

Update on WHO Public Assessment Reports

Regine Lehnert, MD

❖ The WHO Public Assessment Reports (WHOPARs)

- **Why** they are prepared
- **Where** to find them
- **What** they contain
- **How** they are prepared
- **Who** prepares them

**What's new
in 2024**

❖ The product information in the WHOPAR ➡ (SmPC / PIL)

❖ Updates

WHOPARs – Why

World Health Assembly Resolution WHA57.14 (2004)

WHO Public Assessment Reports (WHOPARs) are a **key output** of the WHO Prequalification 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**. As well as **summarizing the assessment** of the data and information provided by the manufacturer, it describes the **quality, safety and efficacy** of the prequalified product. (... .)

<https://extranet.who.int/prequal/medicines>

WHOPARs – Where to find them



Medicines

- About Medicines Prequalification
- What We Do
 - Documents A-Z
 - Prequalification Pipeline
- Prequalified Lists
 - FPPs and APIs Eligible for Prequalification ("EOIs")
- Prequalification Procedures & Fees: FPPs, APIs & QCLs
- Post-prequalification Procedures & Fees: APIs, FPPs, QCLs
- Prequalification Reports
- Collaborative Procedures for Accelerated Registration
- Guidance Documents
- Pilot Prequalification of Biotherapeutic Products
- Support to Manufacturers, CROs and QCLs
- Risk Assessment
- Market Information
- eCTD

Medicines

General Information – WHO List of Prequalified Medicinal Products

Medicines Key Contacts

Notices of Concern (NOCs) - Medicines

Medicines Quality Control Laboratories

Problems with the quality of medicines and their supply led to the creation of WHO medicines prequalification. From a public health perspective, the greatest achievement of medicines prequalification has been to increase access to quality medicines today by millions of people in low- and middle-income countries. Indeed, medicines prequalification ensures that everyone in the world will have access to safe, effective, and affordable medicines.

Perhaps most importantly, it has demonstrated and continues to demonstrate that ensuring the availability of assured medicines is a shared endeavour between regulators, manufacturers, procurers, and donors. The active participation of each of these stakeholders is essential to increasing universal health coverage, protecting people from substandard medicines, and providing people with better health and well-being.

Key activities and standards applied

Medicines key prequalification activities are:

- assessment of product dossiers (for finished pharmaceutical products (FPPs) or master files (for active pharmaceutical ingredients (APIs))
- inspection of manufacturing and clinical sites
- organization of quality control testing of products.

WHO also prequalifies quality control laboratories (QCLs), specifically those QCLs that carry out chemical and microbiological testing of medicines.

The standards used to evaluate FPPs and APIs, and their manufacturing sites, are based on the principles and practices agreed by the world's leading regulatory agencies and adopted by the WHO Expert Committee on Specification for Pharmaceutical Preparations.

Other medicines prequalification activities include:

- training (for manufacturers, regulators and QCLs)
- provision of technical assistance (for manufacturers and QCLs)
- implementation of the collaborative procedure for registration.

On this website...

Here in the medicines part of the WHO prequalification website you can find:

- key prequalification outputs: the lists of prequalified FPPs, APIs and QCLs, and [WHO Public Assessment Reports](#) and [WHO Public Inspection Reports](#)

Information for

Manufacturers

Regulatory agencies

Quality control laboratories

Procurement agencies

**Do not Google them!
It may take you to
outdated versions!**

<https://extranet.who.int/prequal/medicines>

Joint Meeting 2– 6 December 2024

M Medicines

+ About Medicines Prequalification

+ What We Do

Documents A-Z

Prequalification Pipeline

+ Prequalified Lists

FPPs and APIs Eligible for
Prequalification ("EOIs")

+ Prequalification Procedures & Fees:
FPPs, APIs & QCLs

+ Post-prequalification Procedures &
Fees: APIs, FPPs, QCLs

+ **Prequalification Reports**

+ Collaborative Procedures for
Accelerated Registration

+ Guidance Documents

+ Pilot Prequalification of Biotherapeutic
Products

+ Support to Manufacturers, CROs and
QCLs

+ Risk Assessment

Market Information

eCTD

WHO Public Assessment Reports (WHOPARs) Medicines

Each WHO Public Assessment Report is listed by WHO reference number and therapeutic area. Each listing also provides the relevant International Nonproprietary Name (INN), the dosage formulation and dosage strength, and the name of the supplier.

The summary of product characteristics/patient information leaflet included in these WHOPARs focus on uses of the medicines covered by WHO 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.

Refer to the [Contents and structure of a WHOPAR](#) section for information about the value of WHOPARs and the information they contain.

Therapeutic Area

COVID-19

Apply

M [BT-CV001](#)
Tocilizumab 20mg/mL (Each vial contains 80mg of tocilizumab in 4mL) - Concentrate for solution for infusion Roche Registration GmbH 📍 Germany

M [BT-CV002](#)
Tocilizumab 20mg/mL (Each vial contains 200mg of tocilizumab in 10mL) - Concentrate for solution for infusion Roche Registration GmbH 📍 Germany

M [BT-CV003](#)
Tocilizumab 20mg/mL (Each vial contains 400mg of tocilizumab in 20mL) - Concentrate for solution for infusion Roche Registration GmbH 📍 Germany

M [CV004](#)
Dexamethasone (sodium phosphate) 4mg/mL - Solution for injection Farmak JSC 📍 Ukraine

M [CV005](#)
Dexamethasone (sodium phosphate) 3.3mg/mL (1mL) - Solution for injection Noridem Enterprises Ltd 📍 Cyprus

WHOPARs- Where to find them



Overview of WHO Public Assessment Report (WHOPAR)

CV004

WHOPAR

[Part 1](#)

[Part 2](#)

[Part 3](#)

[Part 4](#)

[Part 5](#)

[Part 6](#)

[Part 7](#)

[Part 8](#)

M

Product name

Dexamethasone (sodium phosphate)

Dosage

4mg/ml - Solution for injection

Laboratory

Farmak JSC

Ukraine

Part 1 - Abstract

Part 2 - All accepted presentations (including photo)

** This summary of product characteristics/patient information leaflet focus on uses of the medicine covered by WHO 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.

WHOPARs – How prepared

(focus on product information)

Step
1

- Submission of Product information with application for PQ

2

- Evaluation of quality and crosslinking attributes by PQ assessment team

3

- With positive assessment and inspection outcome compilation of the WHOPAR

4

- Forwarding to applicant for review (soft copies)

5

- Critical review by applicant, including annotations, where required
substantiated by relevant data

6

- Return to WHO (soft copy) – if compressed, only as Zip folder

7

- If acceptable, publication. Otherwise repeat from step 4

WHOPARs – Who prepares them

WHOPAR-Group at PQT/MED

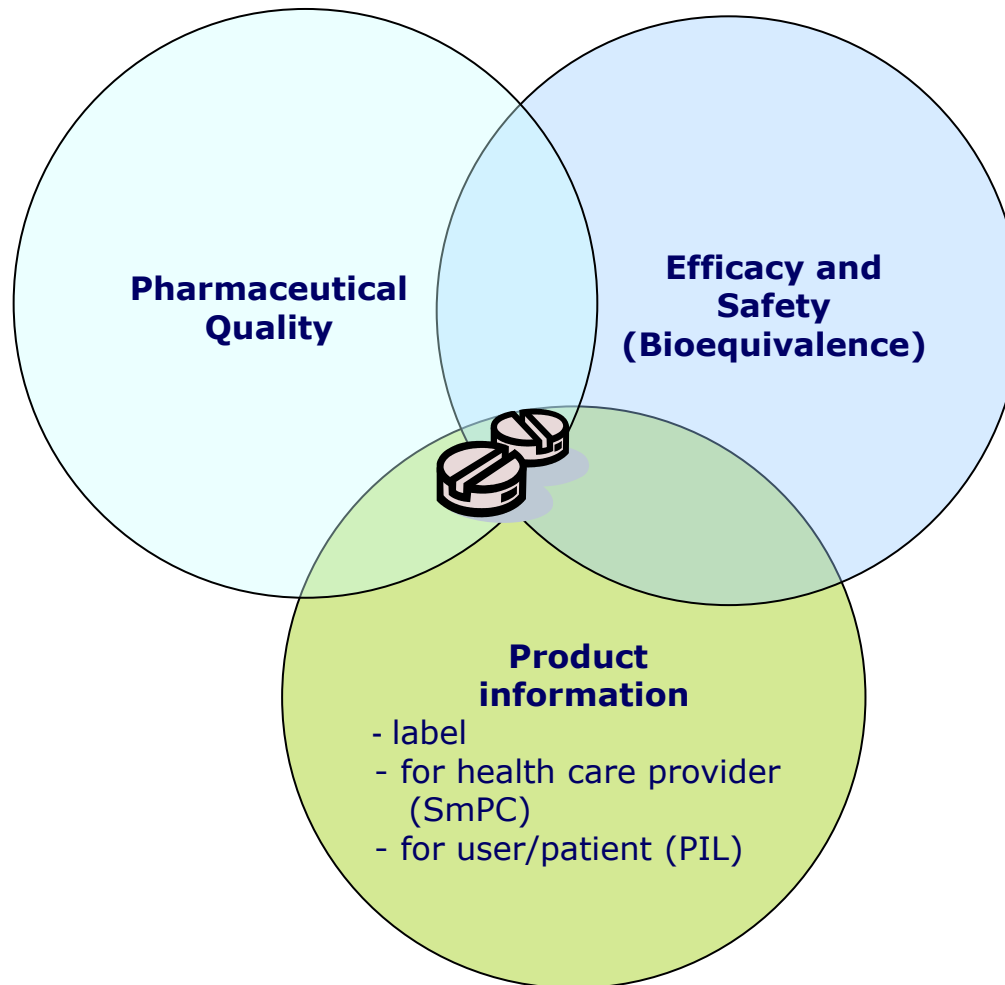
International group of experts
mainly from regulatory authorities
providing output on

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

 Patient safety

- **Parts 3 and 4: Based primarily on comparator product's information and WHO Treatment Guidelines**

A Medicinal Product



WHOPAR Product information clinical and preclinical sections

With time

- Revision of WHO treatment guidelines
- Update of reference product's information
- Availability of novel medical products
- Emergence of new scientific data

- ➡ Information gets **outdated**
- ➡ Same type of product WHOPARs **with differing information**
- ➡ **Products are prequalified that are not recommended by WHO anymore**

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 abacavir-containing products)
- Regular updates begun in 2019:
 - ⚡ **immediately** for major safety updates
otherwise, **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.

Periodic updates

- **First updates of most prequalified products**
of all WHOPAR-parts for formatting updated and including,
e.g. also requalification status
60 "batches", in 2024, e.g. hepatitis antivirals, various
reproductive health medicines, medicines for NTDs
- **Second periodic updates** of **15 "batches"**,
more than **140 WHOPARs**
- **Safety updates** for AQ+S/P containing products

Status 12/2024

WHOPARs not updated

Kanamycin (as ~~an~~ 500mg/2ml Solution for Injection

WHOPAR Part 1

September 2019

WHO Prequalification Programme WHO PUBLIC ASSESSMENT REPORT (WHOPAR)

[redacted] (trade name)¹

Kanamycin (as ~~an~~ 500mg/2ml Solution for Injection¹

Abstract

[redacted] (trade name), manufactured at [redacted] (trade name), was included in the WHO list of prequalified medicinal products for the treatment of tuberculosis on 06 February 2019.

[redacted] (trade name), is indicated in combination with other antituberculosis agents for the treatment of tuberculosis caused by *Mycobacterium tuberculosis*. Kanamycin is only indicated as a second-line antitubercular drug when first-line drugs cannot be used because of resistance or intolerance.

Detailed information on the use of this product is described in the summary of product characteristics (SmPC), which can be found in this WHOPAR.

The active pharmaceutical ingredient (API) of [redacted] (trade name) is the antitubercular agent kanamycin. The API is well established and documented for the treatment of tuberculosis.

The most serious safety concerns with kanamycin are nephrotoxicity and ototoxicity.

Other adverse reactions reported are anaphylaxis, hypersensitivity reactions, rash, anaemia, blood dyscrasias, purpura, headache, nausea, vomiting, diarrhoea, stomatitis, antibiotic-associated colitis, electrolyte disturbances, and effects on liver function. The "malabsorption syndrome" characterized by an increase in faecal fat, decrease in serum carotene, and fall in xylose absorption, has occurred with prolonged therapy.

Local reactions have included pain at the injection site after intramuscular injection.

The efficacy and safety profile of kanamycin is well established based on extensive clinical experience in the treatment of tuberculosis.

On the basis of data submitted and public information on the use of kanamycin in antituberculosis therapy, the team of assessors advised that [redacted] (trade name) is of acceptable quality, efficacy and safety to allow inclusion of [redacted] (trade name), in the list of prequalified medicinal products.

¹ Trade names are not prequalified by WHO. This is the national medicines regulatory authority's responsibility.

Kanamycin (as ~~an~~ 500mg/2ml Solution for Injection

WHOPAR Part 1

September 2019

Summary of Prequalification Status for [redacted] (trade name).

Initial acceptance	Date	Outcome
Status on PQ list, i.e. date of listing	[redacted]	listed
Quality	[redacted]	MR
Biobequivalence	[redacted]	MR
Safety, Efficacy	NA	NA
GMP (re-inspection)	[redacted]	MR
API	[redacted]	MR
FPP	[redacted]	MR
GCP/GLP (re-inspection)	NA	NA

MR: meets requirements

NA: not applicable, not available

Watermarks in parts
1, 3 and 4

Plain language descriptions of oral dosage forms

The description of visual appearance of finished product and packaging provided in the WHOPAR is important.

It can help the patient and health care provider



- To know that the information relates to the correct medicine (for example if a patient has multiple medicines, each with a patient information leaflet)
- to see if there is an obvious problem with the medicine (e.g. tablets are mottled when they are described as plain)
- to identify cases of falsification or error (if the description and the actual medicine do not match)

Descriptions of oral dosage forms

– Issues noted

- Products with similar appearances may be described differently by different suppliers, and it may not be clear exactly what details are helpful to include
- Where technical language is used to describe aspects of the appearance it is likely to be confusing to readers unfamiliar with the terms
- The description is often a single complex sentence that can be hard to read

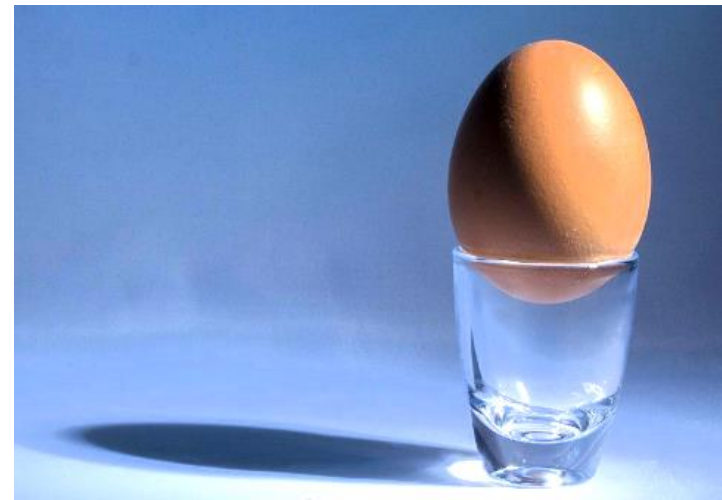
Case Study 1

- Yellow-coloured, circular, uncoated, flat-faced, bevelled edged, matt finished tablets, with a break line on one side and plain on the other side.
- A yellow, round, flat-faced, beveled edge tablet with a break line on one side and plain on the other side
- Yellow, circular, uncoated, matt-finished tablets. They are flat-faced and bevel-edged. The tablets have a break line on one side and are plain on other side.
- Yellow, round, uncoated tablets. They are flat on the top and bottom with a bevelled edge. The tablets are plain on one side and have a score line on the other side.



Case Study 2

- Hard ovoid calcium carbonate capsule, buff to coffee-coloured, containing gallinaceous DNA in a spherical jasmine to gamboge-coloured lipoprotein delivery system suspended in a clear, viscous albuminaceous support solution.



- Brown egg



Similar issue for description of packaging

Plain language descriptions of oral dosage forms - WHO guidance

M

Medicines

About Medicines Prequalification

What We Do

Documents A-Z

Prequalification Pipeline

Prequalified Lists

FPPs and APIs Eligible for Prequalification ("EOLs")

Prequalification Procedures & Fees: FPPs, APIs & QCLs

Post-prequalification Procedures & Fees: APIs, FPPs, QCLs

Prequalification Reports

Collaborative Procedures for Accelerated Registration

Guidance Documents

WHO Technical Report Series

WHO medicines prequalification guidance

International Pharmacopoeia

Pilot Prequalification of Biotherapeutic Products

Support to Manufacturers, CROs and QCLs

Risk Assessment

WHO Medicines Prequalification Guidance

Many of the [guidance documents approved by the WHO Expert Committee on Specifications for Pharmaceutical Preparations \(ECSPP\)](#) are of significant interest and value for manufacturers. But the ECSPP approval process can be lengthy. To be able to respond promptly to demands for new products or for new formulations of existing products, or to incorporate recent pharmaceutical technology developments in their manufacturing processes, manufacturers often require guidance within a much shorter timeframe.

The WHO Prequalification Team therefore works closely and intensively with pharmaceutical experts to develop guidance, as needed, and promptly. In so doing it both facilitates and eases the technical burden associated with quality medicines manufacturer, and expands the range of appropriate products for meeting treatment needs. Moreover, much of the guidance so developed — together with feedback from manufacturers and regulators — forms the basis of guidance documents submitted to ECSPP, thereby also facilitating ECSPP processes.

WHO prequalification guidance documents, application forms and templates are listed below. (Date of issue is given in brackets.) Applicants are also advised to consult [these](#) and the [guidance documents approved by ECSPP](#).

GENERAL ADVICE & PROCEDURAL GUIDANCE

ACTIVE PHARMACEUTICAL INGREDIENTS: GUIDANCE DOCUMENTS, APPLICATION FORMS & TEMPLATES

FINISHED PHARMACEUTICAL PRODUCTS: TECHNICAL GUIDANCE, APPLICATION FORMS & TEMPLATES

BIOEQUIVALENCE: GUIDANCE DOCUMENTS, APPLICATION FORMS & TEMPLATES

PRODUCT-SPECIFIC GUIDANCE, APPLICATION FORM & TEMPLATE

Information for

Manufacturers

Regulatory agencies

Quality control laboratories

Procurement agencies

Do you need assistance?

For assistance regarding prequalification please refer to the [Support to Manufacturers, CROs and QCLs](#) section of this website where we provide technical advice and information about assistance.

WHO PUBLIC ASSESSMENT REPORTS: GUIDANCE DOCUMENTS & TEMPLATES

GUIDANCE DOCUMENTS

Guidance on plain language descriptions of visual appearance for oral dosage forms in WHOPARs (10 October 2023)

Mobile Technologies – QR*code in product information

Pros	Cons

*Quick Response

Mobile Technologies – QR code in product information

- PQT/MED supports the use of mobile technologies where appropriate, provided that
 - ✓ unrestricted access to this information for users, dispensers and prescribers is ensured and
 - ✓ local regulations in each target country are considered
- Decision on acceptance of mobile technologies is with National Regulatory Authorities (NRAs)
- Review of the printed and digital product information rests with the NRAs

Special excipients – in the WHOPARs

PQT/MED refers to EMA-Excipients Guideline:

<https://www.ema.europa.eu/en/annex-european-commission-guideline-excipients-labelling-package-leaflet-medicinal-products-human>

Two exceptions

- Lactose
- Sodium

General statement

If any excipient warnings are included, the WHOPAR product information states:

“It is important to consider the contribution of excipients from all the medicines that the patient is taking.”

Use of these excipients in medicinal products may lead to:

- A restriction in the target population
- Consequences on drug safety

➔ This aspect is now being highlighted in WHOPAR part 1.

- **Avoiding such excipients with recognised undesirable action or effect in certain circumstances might confer advantage**

Example for Part 1 excipient statement

WHO Prequalification Programme WHO PUBLIC ASSESSMENT REPORT (WHOPAR)

[RefNo trade name]¹

API tablets

[RefNo trade name], manufactured at [...] was included in the WHO list of prequalified medicinal products for neglected tropical diseases on ss month yyyy.

[RefNo trade name] is indicated for treatment of [...]. Detailed information on the use of this product is described in the summary of product characteristics (SmPC), which can be found in this WHOPAR.

{RefNo trade name} {DotWP-ProductName} contains <an excipient which restricts> <excipients which restrict> its use <in affected group (e.g. children)>; see WHOPAR part 3 (section 2) and part 4 (section 4.4) for more information.

The active pharmaceutical ingredients of [RefNo trade name] is API.

[...]

Update on „SRA-WHOPARs“

Guidelines on submission of documentation for prequalification of finished pharmaceutical products approved by stringent regulatory authorities

([trs986-annex5.pdf](#))

“WHO may request additional data, when considered necessary for the use of the product in populations, settings or regions relevant for prequalified products. If necessary, this additional information, relevant for use of the product within the scope of the Prequalification Programme, will be included in the WHO public assessment report (WHOPAR) as a separate piece of information. Such information could be communicated to the reference SRA where appropriate.

The SRA-approved product information will not be changed. “

News on „SRA-WHOPARs“

However

SRA-approved product information often not reflective of WHO-recommended uses



- Therapeutic indications, e.g. complicated bacterial infections versus DR-TB
- Target populations
- Dosing regimens
- Use in pregnancy and breastfeeding

News on „SRA-WHOPARs“

Note with respect to WHO PQT/MED Recommended Product Information additional to the SRA Approved Product Information for Products Prequalified via the Abridged (SRA) Route (29 March 2023)*

“Additional information, relevant for use of the product within the scope of the Prequalification Programme ... in the WHO public assessment report (WHOPAR) as a separate piece of information”.

In accordance with this provision, for products prequalified based on SRA approval, **hyperlinks to “WHO-PQ recommended patient information leaflet” and “WHO-PQ recommended summary of product characteristics”, which are generic for the respective kind of product**, e.g. dolutegravir 50mg tablets, as applicable, will be published with the WHOPAR.”

*<http://extranet.who.int/prequal/key-resources/documents/note-respect-who-pqtmed-recommended-product-information-additional-sra>

