

health department and
procurement and logistics division



unrwa quality assurance policy for pharmaceutical products

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guiding principles

The technical requirements described in this document complement, and should be used together with, the UNRWA Standard Tender Documents for procurement of goods and services and general item descriptions as they are provided in bid documents.

1. Purpose:

The purpose of this document is to provide further general technical guidance to bidders and suppliers on the Agency's expectations of quality, safety and efficacy for pharmaceuticals and health supplies that are procured for distribution in the Agency's destination countries. This document is freely available to all bidders/suppliers when completing documents requested for bidding purposes with UNRWA.

2. Related Documents:

This Quality Assurance (QA) requirement document requires that all existing and prospective vendors complete and sign the UNRWA Product Information Questionnaire for FPP (Stringent and Non-Stringent).

3. Key Definitions:

Active pharmaceutical ingredient (API): A substance or compound intended to be used in the manufacture of a pharmaceutical product as a therapeutically active compound/ingredient.

Drug: Any substance or pharmaceutical product for human or veterinary use that is intended to modify or explore physiological systems or pathological states for the benefit of the recipient. In this document, the terms drug, medicine and pharmaceutical product are used interchangeably.

Finished pharmaceutical product: means a medicine presented in its **finished** dosage form that has undergone all stages of production, including packaging in its final container and labelling.

International Non-Proprietary Name (INN): The shortened scientific name based on the active ingredient. The World Health Organization (WHO) is responsible for assigning INNs to pharmaceutical substances.

Marketing authorization: A legal document issued by competent drug regulatory authority for the purpose of marketing or free distribution of a product after evaluation for safety, efficacy and quality.

Quality assurance (QA): QA is a wide-ranging concept covering all matters that individually or collectively influence the quality of a product. It is the totality of the arrangements made to ensure that pharmaceutical products are of the quality required for their intended use.

Quality control (QC): QC is concerned with sampling, specifications and testing, as well as with the procurement agency's documentation and acceptance/rejection procedures that ensure that the necessary and relevant tests are actually carried out and that starting materials, intermediates and finished products are not accepted for use, sale or supply until their quality has been judged to be satisfactory.

Stringent regulatory authority (SRA): means a regulatory authority. In the case of the European Union, both the European Medicines Agency (EMA) and national competent authorities are included, which is (a) a member of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), as specified on its website; (b) an ICH Observer, being the European Free Trade Association (EFTA) as represented by SwissMedic, Health Canada and World Health Organization (WHO) (as may be updated from time to time); or (c) a regulatory authority associated with an ICH member through a legally binding mutual recognition agreement including Australia, Norway, Iceland and Liechtenstein (as may be updated from time to time).

The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S): are two international instruments between countries and pharmaceutical inspection authorities, which together provide active and constructive cooperation in the field of good manufacturing practice (GMP). There are currently 46 Participating Authorities in PIC/S (<http://www.picscheme.org/>).

section 1: quality standards for finished pharmaceutical product

1. Regulatory Requirements (Table 1)

- 1.1 All Finished Pharmaceutical Products (FPPs) should have evidence of registration/marketing authorization in the country of manufacture/origin.
- 1.2 Documentation of a marketing authorization from a stringent regulatory authority (SRA), as defined by the World Health Organization (WHO) or PIC/S, must be provided. Products pre-qualified by WHO or approved by any other UN agency (UNICEF/UNFPA/UNDP/UNOPS) will also be accepted.
- 1.3 Further, FPPs that are not manufactured in an SRA/PIC/S country, but have marketing authorization in any of the SRA/PIC/S member countries can also be accepted if correct documentation is presented.
- 1.4 UNRWA will conduct minimal scrutiny for these products (refer to Section 2) during pre-qualification procedures.
- 1.5 Products that are not approved by the above-mentioned authorities (SRA/PIC/s) will have to undergo a broader scrutiny mechanism during pre-qualification by UNRWA as described in Section 2.
- 1.6 All FPPs should have a Certificate of Pharmaceutical Product (CoPP) according to the WHO Certification Scheme issued by the National Medicines Regulatory Authority and specified as per the relevant WHO Technical Report Series.

Table 1: Stringent standards for key pharmaceutical products

Vaccines	Essential Medicines
<p style="text-align: center;">WHO pre-qualified (PQ) Or Approved by UNICEF, MSF, ICRC Or SRA/PIC/S approved</p>	<p style="text-align: center;">WHO pre-qualified (PQ) Or Approved by Stringent Regulatory Authority (ICH members, observers and associates) – SRA /PIC/S Or Approved by other UN agency</p> <p style="text-align: center;">If products meeting these criteria are not available on the market: Rapid risk review by ERP Or UNRWA in-house qualification</p>

2. Confirmation of Quality Standard

<p>The vendor must confirm if their offered products fall under the standards mentioned above. The list of SRA and PIC/S member countries are given below:</p> <ul style="list-style-type: none"> • Stringent Regulatory Authority (ICH member, observers and associates) • Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, Sweden, The Netherlands, and United Kingdom, Japan and United States. • EFTA as represented by Swiss Medic, Health Canada and World Health Organization (WHO) • Australia, Norway, Iceland and Liechtenstein 	<p>PIC/S member countries:</p> <ul style="list-style-type: none"> • All SRA members, observers and associates are PIC/S members as well. • Argentina, Taiwan, Indonesia, Israel, Republic of Korea, Malaysia, New Zealand, Singapore, South Africa, Ukraine are other PIC/S member countries
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3. Identification

Each FPP must be identified by the International Non-Proprietary Name (INN) and include the following:

- 3.1 The Active Pharmaceutical Ingredient (API) base or the pro-drug compound, salt or ester, as applicable
- 3.2 The pharmaceutical dosage form
- 3.3 The amount of active ingredient in each unit dosage form; where this is given in terms of the salt, ester or pro-drug, the equivalent amount of active moiety must be specified
- 3.4 Route of administration
- 3.5 Inactive ingredients/excipients of medical and/or pharmaceutical relevance and the amount in each dosage unit

Bidders must submit the complete qualitative and quantitative composition of the FPP, including active ingredient(s) and excipients during the pre-qualification process.

4. Monograph Specifications

- 4.1 UNRWA accepts the following pharmacopoeial monographs/standards: The British Pharmacopoeia (*BP*), European Pharmacopoeia (*Ph. Eur.*), International Pharmacopoeia (*Ph. Int.*) or United States Pharmacopoeia (*USP*). Whenever used, the year of publishing of the pharmacopoeia must be specified.
- 4.2 If there is no published pharmaceutical monograph, in-house specifications and validated analytical test methods must be submitted. They must be described in sufficient detail to enable the procedures to be repeated, including biological and microbiological methods where relevant. The results of validation studies, including comments on the choice of routine tests and standards, must be submitted.
- 4.3 For all FPPs, copies of certificates of analysis must be submitted for each batch/lot supplied. General requirements for dosage forms.
- 4.4 Each FPP should comply with the general requirements for dosage forms of the relevant edition of the BP, Ph. Eur, Ph. Int or USP. At the minimum, all dosage forms must be packed:
 - 4.4.1 So as to facilitate course-of-therapy usage, unless specified otherwise.
 - 4.4.2 Together with dose measurement and delivery devices as applicable.
 - 4.4.3 In tamper-evident packaging.
 - 4.4.4 In rigid paperboard boxes, strong enough to resist crushing during transportation and storage.

5. Packaging

- 5.1 A primary package is that which is in direct contact with the dosage form.
- 5.2 A secondary package is not directly in contact with the dosage form. All packaging must be designed so as to protect the dosage form and to render it suitable for the intended use throughout the stated shelf life.
 - 5.2.1 Materials used for packaging must conform to the relevant edition of the *BP*, *USP*, *Ph. Eur* or *Ph. Int* with reference to the specific Active Pharmaceutical Ingredient (API) and dosage form; must be safe for use with the dosage form for the intended route of administration; and be suitable for shipment, storage and worldwide use at extreme temperatures and humidity for ICH Zone II (Subtropical and Mediterranean climate) and Zone III (Hot Dry zone).

- 5.2.2 Packaging must facilitate the distribution to the lowest-level health facilities as well as dispensing to individual patients and their subsequent adherence. Product packaging that facilitates patient adherence is encouraged.
- 5.2.3 The size of the container should be proportional to its contents with the addition of appropriate padding to prevent damage to the product during shipment.
- 5.2.4 Glass containers will not be accepted above a maximum of 250 ml except with prior approval of UNRWA. Glass bottles must be packed individually in cartons.
- 5.2.5 For glass ampoules, single ended, break-off necks are required.

6. Labels

6.1 Label language

All FPP for distribution by must be labelled in the English language with option of Arabic as a secondary language for the secondary packaging materials and inserts. If more than one language is used, the overall readability should not be adversely affected. It is recommended to group different text elements for each language, where appropriate.

6.2 Labelling type

Preferably by lithography direct on container/packaging. Self-adhesive labels should use pharmaceutical defiberized paper (80g/kvm) that is film or UV coated for protection against humidity and be firmly affixed to be tamper-proof and to prevent detachment in Zone II and III.

6.3 Ink/colour

The writing on primary and secondary packs must be in indelible ink, preferably in black on white.

7. Particulars to be Included on the Label

7.1 Outer packaging or, where there is no outer packaging, on the immediate packaging. The label should include at least the following:

- 7.1.1 The International Non-Proprietary Name (INN) or generic name of the FPP, in a bold, clearly visible font size and must not be abbreviated anywhere, including on labels and package inserts.
- 7.1.2 Amount of each Active Pharmaceutical Ingredient present in a dosage unit, unit of volume or unit of weight.

- 7.1.3 Pharmaceutical dosage form and contents of the container, e.g. number of dosage units, weight or volume
- 7.1.4 The pharmacopoeial standard of the FPP and, where not available, as with innovator products, the source of the reference standard must be available on request.
- 7.1.5 Batch number assigned by the manufacturer
- 7.1.6 The manufacturing date in a format that can be easily understood. The recommended format is DD/MM/YYYY. The year of manufacture must be in four digits.
- 7.1.7 The expiry date in a format that can be easily understood. The recommended format is DD/MM/YYYY. The year of expiry must be in four digits.
- 7.1.8 List of excipients known to be a safety concern for some patients, e.g. lactose, gluten, meta-bisulfites, parabens, ethanol or tartrazine. For parenterals and topical preparations, all excipients should be listed.
- 7.1.9 The word 'sterile' if the product is sterile
- 7.1.10 Method and route(s) of administration and the statement, '*Read the patient information leaflet before use.*'
- 7.1.11 Advice on general classification for distribution, e.g., Controlled Medicines, Prescription-Only Medicines, Pharmacy-Only Medicines, Over-the-Counter and General Sales List
- 7.1.12 Special warning that the medicinal product must be stored out of the reach and sight of children ('*Keep out of the reach and sight of children*').
- 7.1.13 Other special warnings and handling precautions, if necessary (e.g. in case of specific toxicity of the agents)
- 7.1.14 Instruction on use
- 7.1.15 Storage conditions and special storage conditions, if applicable
- 7.1.16 Name and address of manufacturer and marketing authorization holder. For contract manufacture, indicate as: manufactured by company X for company Y.
- 7.1.17 Special label of '*For UNRWA Use - Not for Sale*' on the primary packaging, either by stamping or laser print

7.2 Secondary containers must have the following labels:

- 7.2.1 All information on the primary container plus the following:
- 7.2.2 Special precautions for disposal of unused medicinal products or waste material derived from such medicinal products, if appropriate
- 7.2.3 Pharmaceutical dosage form and contents of the container, e.g. number of dosage units, weight or volume
- 7.2.4 Instruction on stacking

7.3 Guidance for small containers

For containers of less than or equal to 10 ml capacity that are marketed in an outer pack such as a carton, and the outer pack bears all the required information, the immediate container should contain at least the following information (added):

- 7.3.1 INN name, strength, pharmaceutical form, active substance(s) and route(s) of administration
- 7.3.2 Method of administration
- 7.3.3 Batch number assigned by the manufacturer
- 7.3.4 Expiry date in a format that can be easily understood. The recommended format is DD/MM/YYYY. The year of expiry must be in four digits.
- 7.3.5 Manufacturing date if space is sufficient
- 7.3.6 Contents by weight, by volume or by unit
- 7.3.7 The name and address of the manufacturing site or a logo that unambiguously identifies the company.
- 7.3.8 Directions for use and any warnings or precautions that may be necessary
- 7.3.9 Storage conditions

7.4 Guidance for blisters and strips

Blisters and strips should include, as a minimum, the following information (printed directly):

- 7.4.1 Name, strength and pharmaceutical form of the FPP
- 7.4.2 Name and physical address of the manufacturing site (the site responsible for release of the finished product)

- 7.4.3 The batch number assigned by the manufacturer
- 7.4.4 The expiry date [Note that for co-blistered products, the expiry date is that of the product which expires first.]
- 7.4.5 The manufacturing date, if space is enough
- 7.4.6 Directions for use and any warnings or precautions that may be necessary.

This desired label format is expected at the time of supply, subject to acceptable variations according to each order. The bidder is expected to confirm that they are able to do such labelling, should their samples submitted for technical evaluation be different.

8. Guidance on Information Leaflet

All products must be accompanied by package inserts/patient information, leaflets, and summary information about the product as per the underlying pharmacopeia standards. The leaflet should be available in English and Arabic.

9. Shelf-Life and Stability

The following shall apply at all times without exception:

- 9.1 Document for shelf-life: the supplier to guarantee remaining shelf life at 75 per cent at time of arrival in the country of destination (85 per cent is preferable).
- 9.2 Product should be suitable for use in *Zone II: Subtropical and Mediterranean* *Zone III: Hot Dry Climate*. UNRWA may request proof of stability in this zone in form of either real-time or accelerated stability studies.

section 2: pharmaceutical product pre-qualification

1. Pre-Qualification Standards Used

Products pre-qualified by other UN agencies or approved by SRA or PIC/S member country: UNRWA recognizes all products registered by a SRA and/or PIC/S member country and all products already pre-qualified by a UN agency under Long-Term Agreement (LTA). In such cases, the following applies to the pre-qualification:

- 1.1 Suppliers need to submit the 'UNRWA Finished Pharmaceutical Product Information Questionnaire (for SRA/PIC/S/UN approved products)'
- 1.2 Vendor is required to submit completed documentary evidence of pre-qualification with the relevant UN agency or SRA or PIC/S approval certificate indicating clearly the period of validity of such pre-qualification
- 1.3 UNRWA will conduct a due diligence check to confirm the pre-qualification/approval status

2. Products without Pre-Qualification

Products which are 'not' pre-qualified by any UN agency or are not approved by any SRA or PIC/S member country: UNRWA will conduct a broader scrutiny for all these products. The steps for prequalification are as follows:

- 2.1 Submission of Product Information Questionnaire (non-stringent) for assessment by UNRWA. The suppliers should submit the 'UNRWA Finished Pharmaceutical Product Questionnaire' along with the necessary supporting documents and a sample for quality testing. The major evaluation points in the questionnaire are:
 - 2.1.1 Formulation of the product (complete qualitative and quantitative composition including active ingredient(s) and excipients)
 - 2.1.2 GMP certificate of FPP manufacturing site – issued by the Drug Regulatory Authority of the manufacturing country
 - 2.1.3 Certificate of Pharmaceutical Product (CPP) according to the WHO Certification Scheme
 - 2.1.4 Copy of the certificate of analysis for the last three batches released
 - 2.1.5 Validated analytical methods if specifications for finished product are in-house specifications, different from BP, USP and Ph. Int.

- 2.1.6 Protocol and report for accelerated and real-time stability testing
- 2.1.7 Sample of the finished product(s) offered
- 2.1.8 Packaging and label artwork
- 2.1.9 Package insert/Patient Information Leaflet
- 2.1.10 GMP certificate(s) of API manufacturing site – issued by the Drug Regulatory Authority of the manufacturing country
- 2.1.11 Validated analytical methods in case of in-house API specifications
- 2.1.12 Copy of the certificate(s) of analysis of the API from the API manufacturer, as well as from the FPP manufacturer
- 2.1.13 Evidence of product registration or marketing authorization in country of manufacture/origin
- 2.1.14 List of other countries where the product is registered, giving license number, and registration date and validity period
- 2.1.15 Copy of internal finished product specifications



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