Update on WHO Public Assessment Reports

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Outline

- The WHO Public Assessment Reports (WHOPARs)
  - What do they contain?
  - How are they prepared?

- The Product information in the WHOPAR (SmPC/PIL)
  - Past → Present → Future
WHOPARs – What do they contain?

Contents and Structure of a WHOPAR

WHO Public Assessment Reports (WHOPARs) are a key output of PQTm. They are a Team: medicines, providing insight and transparency as to the process followed to prequalify the finished pharmaceutical products (FPPs) concerned.

A WHOPAR is of great value for regulators and procurers. The data and information provided by the manufacturer, it describes the quality, safety and efficacy of the preq prequalified FPP.

the product information is an essential component of a prequalified FPP

https://extranet.who.int/prequal
WHOPARs – How are they prepared

Steps in developing a WHOPAR

The sequence for developing a WHOPAR following prequalification of an FPP is as follows:

**Step 1:** The applicant submits documents required for the WHOPAR as part of the initial submission for evaluation for prequalification to WHO.

**Step 2:** WHO compiles the draft WHOPAR when the assessment and inspections have been completed successfully.

**Step 3:** WHO forwards the draft WHOPAR to the applicant for review. (Documents are exchanged in electronic format by the applicant and WHO, generally by email.)

**Step 4:** The applicant reviews and comments on (annotates) the draft WHOPAR, in particular to ensure that the WHOPAR does not contain any proprietary or confidential information.
WHOPARs – How are they prepared
What’s new in 2019

Steps in developing a WHOPAR

Step 5: The applicant returns the annotated draft WHOPAR to WHO.

Step 6: WHO reviews the annotated text — Steps 3 to 6 may need to be repeated if an item requires further clarification — and finalizes the WHOPAR.

Step 7: If the FPP, as produced at the specified manufacturing site(s), meets the prequalification requirements, WHO accepts the FPP for inclusion in the WHO List of Prequalified Medicinal Products (i.e. prequalifies it) publishes the WHOPAR and informs the applicant accordingly.

Step 8: Within three months after acceptance/publication of the WHOPAR, the applicant provides a mock-up of the final PII, taking into consideration the recommendations as described in the European Commission’s guideline on the readability of the labelling and the package leaflet of medicinal products for human use.
A WHOPAR consists of eight parts:

- **Part 1**: Abstract
- **Part 2a**: All accepted presentations
- **Part 2b**: Appearance of Product
- **Part 3**: WHO-PQ recommended product information for the user (PIL)
- **Part 4**: WHO-PQ recommended information for the health care provider (SmPC)
- **Part 5**: Labelling
- **Part 6**: Scientific discussion
- **Part 7**: Steps taken for prequalification
- **Part 8**: Steps taken following prequalification.
A “Good” Medicinal Product
Not new in 2019

Pharmaceutical Quality

Efficacy and Safety (Bioequivalence)

Product information
- label
- for health care professional
- for user/patient

Copenhagen, Denmark 2-5 December 2019
The WHOPAR product information

Since more than 15 years a group of international experts mainly from regulatory authorities have spent effort in producing high-quality output on

- Prequalification processes and outcomes
- Information on efficacy and safety of prequalified products
- Focus on product information

Patient safety
WHOPAR Product Information
- Full PQ assessment

Comparator product’s / products’ (for FDCs) SmPC/PIL as basis

- Due to similarities in the structure with the WHOPAR format, preferably EU texts
- Current WHO-treatment guidelines
- Relevant regulatory guidance
- Supplemented with data from scientific literature

Reference list at the end of part 4 (SmPC)
Special consideration: Relevance of the information for the safe use in resource constrained settings.

Examples include

unambiguous and practical recommendations for:

- handling of drug interactions; whenever possible, avoid costly and not widely available investigations, e.g. regular monitoring of drug plasma levels (TDM), instead detailed information on optimized clinical monitoring
- pregnancy and breast-feeding
- warnings/contraindications, in view of available alternative therapies and their benefits and risks.
Over time

- WHO treatment guidelines change
- Innovators’ product information gets updated
- New drugs and new scientific data become available

2019

WHOPARs normally get published shortly after prequalification
Users of WHOPARs (procurers/health care providers) sometimes faced with inconsistent/outdated/conflicting information in different WHOPARs

PQTm faced with many applications for changes of the product information “variations”, all of which have to be assessed individually – resource-intense effort!

What is the solution?
Preparation of WHO-PQ recommended (generic) texts of clinical and preclinical medicines information

- In a rolling system (one product type/kind at a time, e.g. all lamivudine-containing products)
- Regular updates begun in 2019:
  - immediately for major safety updates
  - otherwise, yearly checks, updates as needed

Of note: This service provided by WHO does not in any way preclude the supplier’s responsibility and liability in terms of keeping the product information of the supplied medicinal product correct and updated.
Preparation and publication of WHO-PQ recommended "Model texts of clinical and preclinical medicines information"

Instead: News item on PQTm-website informing about update of texts.

Example:

„For all prequalified lamivudine- and lamivudine/zidovudine-containing products the SmPC and PIL in the WHOPARs (parts 3 and 4) have been updated to reflect current WHO treatment guidelines and present state of scientific knowledge.“
Text appearing on PQTm-website and within the WHOPARs:

“This <product information text> focuses on uses of the medicine covered by WHO’s prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information from stringent regulatory authorities (term to be revised). The medicine may be authorised for additional or different uses by national medicines regulatory authorities.”
WHOPAR - Product Information

What's new in 2019

Readability

Links to non-WHO guidance documents that can be consulted when preparing product information

EC guideline on the readability of the labelling and the package leaflet of medicinal products for human use (2009)


Mock-ups of the patient information leaflet to be submitted to PQTm for proving readability

Responsibility of the National Medicines Regulatory Authority

Copenhagen, Denmark | 2-5 December 2019
Clarifications regarding carton free supply of prequalified products packaged in bottles

- Advantages of carton free supply of medicinal products acknowledged
- Acceptable to PQTm, when the immediate container label (bottle label) contains all the product information required to be on the outer carton and immediate container labels.
- Essential that every bottle dispensed to users/patients is accompanied by a patient information leaflet
- Products not supplied with the required number of patient information leaflets shall not be regarded as prequalified