)
- MEDDEV 2.12/2 rev.2 (Post Market Clinical Follow-up studies)
Similarities and Differences

• Yes, there are similarities. The rough outline of the processes are the same.
  - It would be tempting to use the same system/organisation
  - Very useful for Drug-Device combinations

• Yes, there are distinct differences
  - Event analysis and reporting
  - Huge number of different medical devices and their respective methods for application require specific expertise

• It can be handled by (pharmaco-)vigilance team
  - Specific Documented Procedures to ensure compliance
  - Training
  - Audits
In Summary

• The assessment process certainly has similarities. The same process flow could be followed for pharma and medical device events.

• For the assessment, Medical Device Expertise is essential due to the large number of devices and their respective complexities in application.

• Analysis, trending and reporting do have similarities and could be handled by the vigilance team.