NOTIFIED BODIES AND THEIR ROLE IN ASSESSING QUALITY OF DRUG DELIVERY DEVICES

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Background to notified bodies and differences to pharma regulatory system

Notified body involvement on quality, safety and performance of delivery devices

GSPRs and risk-based review of different types of delivery devices
Background to notified bodies and differences to pharma regulatory system
The higher the risk of the product, the greater is the level of intervention of the Public Authorities in their assessment.

For certain products, the Authorities "delegate" the certification activity to organizations called notified bodies (NB).

A certificate issued by a NB is recognized throughout the European Union.

Notification is an act whereby a Member State (ME) informs the Commission (EC) that a body has been designated to carry out conformity assessment.
The ‘New Approach’ developed in 1985 restricted the content of legislation to ‘essential requirements’ (ER) that products must meet when they are put on the market, leaving the technical details to European harmonised standards.

For Medical devices, compliance to ER shall also include monographs of the European Pharmacopoeia.

Regulation (EU) 2017/745 on Medical Devices (MDR)
ER are therefore written in such a way that they remain valid over time, and do not become obsolete with technical progress.

In the MDR the ER are called General Safety and Performance Requirements (GSPR).

Some examples of GSPR:

5. In eliminating or reducing risks related to use error, the manufacturer shall:
   (a) reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety), and
   (b) give consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users).

15. Devices with a diagnostic or measuring function

15.1. Diagnostic devices and devices with a measuring function, shall be designed and manufactured in such a way as to provide sufficient accuracy, precision and stability for their intended purpose, based on appropriate scientific and technical methods. The limits of accuracy shall be indicated by the manufacturer.

ISO – IEC 62366-1: Usability Engineering for Medical Devices

ISO 7886-1: Sterile hypodermic syringes for single use
The MDR foresees the existence of public notified bodies:

1.2.6. If a notified body is owned by a public entity or institution, independence and absence of any conflict of interest shall be ensured and documented between, on the one hand, the authority responsible for notified bodies and/or the competent authority and, on the other hand, the notified body.

Current scenario:

• To reinforce independence a new administrative situation is in process...
Notified body involvement on quality, safety and performance of delivery devices
CERTIFICATION PROCESS IN BRIEF

Application review and contract

Allocation of resources

Assessment of the technical documentation

Quality management system auditing

Final review and Certification Decision
The NB review of non-high-risk products can be carried out by establishing a sampling plan in which a representative sample is selected and reviewed.

The manufacturer is expected to take into account the deficiencies detected in the review of the sample and apply them to the rest of the files.
➢ NB review covers 100% of Class III products

➢ Class IIb are sampled by choosing a representative product from a generic group

➢ Class IIa by choosing a representative product from a category

➢ For Class I devices the NB intervention is limited to the aspects relating to establishing, securing and maintaining sterile conditions or to the aspects relating to the conformity of the devices with the metrological requirements;
What is considered a category?

3.1. Category of devices: category of devices should be understood as the relevant MDA/MDN codes (MDR) or IVR codes (IVDR) according to Regulation (EU) 2017/2185 on the codes for the designation of notified bodies.


What is considered a generic group?

3.2. Generic device group: is to be understood:
- in respect of the MDR as the 4th level of the European Nomenclature on Medical Devices (EMDN) (i.e. combination of one letter plus 6 digits), and

md_q-a_emdn_en.pdf (europa.eu)

MDCG 2019-13
Guidance on sampling of MDR Class IIa / Class IIb and IVDR Class B / Class C devices for the assessment of the technical documentation

December 2019
As part of the surveillance activities carried out by the NB it is required to conduct:

- Surveillance audits of the manufacturer on at least an annual basis

- Sample and test devices and technical documentation, during audits, according to pre-defined sampling criteria and testing procedures to ensure that the manufacturer continuously applies the approved quality management system.

In choosing representative samples, the NB shall take into account the novelty of the technology, similarities in design, technology, manufacturing and sterilisation methods, the intended purpose and the results of any previous relevant assessments such as with regard to physical, chemical, biological or clinical properties.
GSPRs and risk-based review of different types of delivery devices
Technical documentation must allow the conformity of the device with the requirements of the MDR to be assessed. The technical documentation shall include the following elements:

1. Device Description and Specification
2. Information to be Supplied by the MF
3. Design and Manufacturing Information
4. GSPR
5. Benefit-Risk Analysis and Risk Management
6. Product Verification and Validation

All products regardless of their class must demonstrate compliance with the applicable requirements.

The level of clinical evidence necessary to demonstrate conformity with the relevant GSPR shall be appropriate in view of the characteristics of the device and its intended purpose.
Section 6. PRODUCT VERIFICATION AND VALIDATION

This section is expected to contain the results and critical analyses of all verifications and validation tests and/or studies undertaken to demonstrate conformity of:

— Biocompatibility of the device including the identification of all materials in direct or indirect contact with the patient or user;
— physical, chemical and microbiological characterisation;
— stability, including shelf life;
— Performance and safety
— Ect..
Section 6. PRODUCT VERIFICATION AND VALIDATION

e.g: GSPR 15 – (Section 6.2.f of TD) – Measuring function of a single use syringe

(f) In the case of devices placed on the market with a measuring function, a description of the methods used in order to ensure the accuracy as given in the specifications.

The error varies as the delivery volume changes for different size syringes.

ISO 7886-1: “Sterile hypodermic syringes for single use” provides tables with the acceptance criteria for Expelled Volume test or dead space.

<table>
<thead>
<tr>
<th>Syringe Size</th>
<th>Expelled Vol</th>
<th>Tolerance ± (ml)</th>
<th>Tolerance ± (%)</th>
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<td>0.017</td>
<td>17.00</td>
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<tr>
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<td>0.20</td>
<td>0.019</td>
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<tr>
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<td>0.050</td>
<td>5.00</td>
</tr>
</tbody>
</table>

Table 1: Syringe Accuracy Vol - Syringe Size = 1 ml
Thank you!

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