Agenda

• Background:
  • Definition, role and responsibilities of a Pharma Qualified Person
  • Translation of this concept into the Medical Device and in Vitro Diagnostic draft Regulations

• What does it mean in practice?

Note: This presentation is based on the current available draft of the Medical Devices and In Vitro Diagnostic Medical Devices Regulations, Council version dated 27Jun2016.
Previous drafts of the MDR/IVDR used the term: **QUALIFIED PERSON**.

Since Council draft of Sep2015, wording has changed to:

**PERSON RESPONSIBLE FOR REGULATORY COMPLIANCE**
Pharma Qualified Person
Qualified Person in the « pharma world »

basic concept of the European Pharmaceutical legislation:

Each holder of a manufacturing authorization has "permanently and continuously at his disposal the services of at least one qualified person."

⇒ one individually responsible person for batch certification and release required at site.

Regulatory framework:

European Directive 2001/83/EC, relating to medicinal products
European Directive 2001/82/EC relating to veterinary products
Superior European pharmaceutical directives define the additional personal responsibility and liability of the "qualified person" (QP)

Vol 9A of the Rules Governing Medicinal Products in the European Union
Qualified Person in the « pharma world »

EU QP concept is unique

The personal responsibility and liability of the EU QP is a very specific requirement.

Every QP needs to be registered/appointed/approved with the competent authority of the EU member state in which he or she is operating.

⇒ not only the pharmaceutical company for which he or she is acting, but also the registered QP, is personally responsible for his or her duties.

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Qualified Person in the « pharma world »

Qualification

A completed four years **theoretical and practical university** study in pharmacy. Or a university study in medicine, veterinary medicine, chemistry, pharmaceutical chemistry and technology, or biology + additional relevant studies

+ **practical experience during at least 2 years** at one or more companies authorized to manufacture medicinal products in the EU, covering qualitative analysis of medicinal products, quantitative analysis of active substances, and testing and checking the quality of medicinal products. (1-year or 6-month in specific cases)

* for Pharmacovigilance QP, 1-year of PV experience

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Qualified Person in the « pharma world »

Registration with national Competent Authority

To perform his or her responsibilities, a qualified person must be registered (or approved, depending on the member state's legislation) by the competent authority of the EU member state where the manufacturing license of the pharmaceutical company was issued and the QP is acting.

⇒ providing the competent national authorities a perfect recourse within a short timeframe in case of any issue with a batch certified and released by a particular QP.
Qualified Person in the « pharma world »

Responsibilities - article 51 of Directive 2001/83

• **Certify prior to the release** for sale, placing on the market, or export in a register (or equivalent), **that each batch** of the medicinal product has been manufactured and checked in compliance with the laws of that member state and in accordance with the requirements of the **marketing authorization**.

• Similar responsibilities for IMPs (investigational Medicinal Products) - Directive 2005/28/EC (good clinical practice)

• “QP import” in the case of medicinal products coming from third countries.

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Qualified Person in the « pharma world »

Pharmacovigilance Qualified Person (QPPV)

QPPV is responsible for the “overall pharmacovigilance for all medicinal products for which the company holds marketing authorizations within the EU.”

The QPPV has three main areas of responsibility:

- to ensure the Marketing Authorization holder has an appropriate pharmacovigilance system in place
- to have an overview of a safety profile for the products for which the company holds a Marketing Authorization
- to be the point of contact with the competent authorities
MD and IVD Regulations

Adapting the QP concept to Medical Devices
In Vitro Diagnostic Medical Devices Regulation

**Identical requirements for MDR and IVDR**

<table>
<thead>
<tr>
<th>IVDR</th>
<th>MDR</th>
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<tr>
<td><em>In Vitro Diagnostic</em> Medical Devices</td>
<td>Medical Devices</td>
</tr>
<tr>
<td>devices for performance studies intended to be used in the context of interventional clinical performance studies or other <strong>performance studies</strong> involving risks for the subjects</td>
<td>investigational devices</td>
</tr>
<tr>
<td>reporting obligations in accordance with Articles 59 to 64</td>
<td>reporting obligations in accordance with Articles 61 to 66</td>
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</table>
Medical Device Regulation

Whereas (27)
It should be ensured that **supervision and control** of
**the manufacture of** and
**the post-market surveillance** and
**vigilance activities**
of medical devices are carried out within the manufacturer's
organization by a **person responsible for regulatory compliance**
who fulfils minimum conditions of qualification.
MDR Article 13

1. Manufacturers shall have available within their organization at least one person responsible for regulatory compliance who possesses the requisite expertise in the field of medical devices. The requisite expertise shall be demonstrated by either of the following qualifications:

(a) a diploma, certificate or other evidence of formal qualification awarded on completion of a university degree or of a course of study recognized as equivalent by the Member State concerned, in law, medicine, pharmacy, engineering or another relevant scientific discipline, and at least one year of professional experience in regulatory affairs or in quality management systems relating to medical devices;

(b) four years of professional experience in regulatory affairs or in quality management systems relating to medical devices.
Without prejudice to national provisions regarding professional qualifications, manufacturers of custom-made devices may demonstrate their requisite expertise referred to in the first subparagraph by at least two years of professional experience within the relevant field of manufacture. 
(This paragraph is not applicable to IVDR.)

1a. Micro and small enterprises within the meaning of Commission Recommendation 2003/361/EC are not required to have the person responsible for regulatory compliance within their organization but shall have such person permanently and continuously at their disposal.

2003/361/EC defines small and micro enterprises categories as follows: 
Small entreprise: < 50 employees, annual turnover < 10 M €
Micro entreprise: < 10 employees, annual turnover < 2 M €
2. The person responsible for regulatory compliance shall **at least be responsible for ensuring** the following matters:

(a) that the **conformity** of the devices is **appropriately checked** in accordance with the quality management system under which these devices are manufactured before a product is released;

(b) that the **technical documentation** and the **declaration of conformity** are drawn up and **kept up-to-date**;

(ba) that the **post-market surveillance** obligations in accordance with Article 8(6) are complied with;

(c) that the **reporting** obligations in accordance with Articles 61 to 66 are fulfilled;

(d) in the case of **investigational devices**, that the statement referred to in point 4.1 of Chapter II of Annex XIV is issued.
If a number of persons are **jointly responsible** for regulatory compliance in accordance with paragraphs 1 and 2, their **respective areas of responsibility** shall be **stipulated in writing**.

3. The person responsible for regulatory compliance shall **suffer no disadvantage** within the manufacturer's organization in relation to the proper fulfillment of his duties, regardless of whether or not he is an employee of the organization.
Article 2 - (20): ‘authorised representative’ means any natural or legal person established within the Union who has received and accepted a written mandate from a manufacturer, located outside the European Union, to act on his behalf in relation to specified tasks with regard to the latter's obligations under this Regulation;

⇒ No change in definition from MDD/AIMD/IVDD
Authorised representative

Whereas (28)

For manufacturers who are not established in the Union, the authorised representative plays a pivotal role in ensuring the compliance of the medical devices produced by those manufacturers and in serving as their contact person established in the Union. Given that pivotal role, for the purposes of enforcement it is appropriate to make the authorised representative legally liable for defective medical devices in case a manufacturer established outside the Union has not complied with its general obligations. The liability of the authorised representative provided for in this Regulation is without prejudice to the provisions of Council Directive 85/374/EEC, and accordingly the authorised representative is jointly and severally liable with the importer and the manufacturer.

The tasks of an authorised representative should be defined in a written mandate. Considering the role of authorised representatives, the minimum requirements to be met by them should be clearly defined, including the requirement of having available a person who fulfils minimum conditions of qualification which should be similar to those for a manufacturer's person responsible for regulatory compliance.
4. Authorised representatives shall have **permanently and continuously at their disposal at least one person** responsible for regulatory compliance who possesses the requisite expertise regarding the regulatory requirements for medical devices in the Union. The requisite expertise shall be demonstrated by either of the following qualifications:

(a) diploma, certificate or other **evidence of formal qualification** awarded on completion of a university degree or of a course of study recognised as equivalent by the Member State concerned, in **law, medicine, pharmacy, engineering or another relevant scientific discipline**, and **at least one year** of professional experience in regulatory affairs or in quality management systems relating to medical devices;

(b) **four years** of professional experience in regulatory affairs or in quality management systems relating to medical devices.
In practice...
ISO 13485:2016

5.5.1 Responsibility and authority

Top management shall ensure that responsibilities and authorities are defined, documented and communicated within the organization.

Top management shall document the interrelation of all personnel who manage, perform and verify work affecting quality and shall ensure the independence and authority necessary to perform these tasks.

6.2 Human resources

Personnel performing work affecting product quality shall be competent on the basis of appropriate education, training, skills and experience.

The organization shall document the process(es) for establishing competence, providing needed training, and ensuring awareness of personnel.

The organization shall:

a) determine the necessary competence for personnel performing work affecting product quality;
b) provide training or take other actions to achieve or maintain the necessary competence;
c) evaluate the effectiveness of the actions taken;
d) ensure that its personnel are aware of the relevance and importance of their activities and how they contribute to the achievement of the quality objectives;
e) maintain appropriate records of education, training, skills and experience (see 4.2.5).

NOTE The methodology used to check effectiveness is proportionate to the risk associated with the work for which the training or other action is being provided.

⇒ Areas of responsibilities defined and documented
⇒ “suffer no disadvantage within the manufacturer's organisation in relation to the proper fulfilment of his duties”
⇒ Qualification and expertise documented and maintained
The PRRC is responsible for ensuring: (a)

that the **conformity** of the devices is **appropriately checked** in accordance with the quality management system under which these devices are manufactured before a product is released.

⇒ ISO 13485 applicable revision + Requirements of MDR/IVDR (Article 8.5)

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**8.2.6 Monitoring and measurement of product**

The organization shall monitor and measure the characteristics of the product to verify that product requirements have been met. This shall be carried out at applicable stages of the product realization process in accordance with the planned and documented arrangements and documented procedures.

Evidence of conformity to the acceptance criteria shall be maintained. The identity of the person authorizing release of product shall be recorded (see 4.2.5). As appropriate, records shall identify the test equipment used to perform measurement activities.

Product release and service delivery shall not proceed until the planned and documented arrangements have been satisfactorily completed.
The PRRC is responsible for ensuring: (b)

that the technical documentation and the declaration of conformity are drawn up and kept up-to-date;

⇒ MDR/IVDR Annex II:

1. DEVICE DESCRIPTION, SPECIFICATION, VARIANTS & ACCESSORIES
   - Device description and specification
   - Reference to previous / similar generations of the device

2. INFORMATION SUPPLIED BY THE MANUFACTURER

3. DESIGN AND MANUFACTURING INFORMATION

4. GENERAL SAFETY AND PERFORMANCE REQUIREMENTS

5. RISK/BENEFIT ANALYSIS AND RISK MANAGEMENT

6. PRODUCT VERIFICATION AND VALIDATION
   - Pre-clinical and clinical data / Analytical Performance and Clinical Performance Evaluation / Stability / Software verification and validation
   - Additional information in specific cases
The PRRC is responsible for ensuring: (b)

*that the technical documentation and the declaration of conformity are drawn up and kept up-to-date;*

⇒ MDR/IVDR Annex IIa: Technical Documentation on PMS

- PMS plan
- PMS report
- PSUR – Periodic safety update report
The PRRC is responsible for ensuring: (b) *that the technical documentation and the declaration of conformity are drawn up and kept up-to-date*

⇒ MDR/IVDR Annex III: Declaration of Conformity provides details on information required on the DoC
The PRRC is responsible for ensuring: (ba)

*that the post-market surveillance obligations in accordance with Article 8(6) are complied with;*

Article 8 – General Obligations of the manufacturer.

6. *Proportionate to the risk class and the type of device*, manufacturers of devices shall implement and keep up to date the post-market surveillance system referred to in Article 60a/58a.

Article 60a/58a:

For *any device*, *proportionate to the risk class* and appropriate for the type of device, manufacturers shall plan, establish, document, implement, maintain and update a post-market surveillance system which shall be an integral part of the manufacturer’s quality management system...

... suitable to *actively and systematically* gather, record and analyse relevant data on the *quality, performance and safety* of a device throughout its *entire lifetime*, to draw the necessary conclusions and to determine, implement and monitor any preventive and corrective actions.

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The PRRC is responsible for ensuring: (ba)

that the **post-market surveillance obligations** in accordance with Article 8(6) are complied with;
The PRRC is responsible for ensuring: (c) that the **reporting obligations** in accordance with Articles 61 to 66 / 59 to 64 are fulfilled;

- QMS
- PMS Article 60a / 58a
- Vigilance Article 61-66 / 59-64
- Passive PMS
- Active PMS
- PMCF / PMPF
- Annex XIII / XII

Applies to every class of device under every route of conformity.
<table>
<thead>
<tr>
<th>Who reports?</th>
<th>Manufacturers of devices, made available on the Union market, other than investigational/performance evaluation devices</th>
</tr>
</thead>
</table>
| What to report? | a) any **serious incident** involving devices made available on the Union market, except expected side-effects/erroneous results which are clearly documented in the product information and quantified in the technical documentation and are subject to **trend reporting** pursuant to Article 61a/59a;  

b) any **field safety corrective action** in respect of devices made available on the Union market, including any field safety corrective action undertaken in a **third country** in relation to a device which is also legally made available on the Union market, if the reason for the field safety corrective action is not limited to the device made available in the third country. |
| Periodic summary reports – if agreed with Competent Authority(ies) |
### Trends reporting

Statistically significant increase in the frequency or severity of incidents that are not serious incidents or of expected undesirable side-effects that could have a significant impact on the risk-benefit analysis... and which have led or may lead to unacceptable risks to the health or safety of patients, users or other persons when weighted against the intended benefits.

The significant increase shall be established in comparison to the foreseeable frequency or severity of such incidents or expected undesirable side-effects in respect of the device, or category or group of devices, in question during a specific time period as specified in the technical documentation and product information.

The manufacturer shall define how to manage these incidents and the methodology used for determining any statistically significant increase in the frequency or severity of these incidents, as well as the observation period, in the post-market surveillance plan.
Reporting obligations – Vigilance *Articles 61 to 66 / 59 to 64*

<table>
<thead>
<tr>
<th>When to report?</th>
<th>As a general rule, the time period for reporting shall take account of the severity of the serious incident.</th>
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<tbody>
<tr>
<td><strong>IMMEDIATELY</strong></td>
<td>immediately after causal relationship is suspected.</td>
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<tr>
<td><strong>serious public health threat:</strong></td>
<td>no later than <strong>2 days</strong> from awareness of threat.</td>
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<tr>
<td><strong>death or unanticipated serious deterioration in health:</strong></td>
<td>no later than <strong>10 days</strong> from awareness of incident.</td>
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<tr>
<td>In all other cases:</td>
<td>no later than <strong>15 days</strong> from awareness of incident.</td>
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<tr>
<td>Where necessary to ensure timely reporting, the manufacturer may submit an initial incomplete report followed up by a complete report.</td>
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<tr>
<td>If after becoming aware of a potentially reportable incident there is still uncertainty about whether the incident is reportable, the manufacturer shall submit a report within the timeframe required for that type of incident.</td>
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</tbody>
</table>
### Reporting obligations – Vigilance *Articles 61 to 66 / 59 to 64*

<table>
<thead>
<tr>
<th>How/Where to report?</th>
<th>Article 66a - Electronic system on vigilance (EUDAMED)</th>
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<tbody>
<tr>
<td></td>
<td>implementing acts with details of modalities and procedural aspects</td>
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<tr>
<td></td>
<td>The information collated and processed by the electronic system shall be accessible to the competent authorities of the Member States, to the Commission and to the notified bodies that issued a certificate for the device in question.</td>
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<tr>
<td></td>
<td>⇒ Manufacturer will need to report in a timely manner to the centralised EUDAMED which will notify the relevant actors (CA of MS where incident/FSA occurred, CA of MS where manufacturer/EC Rep is located, Notified Body...)</td>
</tr>
</tbody>
</table>
The PRRC is responsible for ensuring: (d)

*in the case of investigational devices / devices for performance study, that the statement referred to in point 4.1 of Chapter II of Annex XIV / Annex XIII is issued.*

4.1. A signed statement by the natural or legal person responsible for the manufacture of the investigational device / device for performance study that the device in question conforms to the general safety and performance requirements apart from the aspects covered by the clinical investigation / clinical performance study and that, with regard to these aspects, every precaution has been taken to protect the health and safety of the subject.

The device in question conforms to the general safety and performance requirements apart from the aspects covered by the clinical investigation / clinical performance study. Every precaution has been taken to protect the health and safety of the subject.

bsi.

*Person Responsible For Regulatory Compliance*
Annex I – Safety & Performance Requirements

1. Safe, Effective, State of the Art

1a. Reduce risks as far as possible, without adversely affecting risk:benefit

   Risk Management, Risk Control, Including Use Error

3. Lifetime

4. Packaging

5. Evaluated Benefits of achieved performance > Known and Foreseeable Risks & Undesirable Side Effects

6. Devices with no medical purpose – “shall not present any risk or no more than the maximum acceptable risks”

Annex I – Safety & Performance Requirements

7. Chemical, Physical & Biological Properties

8. Infection & Microbial Contamination

9. Devices incorporating a medicinal product and devices composed of substances that are absorbed by or locally dispersed in the human body

10. Devices incorporating materials of biological origin

11. Construction and interaction with environment

12. Devices with a diagnostic or measuring function

13. Protection against radiation
Annex I – Safety & Performance Requirements

14. Electronic programmable systems

15. Active devices and devices connected to them

15a. Particular requirements for active implantable devices

16. Protection against mechanical and thermal risks

17. Protection against the risks posed to the patient or user by supplied energy or substances

18. Protection against the risks posed by medical devices intended by the manufacturer for use by lay persons

19. Information Supplied by the Manufacturer + Implant Card (Article 16) + Promotional Material CE Marked (Article 18) + UDI (Article 24)
Questions & Answers