Vaccine Safety Monitoring and Pharmacovigilance Tools
Advanced Pharmacovigilance Mini E-Workshop
16-18 March 2020

dcvmn
Developing Countries Vaccine Manufacturers Network

# Handling of Product Quality Complaints with respective Safety Implications

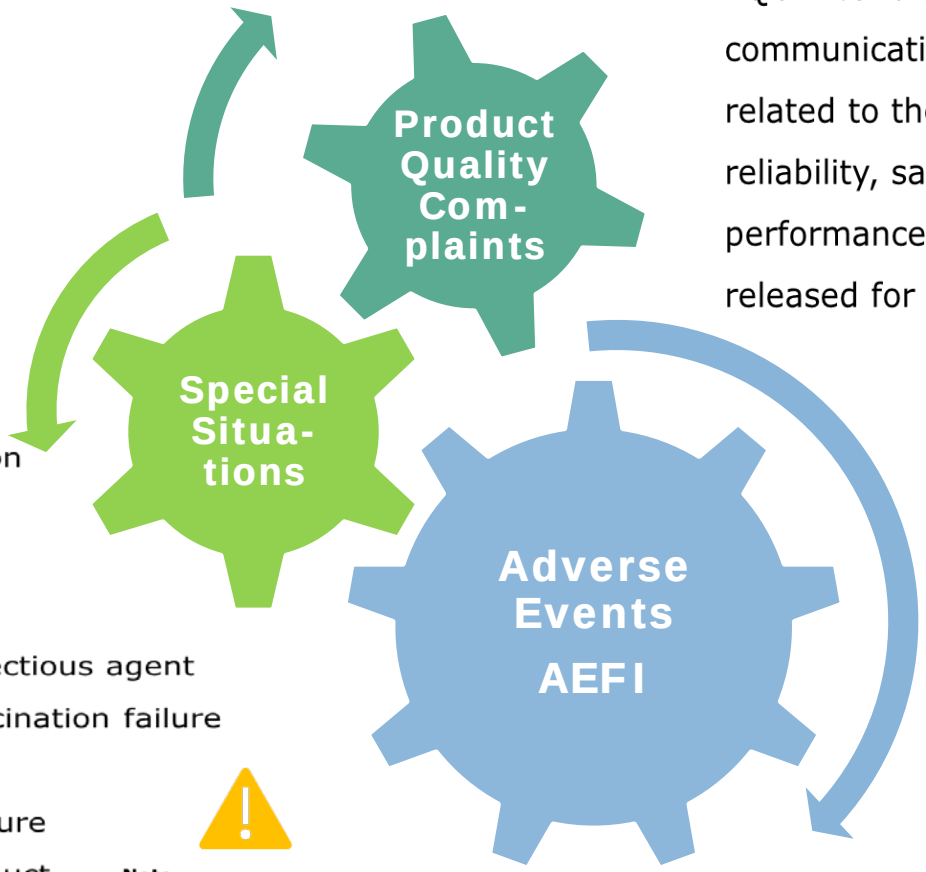
## Best Practices

Katharina Hartmann

# Types of reports

**Product Quality Complaint (PQC):**

PQC means any written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness or performance of the Product after it is released for distribution.

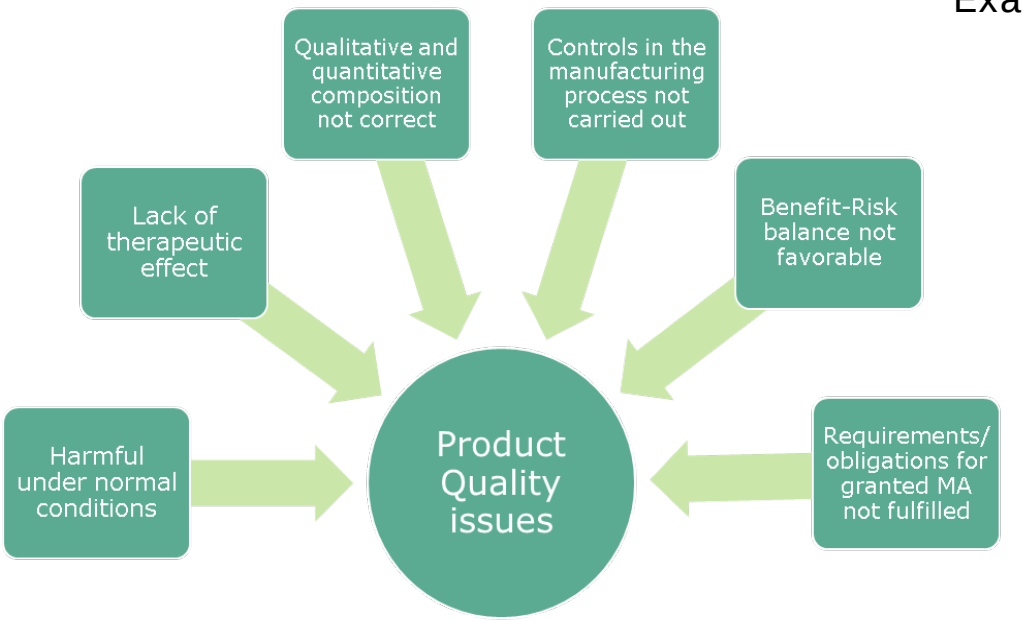



**Special Situations:**

- Pregnancy / lactation
- Overdose
- Misuse / abuse
- Medication error
- Transmission of infectious agent
- Lack of effect / vaccination failure
- Off-label use
- Occupational exposure
- Use of falsified product

**Note**
not all Special Situations may occur with vaccines

# Examples of Product Quality issues




Examples of PQCs also include:

- ✓ Damaged package or syringe
- ✓ Evidence of contamination
- ✓ Presence of a visible foreign substance / particles
- ✓ Missing lot number
- ✓ Missing or incorrect product label
- ✓ Missing package insert
- ✓ Color /appearance abnormal
- ✓ Accidental injury when handling / reconstituting

Note:
Lack of effect / vaccination failure is considered a serious unexpected AE

# Classes of quality defects

Class I: Defects that are potentially life-threatening or could cause a serious risk to health

Class II: Defects that could cause illness or mistreatment, but are not class I

Class III: Defects that may not pose a significant hazard to heath but where withdrawal of the medicine may be indicated for some other reason, but which are not class I or II

Directive 2003/94/EC
Art. 13

# Why report Product Complaints?

## ICH Q7 Good Manufacturing Practice Guide / Complaints and Recall requirements

All quality related complaints, whether received orally or in writing, should be recorded and investigated according to a written procedure.

Content of Complaint Records as defined by ICH Q7 / EMA Defective Product Report.

Records of complaints to be retained to evaluate trends, product-related frequencies, and severity with a view to taking additional, and if appropriate, immediate corrective action.

In the event of a serious or potentially life-threatening situation, local, national, and/or international authorities should be informed.

Vaccines have a complex production process and small changes may impact safety profile: Requirement to perform batch-related safety surveillance.

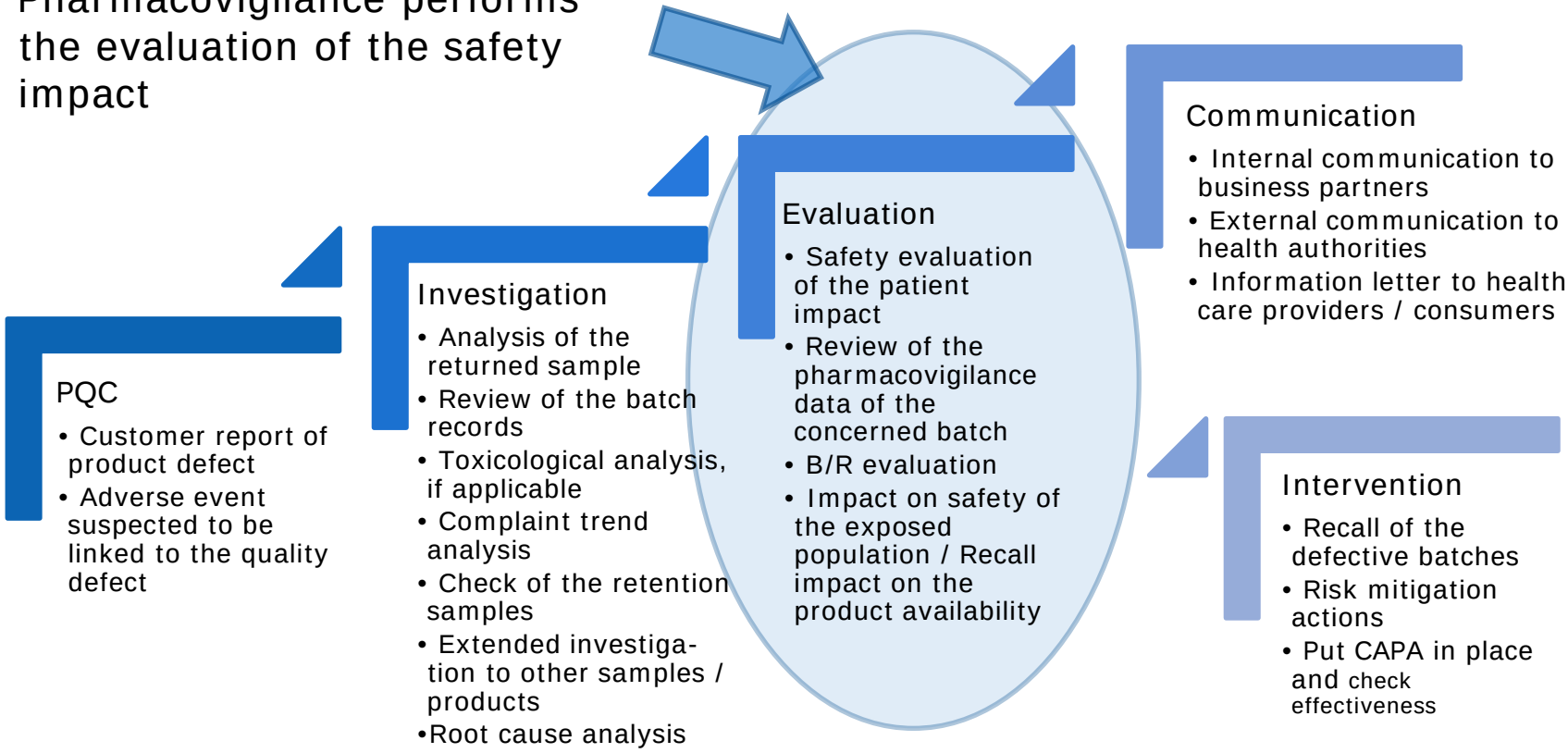
# What information is required for a PQC Report?

- Name and phone number of initial reporter
- Product name, strength and pack size
- Batch/Lot number & Expiry Date
- Details of retailer (wholesaler, hospital, pharmacy)
- Brief description of the product complaint
  - Including details of suspected adverse events
- Investigation, action details, root cause, proposed / taken CAPA
- Patient details (initials, date of birth, sex, age or age group) where relevant


6

# Quality complaint management

Pharmacovigilance performs the evaluation of the safety impact



# Pharmacovigilance role in PCQ management

## Detection of quality defects

A quality defect may have an impact on a subject's safety, if defective vaccine is administered.

PV monitoring is important to identify safety signals due to quality defects.

Manufacturers / MAH are required by NRAs to have processes in place that are capable to detect quality defects.

Assessment of AEFI reports associated with quality defects to determine the causal relationship and the potential extent of the safety impact

- E.g. a case of injection site pain due to a problem of a dull needle with a specific batch needs a trend review of all similar cases reported with the affected needle

Specific signal detection methods are necessary to identify, differentiate and assess potential quality defects linked to the medicinal product.

- Medical evaluation of individual AEFI
- Analyses of AEFI clusters possibly linked to a manufacturing period
- Disproportionality analyses at product batch level
- Analyses of AEFI reporting rate differences between regions / countries

# Which signals could be linked to a quality issue?

Reports of infections

Infections caused by a sterility problem

- with the vaccine itself
- with any part of the syringe
- with the handling of the vaccine preparation / vaccine administration
- suspected transmission of infectious agent

Unusual increase of reports of expected or serious AEFIs (e.g., clusters)

E.g., anaphylaxis linked to contamination of the product in any phase of the manufacturing process.

Efficacy problem / vaccination failure

Due to decrease of vaccine potency within its shelf life.

Vaccine exposed to inappropriate temperature during transport or storage.

In case of a sterility issue, e.g. *R. mannitolilytica* PV to analyze all available AEFI information from vaccinees that received the contaminated lot. The analysis of the data takes into consideration a potential contamination with particular focus on the SOCs Infections and Infestations, General Disorders and Administration Site Conditions (which contains the preferred terms pyrexia and chills), and Respiratory Thoracic and Mediastinal Disorder.

# Evaluation of the safety impact
## Example for a Health Hazard Evaluation HHE

**1. Introduction:**

[Describe the product under investigation including the usage indication(s) and license information for the country(ies) concerned. Include the product manufacturer information (e.g., information and the issue or concern, the scope of the issue and the potential safety implications—specify whether the evaluation is across all lots and manufacturing locations or confined to specified lots and manufacturing sites). This section also includes the purpose of the Report (i.e., to review the safety data relevant to an identified issue and to make a medical assessment regarding any potential safety issues involving the product.]

**2. Methods of Investigation:**

[Include the specifics of the investigation conducted whether safety database search(es) or literature search(es) (e.g., search by product lot(s), types of cases, specific adverse event terms)]

**3. Source:**

[Outline the sources of information used for the HHE (e.g., the Safety Database search and the literature search)]

**4. Summary of Results/Findings:**

[Describe in brief the results of the data search (e.g., number of AEFIs found, other safety findings)]

**5. Evaluation:**

[Describe how the issue has been evaluated. Support all conclusions as completely as possible with scientific documentation and/or a statement that the conclusion is the opinion of the individual(s) making the health hazard assessment determination.]

- Were case reports retrieved from the Safety Database?
  **Evaluation Results:**

- Have disease or injury already occurred from the use of the product with this specific issue or concern?
  **Evaluation Results:**

- Are there existing conditions in relation to the issue or concern that could contribute to a situation potentially exposing humans or animals to a health hazard?
  **Evaluation Results:**

- What is the perceived hazard to various segments of the population (e.g., children, surgical patients) expected to be exposed to the Product? [Focus on those with the greatest risk.]
  **Evaluation Results:**

- What is the degree of seriousness of the health hazard to which the populations at risk would be exposed?
  **Evaluation Results:**

- What is the likely occurrence of the hazard?
  **Evaluation Results:**

- What are the immediate and/or long-term consequences if the health hazard occurs?
  **Evaluation Results:**

- What is the benefit-risk analysis for the population at risk?
  **Evaluation Results:**


11

# Example for a Health Hazard Evaluation HHE cont.

**6. Conclusion:**

[Provide a conclusion of the medical assessment on whether a potential safety health hazard is posed by the issue under investigation.]

**Approval of Health Hazard Evaluation Report:**

| | |
|---|---|
| **Product:** | **Requester:** [Individual requesting safety investigation] |
| **Document Issue Date:** | |
| **Attachments:** [List and provide all supporting documentation such as tables, graphs, line listings reports, database search outputs and literature search results.] | |