Common Quality Issues - Challenges

Dossier assessments, GMP audits, Complaints & Recalls

Presenters
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Common Quality Issues - Challenges
Dossier assessments, GMP audits, Complaints & Recalls

Interagency finished pharmaceutical product questionnaire

- Dossier Assessments - Challenges
  - ✓ Product Dossiers (Technical)
- Site Document Dossiers, GMP Audits, Complaints & Recalls (QAC)

Product Dossier Assessments - Challenges

Interagency Finished Pharmaceutical Product Questionnaire (IAFPPQ)

❑ Completion of IAFPPQ

When completing the automated IAFPPQ questionnaire, it is mandatory to enter comprehensive information in the form itself and not refer/redirect to Annexures/external documents.

- ✓ Otherwise, there will be gaps in the information, when it is converted into an Excel spreadsheet for technical assessment.
- ✓ Will prevent follow up with the bidder, which leads to delays in the evaluation process.

1.6.2 Product registration in other countries

List other countries where the product is **registered and is currently marketed** in the table below.

Country	Competent Authority	Licence number
please refer to Annex D - List of Countries		

Product Dossier- Annex 2c Inter Agency Pharmaceutical Product Questionnaire (**IAFPPQ**)

IAFPPQ - Product Dossier Assessments - Challenges

❑1.3. Packaging- Include Primary & Secondary pack details ONLY specific to the offered product

1.3 Packaging

1.3.1 Primary packaging

Pack size (e.g. blister pack of 10 tablets, or 10 ml ampoule):
Description of package (bottle, ampoule, other):
Materials used for primary packing:

1.3.2 Secondary packaging

Total pack size (e.g. 100 tablets per box = 10 tablets x 10 blister cards):
Description of package (box, bag, other):
Materials used for primary packing:

❑1.4 Contact details- 1.4.1 Supplier/Bidder identification

✓Supplier/Bidder to include details of the Head/commercial office site i.e., responsible for signing the LTA, P.O, receiving payments etc.

✓ This site also could be same as the manufacturing site
e.g. Head/commercial office and the mfg. site are located at the same address.

✓Vendors (Nos.) are created for both head office/commercial office and manufacturing site (as applicable) and are interconnected in the internal system.

Product Dossier- Annex 2c Interagency Pharmaceutical Product Questionnaire (**IAFPPQ**)

IAFPPQ – Product Dossier Assessments - Challenges

- 1.5 Manufacturer identification

  - ✓ Only manufacturing site details to be included here.
  - ✓ If the Supplier/Bidder address is the same as Manufacturing site, please skip this section.
  - ✓ Please provide detailed information of manufacturing line/site e.g., Workshop # or Unit #

- Finished Product Certificate of Analysis (FPP CoA)

  - ✓ Should be provided for the Finished Pharmaceutical Product (i.e. packed in primary container) and NOT for bulk batch release.
  - ✓ Specification (method/standard) reference (B.P, USP, Ph. Eur. or IH) should be included for EACH tests mentioned in the FPP CoA.

Bulk Batches- Means Bulk finished product e.g.. Tablets, Capsules, Liquids not yet packed in primary container
Finished Pharmaceutical Product (FPP)- A product that has undergone all stages of production, including packaging in its final container and labelling

IAFPPQ – Product Dossier Assessments - Challenges

- Terminal Sterilization is preferred for Injectables (wherever applicable).

- FPP Stability Reports

Should include,

- ✓ API Grade & API Manufacturer name & country.
- ✓ Sample pull-out dates of testing.
- ✓ Specification (Method/standard) reference should be included for EACH test mentioned in the stability report.
- ✓ Recent stability reports should be provided.

Finished Pharmaceutical Product (FPP)- A product that has undergone all stages of production, including packaging in its final container and labelling

IAFPPQ – Product Dossier Assessments - Challenges

- APIs & API sources
  - ✓ Only API sources that contribute directly to the submitted stability data should be included.
  - ✓ For sterile APIs, it is mandatory to include the media fill validation report received from the API source.
  - ✓ Post LTA changes, affecting API should be approved by UNICEF SD.
  - ✓ API sources should be audited onsite by FPP manufacturer. Exemption include SRA/WHO PQ API sources.

- Annex W: Stability Declaration (API used)
  - ✓ Annex W requires a detailed declaration confirming the completion or progress of stability studies with all specified API sources.
  - ✓ This declaration should contain specific information, including batch numbers and the full names and addresses of the API sources used.

Finished Pharmaceutical Product (FPP)- A product that has undergone all stages of production, including packaging in its final container and labelling
API- Active Pharmaceutical Ingredient
SRA- Stringent Regulatory Authority

IAFPPQ – Product Dossier Assessments - Challenges

- Annex 2g Technical Commitment declaration
  - ✓ Outline any differences between the product offered and the product previously supplied or registered in other reference countries that are listed in the IAFPPQ.
  - ✓ Clearly state and highlight these differences to enable a clear understanding of the differences.
- Uploading documents to the share point library
  - ✓ Do not create additional folders; other than the provided folders.
  - ✓ Upload documents, name and tag appropriately.

IAFPPQ – Product Dossier Assessments - Challenges

- Criteria- SRA approved/registered products-

  - ✓ Should be supplied in SRA approved packs.
  - ✓ SRA approved packs must carry MA number and MAH details.
  - ✓ QP released (FPP CoA issued) from country of SRA only.
  - ✓ Supplied from country of SRA only.

- Offering SRA approved/registered products-

  Supplier must sign the following forms (manually or electronically)

  - ✓ Technical Offer Form (2f) and
  - ✓ Commitment Declaration form (2g)

Finished Pharmaceutical Product (FPP)- A product that has undergone all stages of production, including packaging in its final container and labelling
CoA- Certificate of Analysis

Common Quality Issues - QAC

- ❑ Dossier Assessments - Challenges
  - ✓ Product Dossiers (Technical)
  - ✓ Site Document Dossiers (QAC)
- ❑ GMP Audits (QAC)
- ❑ Complaints & Recalls (QAC)

Site Document Dossier Assessments - Challenges

Technical Questionnaire for Pharmaceutical Manufacturers and Wholesalers

- Purpose of Technical Questionnaire(s)

Information provided in the technical questionnaire needs to be as comprehensive and transparent as possible because it is used for the following key purposes:

- ✓ To perform a GMP / GDP evaluation of the company using a quality risk management tool which will determine:
  - The need for a GMP / GDP audit.
  - The frequency, scope and duration of the GMP / GDP audit.
- ✓ Forms part of the document assessment in preparation for a GMP / GDP audit.

Site Document Dossier Assessments - Challenges

Technical Questionnaire for Pharmaceutical Manufacturers and Wholesalers

- Most common challenges experienced during review of Technical Questionnaires
  - Completing the incorrect Technical Questionnaire
    - ✓ Technical Questionnaire for Pharmaceutical Manufacturers
    - ✓ Technical Questionnaire for Pharmaceutical Wholesalers

Site Document Dossier Assessments - Challenges

Technical Questionnaire for Pharmaceutical Manufacturers

- Most common challenges experienced during review of Technical Questionnaires

  - 3.2 Manufacturing license for medicinal products

    - ✓ Current manufacturing license <u>with attachments</u>
    - ✓ Where applicable, also provide the current GMP certificate(s)

Site Document Dossier Assessments - Challenges

Technical Questionnaire for Pharmaceutical Manufacturers

- Most common challenges experienced during review of Technical Questionnaire

  - 3.3 Inspection

    Names of all other Regulatory Authorities and International Organisations who have inspected the company. Please also state the outcome of the inspection.

    - ✓ List <u>at least</u> the following:

Authority / International Organisation Name	Country	Audit Date(s)	Manufacturing Unit Audited	Audit Scope	Audit Outcome (approved / not approved)

    - ✓ <u>Date of last inspection</u> by the National Regulatory Authority

Site Document Dossier Assessments - Challenges

Technical Questionnaire for Pharmaceutical Manufacturers

- Most common challenges experienced during review of Technical Questionnaire

  - 4.1 Manufacturing Site

    Please state all addresses at which manufacturing of pharmaceutical products takes place and indicate which year the factory was built (complete one questionnaire for each site).

    - ✓ This also applies to where one site has multiple manufacturing units.
    - ✓ Where there is only one SMF per site with multiple manufacturing units it is important that the SMF:
      - Clearly distinguish between different activities performed by each manufacturing unit.
      - Specifies which activities or areas are shared by the units.
      - Include all annexes and layouts for all the different units.

Site Document Dossier Assessments - Challenges

Technical Questionnaire for Pharmaceutical Manufacturers

- Most common challenges during completion of Technical Questionnaire

  - 6 GMP Inspection
    - ✓ Can UNICEF or any other representative designated by UNICEF perform an inspection of the Manufacturing site?
      ☐Yes ☐No
    - ✓ Can the National Regulatory Authority participate as observers in the audit?
      ☐Yes ☐No
    - ✓ May UNICEF share the inspection report with its partners WHO Geneva, MSF France, ICRC Geneva and PIC-S member states upon request? (Your company will be notified in case the report is shared.)
      ☐Yes ☐No

Common Quality Issues - QAC

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GMP Audits

- Examples of most common GMP observations relates to:
  - Contract production, analysis and other activities
    - No technical agreements, or lack of information covered
    - Inadequate, or lack of supplier qualification
    - Not auditing (critical) suppliers
  - Cleaning Validation
    - No consideration of Health-Based Exposure Limits (HBELs)
  - Suitability of storage conditions during distribution
    - Lack of adequate storage conditions and monitoring of shipments during transportation

GMP Audits

- Examples of most common GMP observations relates to:
  - Quality Risk Management
    - Selective use of Quality Risk Management
    - Using risk assessment to justify GMP non-compliances
  - Data Integrity
    - Lack of, or inadequate implementation of data integrity across all systems in the facility, not only QC
  - Facilities
    - Facility layouts are not a true reflection, or up-to-date
    - Inadequate design to ensure containment where required

GMP Audits

- Examples of most common GMP observations relates to:
  - Mock Recalls
    - Inadequate frequency of performing mock recalls
    - Insufficient selection of product / market to represent mock recalls
  - Analytical Method Verification / Validation
    - Lack of systems for review / revalidation
  - Product Quality Review
    - Lack of adequate review of the reports with missing or incorrect information
    - Lack of, or inadequate use of statistical analyses

Common Quality Issues - QAC

- ❑ Dossier Assessments - Challenges
  - ✓ Product Dossiers (Technical)
  - ✓ Site Document Dossiers (QAC)
- ❑ GMP Audits (QAC)
- ❑ Complaints & Recalls (QAC)

Complaints & Recalls

- Most common challenges during complaint & recall investigations
  - Difficulty to obtain samples to perform the investigation (logistical mostly)
  - “Superficial” investigation reports with lack of finding the root cause
  - Tendency to blame incorrect storage conditions as an immediate root cause, especially in the case of shipments sent under DAP terms.
  - Lack of adequate storage conditions and monitoring of shipments during transportation

Questions?

THANK YOU

29th Nov 2023- 14:30-15:00 hrs plenary session 9

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