

Pharmaceutical product technical requirements and the Interagency pharmaceutical product questionnaire

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Product evaluation is a key tool to ensure product quality

- Recent publications underlines the continued problem with substandard drugs in many countries:

Caudron JM, Ford N, Henkens M et al (2008), *Substandard medicines in resource-poor settings: a problem that can no longer be ignored*. Tropical Medicine and International Health, 13(8): 1062-1072

⇒ **Quality Assessments (GMP and product specific) from procurement agencies remain a key to assuring the quality of medicines in countries and projects**



Presentation outline

- The Interagency Pharmaceutical Product questionnaire
- UNICEF technical requirements for pharmaceutical products

The Interagency Pharmaceutical Product Questionnaire





WHY Interagency?

- Improve overall product quality in the market
- Standardization and Harmonization
- Information sharing
- Shared workload
- Coordinated feedback to manufacturers
- Joint review meetings twice a year



Benefits of Questionnaire

- Standardized technical evaluation of suppliers and commodities.
- Products from different suppliers technically compared in a standard format.
- Faster technical evaluation and approval
- Faster supply to organizations
- Reduced workload for both the bidder and agencies



Use of the questionnaire

- Considered as the basic minimum
- Currently part of the WHO Model QA system for procurement agencies
<http://www.who.int/medicines/publications/ModelQualityAssurance.pdf>
- Agencies to maintain own validation procedures:
 - Organizations may ask additional questions to manufacturers depending on validation scheme



Shared data base

- Outcomes of GMP inspection
- Technical evaluations
- Tools
- Others



Challenges

- Incomplete Questionnaire
- Inadequate information
- Different information to agencies on the same product
- Variation to approved product at the time of supply



Challenges; Incomplete questionnaire

- Questionnaire not completely filled. **Why?**
Usually filled by business unit in the company while questionnaire is technical
- Information and supporting documentation not submitted. **Should this be done before an offer is requested?**
- Supporting documentation not submitted according to requirements as specified



Challenges: inadequate information

■ E.g stability studies

- Not always available in the formulation or packaging proposed to be supplied
- Information on batch size not always included
- Batch analysis do not always include all required tests as per pharmacopoeial reference or in-house FPP specifications
 - at least for initial batch release and analysis at end of proposed shelf-life period, e.g. related substances, bacterial endotoxins



Challenges: Different information to agencies on the same product

- Stability studies
- API sources
- Manufacturing sites



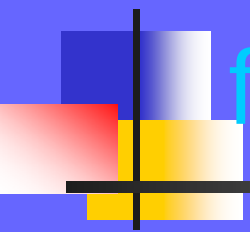
Challenges; Variation to approved products at the time of supply

- Packaging, brand names, pack color
- Shelf life
- Manufacture site
- API sources
- How best to handle this?
 - New technical evaluation required
 - Time consuming, leads to delays in supply
 - Cost implications-new commercial evaluation required



Challenges from agencies perspective

- How to keep track of the documentation and information for subsequent bids
- Questionnaire requires manual filling in
 - Electronic version being considered



UNICEF technical requirements for pharmaceuticals



Technical requirements

- Outlines UNICEF's expectations of safety, efficacy and quality
- Solicits supporting documentation to verify product and manufacturer status
- Based on current international standards and best practice for FPP specifications and the enabling manufacturing environment
- Accompanies every bid for pharmaceutical commodities



Documents required

- Complete Tech Questionnaire for Pharmaceutical manufacturers
- WHO-GMP certificate
- Complete IAPPQ
- CoPP
- Standards for API- CEP/DMF
- FPP specifications, monograph
- Marketing authorization in source country
- Manufacture licence
- Results of
 - FPP stability studies
 - bioequivalence/bioavailability as applicable
- COA of 5 production batches or model cert

IMPORTANT

- Documents to be filed/bound in an orderly manner as specified
- Documents not in English must have certified Professional translation to English



What we are looking for

- Manufacturing standards for API, FPP
 - WHO-GMP
- FPP Standards
 - Registration by stringent DRA (ICH)
 - WHO prequalification
- FPP specifications for
 - dosage forms
 - Primary & secondary packaging, closure systems
 - Labels, pack inserts
- Shelf life, stability, storage
- Product samples as will be supplied on order



Manufacturing standards

- GMP for all relevant manufacture sites
- API compliance with monographs,
Confirmatory COA valid for shelf life of FPP
- Contract manufacture
- Changes in manufacture site require re-evaluation
- UNICEF to carry out GMP inspection and audits where applicable



Pharmaceutical dosage forms

- Each dosage form to comply with relevant section of Ph.Int, Ph.Eur, USP, BP
- Fit-for-purpose, usability e.g.
 - break marks for solid tablets
 - packing injectables together with special diluents
 - Packing oral liquids with dose measuring devices
 - Individual sealing of vaginal/ rectal suppositories
- Instructions for reconstitution, storage, use



Packaging, container closure systems

- Stability studies done in final packaging
- Conforms with relevant monograph with respect to the specific medicine
- Zone IVa/b stability
- Facilitates distribution, dispensing, adherence
- Size of container proportional to its contents

Labels, pack inserts, patient information leaflets



- Language- English and French, as specified
- Minimum required information on primary and secondary label,
 - Amodiaquine 200mg
 - Amodiaquine HCl 200mg
 - Amodiaquine 153mg
 - Amodiaquine 153mg (as HCl)
 - Amodiaquine HCl 200mg equivalent to Amodiaquine 153mg base
- No abbreviation of INNs
- Expiry date format dd/mm/yyyy
- Label format-Visibility of important information for users
- Pack inserts/patient info leaflets as per standards
- Suitability of brand names assessed



Shelf life, stability, storage

- State numerical results instead of “complies”, “conforms”
- Specifications and methods used for stability studies (Monograph), if different, method validation.
- Real time, accelerated studies as per WHO
- Shelf life conclusions drawn from stability studies