

Technical Requirements for Pharmaceutical and Nutrition Products

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Table of Contents

Abbreviations & Acronyms	1
Glossary	2
Background	5
1. General requirements	7
1.1 Product identification	7
1.1.1 Biologicals	8
1.1.2 Packaging	9
1.2 Regulatory Compliance.....	9
1.2.1 Regulatory (Licensing) status.....	9
1.2.2 Pharmacopoeial standards	9
1.2.3 Analytical methods-In house methods.....	10
2. Active pharmaceutical ingredients (s), intermediates and excipients	11
2.1 Active Pharmaceutical Ingredients.....	12
2.1.1 Active Pharmaceutical Ingredient comparability across multiple sources	14
2.2 Excipients.....	15
2.3 Nitrosamines.....	15
3. Finished Pharmaceutical Product (FPP).....	17
3.1 General requirements for dosage forms.....	17
3.2 Manufacturing site(s) GMDP status	17
3.2.1 Contract manufacturing.....	18
3.2.2 Inspection.....	18
3.3 Manufacturing process and process validation.....	19
3.3.1 Batch formula	20
3.4 Specifications of Finished Pharmaceutical Product (FPP).....	21
3.4.1 Analytical procedures used for testing the FPP and their validation	21

3.4.2 Certificates of Analysis	22
3.5 Stability	23
3.5.1 Shelf-life and storage requirements	27
3.5.2 Stability requirements when considering long shipment of intermediates	28
3.6 Container-closure systems.....	29
3.6.1 Primary Packaging.....	30
3.6.2 Secondary packaging	31
3.7 Labels.....	33
3.7.1 Minimum Labelling Requirements.....	34
3.7.2 Summary of product characteristics, pack inserts/patient information leaflets.....	37
3.8 Safety, efficacy and/or therapeutic equivalence.....	38
3.9 Suitability of invented/brand names or registered trade names	40
3.10 Samples	40
3.11 Track and Trace	41
3.12 Transport and transit storage requirements.....	41
3.13 Reporting of Complaints/Adverse events	44
3.14 Emergencies.....	44
3.15 Periodic Safety Update Reports	45
4. Sustainability	46
5. COMMITMENT	48
Appendix 1: Technical Instructions, Questionnaires and Annexes.....	49
Appendix 2: UNICEF'S Supplier Qualification Process Diagram	52
References	54

Abbreviations & Acronyms

CoA: Certificate of Analysis

CoPP: Certificate of Pharmaceutical Product. Also referred to as CPP

ICH: International council for Harmonization of Technical Requirements for Pharmaceuticals for human use.

LTA: Long-term Agreement

PO: Purchase order

MQAS: WHO's Model Quality Assurance Scheme

RFP: Request for Proposal

RFQ: Request for Quotation

RFP: US FDAs Reference listed product. Also referred to by WHO as comparator product.

SO: Sales Order

UNGM: United Nations Global Marketplace

WHO: World Health Organization

WHO PQ: World Health Organization prequalification

WLA: WHO Listed Authority

SRA: Stringent Regulatory Authority

Glossary

API supplier qualification is a formal: is a risk-based approach to assess, approve, and monitor suppliers, ensuring they meet current good manufacturing practices (cGMP), regulatory, and quality standards for pharmaceutical ingredients. It encompasses technical audits, document review, and performance monitoring to ensure compliance.

Biopharmaceutical Classification System (BCS): A scientific framework for classifying active pharmaceutical ingredients (APIs) regarding their solubility (in physiologically relevant medium) and permeability across the intestinal mucosa.

Comparator: A product which is proposed for use in a bioequivalence study for the purpose of proving therapeutic equivalence and therefore product interchangeability. A comparator product is normally the innovator product (Whenever the innovator product is not available, it is advisable to follow the WHO criteria for “comparator” as applicable at the time e.g. WHO Technical report series No. 992, annex 8 (2015). The US FDA refers this as “Reference listed Product”.

Drug substance: The active moiety in a pharmaceutical dosage form e.g. active pharmaceutical ingredient or biological substance.

Dosage form: The form of a completed pharmaceutical product e.g. tablets.

Drug product: A completed pharmaceutical product i.e., a dosage form in its final packaging. Also referred to as finished pharmaceutical product.

Good Manufacturing practice (GMP): is a system for ensuring that the products are consistently produced and controlled to quality standards.

Good Storage/Distribution Practices: refers to the part of quality assurance that ensures that the quality of medical products is maintained by means of adequate control throughout the storage thereof and throughout the numerous activities which occur during the distribution process.

Interchangeable product: A pharmaceutical product that is therapeutically equivalent to a comparator product and thus can be used in place of a comparator product in clinical use.

Innovator Pharmaceutical Product: Generally, the first authorized for marketing with complete documentation for Quality, safety and efficacy as New Chemical Product or New Biological product.

Multisource (generic) finished pharmaceutical products (FPPs): Pharmaceutically equivalent or alternative products that may be (or not) therapeutically equivalent.

National Medicines Regulatory Authority (NMRA): the official regulatory authority of a country designated to administer the regulatory activities related to Medicines. This term is interchangeable with NRA i.e. National Regulatory Authority.

Pharmaceutical defibred paper (80gsm): a high-performance, medical-grade material used primarily for pharmaceutical leaflets and sterile packaging.

Pharmaceutical Inspection Cooperation (PIC/S): is a group to improve co-operation in good manufacturing practices between regulatory authorities performing GMP inspections.

Pharmacopoeial Standards: Refers to claimed quality standard with relation to an active pharmaceutical ingredient, finished pharmaceutical product or an excipient.

Regional regulatory system (RRS): means a system comprised of individual regulatory authorities, or a regional grouping composed of individual regulatory authorities, operating under a common regulatory framework including harmonized procedures and including or excluding a common legal framework. The common regulatory framework must at least ensure convergence between the members in terms of regulatory requirements, practices, and quality assurance policies.

Specifications: Is a quality standard to which a drug substance or drug product should conform to be considered acceptable and normally includes a list of tests, references to pharmacopoeial or inhouse standards, analytical procedures and appropriate acceptance criteria.

Stringent Regulatory Authority (SRA): means a regulatory authority which was, prior to 23 October 2015:

(a) a member of the ICH; or

(b) an ICH Observer, being the European Free Trade Association (EFTA) as represented by Swiss Medic and Health Canada; 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).

Therapeutic equivalence: Pharmaceutically equivalent or pharmaceutical alternative products are two products which upon administration in the same molar dose, to the same study subjects or patients and in line with label instructions, demonstrate the same efficacy and safety.

Variation herein considered a post LTA change: is a post approval amendment that details the proposed change(s) to information appertaining to approved documentation for the purpose of updating the details of the approved Long-term Agreement.

WHO Emergency Use Listing (EUL): means WHO's risk-based procedure for assessing and listing unlicensed vaccines, therapeutics, and in vitro diagnostics with the aim of expediting the availability of these products to people affected by a public health emergency.

WHO Listed Authority (WLA): means a regulatory authority or a Regional regulatory system which has been listed by WHO to comply with all the relevant Global Benchmarking tool indicators and performance requirements specified by WHO for the requested scope of listing based on an established benchmarking and performance evaluation process¹.

WHO normative standards and guidelines: Means guidance (on specific thematic area) based on sound scientific evidence and developed by global experts to address needs by WHO's member states or other stakeholders in developing public health policies or practices.

WHO Prequalification means the programme managed by WHO which prequalifies (a) medicines that are acceptable for procurement by the United Nations and specialized agencies; and (b) quality control laboratories for medicines.

¹ [List of WHO Listed Authorities WLAs](#)

Background

UNICEF aims to ensure timely and affordable access to safe, effective, quality medicines and nutrition products in both development and humanitarian contexts. UNICEF's product portfolio is designed to meet global demand while also addressing specific needs of countries and partners. The [UNICEF Supply Catalogue](#) lists the standard range of products available for routine procurement, while additional non-standard products may be sourced on behalf of governments, UN agencies, non-governmental organizations, philanthropic foundations, and academic institutions.

UNICEF procures and supplies products that have undergone quality assessment and are found acceptable by UNICEF or other entities recognized by UNICEF. UNICEF procures directly from manufacturers; procurement from wholesalers occurs only in exceptional circumstances. UNICEF Quality management system is comprehensive from the assessment of individual risks related to specific products and starting materials. This guidance implements the principles for pre-qualifying and approving pharmaceutical suppliers and products as established in the WHO Model Quality Assurance System (MQAS) for Procurement Agencies (*WHO Technical Report Series No. 986*).

In principle, UNICEF products are aligned with WHO normative standards and guidelines and designed to facilitate rational use to the lowest level of health care service delivery. The latest *WHO Model List of Essential Medicines (EML)* and disease specific treatment guidelines inform UNICEF product selection.

This document and all other related information for pharmaceuticals and nutrition products, including questionnaires, can be accessed at [Questionnaires and requirements for pharmaceutical and nutrition products | UNICEF Supply Division](#)

The nutrition products in this document refer to all parenteral nutrition products designed to prevent and/or treat nutrient deficiencies, manufactured according to standards for pharmaceutical finished products.

This Technical Requirements document provides further explanations for what is described in the most recent version of the IAFPPQ. It captures specifications and requirements that apply in general to every pharmaceutical product or dosage form. Specifications unique to a product are elaborated in each solicitation activity, Long-term Arrangement Contract (LTA) and Purchase Order (PO). Vendors are reminded to pay close attention to both unique

specifications for each product and the general requirements in this document as they complement each other.

As a default, information required for product assessment is submitted by the bidder (manufacturer, wholesaler, distributor, marketing license holder) through the **Interagency Finished Pharmaceutical Product Questionnaire (IAFPPQ)** [Interagency finished pharmaceutical product questionnaire | UNICEF Supply Division](#) which is based on the *WHO Technical Report Series No. 986, 2024 – Appendix 6: WHO Model quality assurance system for procurement agencies*.

Manufacturer's GMP related information is collected through the **UNICEF Technical Questionnaire for Pharmaceutical Manufacturers** [Technical questionnaire for pharmaceutical manufacturers | UNICEF Supply Division](#). Additionally, wholesalers/distributors should fill in the **UNICEF Technical Questionnaire for Pharmaceutical Wholesalers**.

This document is intended to help suppliers, primarily manufacturers of finished pharmaceutical products (FPP), participating in UNICEF tenders. Adequately prepared technical documentation/product dossier for a tender facilitates the process and saves time and effort on both sides. Vendors are encouraged to carefully read this document and all documents referred to in the text and seek clarification in advance of any solicitation/tender process.

All the documentation should be submitted to the online document repository. If at time of submission an Annex (for product or site or other documents) to be uploaded is not available, please mention the specific reason for the same on a word /pdf file and upload the same with respective Annex name, e.g. Not Applicable or Will submit the document later (by XXXX date) or Document cannot be provided or NOT available or any other reason as applicable. Bidders may be required to submit a full copy of the most recent inspection report by the National Regulatory Authority or other agencies as listed in the IAFPPQ.

For clear comprehension of the expected compliance with the requirements laid in this document, the following verbal forms are used:

- "must" or "shall" indicates a requirement.
- "should" indicates a recommendation.
- "can" or "may" indicates a possibility.

1. General requirements

1.1 Product identification

These requirements are to be included under section 1.1 of the IAFPPQ.

Each Finished pharmaceutical product (FPP) must be fully identified as stipulated in the most current version of the Interagency Finished Pharmaceutical Product Questionnaire (IAFPPQ) Annex 2c or Technical offer form Annex 2f the following additional explanations:

1. Each **Finished Pharmaceutical Product** (FPP) should be identified by its International Non-proprietary Name(s) (INN). Additionally, other generic name(s) such as British Approved Name(s) (BAN) should be stated if different from INN and relevant to the submission.
2. The **Active Pharmaceutical Ingredient(s)** (API) should be fully identified by their INN along with their pharmacopeial monograph reference and chemical form such as base, salt, ester or pro-drug compound as applicable.
3. Bidders should include relevant pharmaceutical **dosage form and dosage form attributes** e.g., if tablets are functionally scored “evidenced through dose divisibility studies”, dispersible, enteric coated, bi-layered, film coated, sugar coated, what release mechanism the product has (immediate or modified).
4. The **strength per dosage unit** or the amount of active ingredient per dosage unit must be specified. Where this is given in terms of salt, ester or pro-drug, the equivalent amount of active moiety must be specified. For further guidance refer to *WHO Technical Report Series No. 957, 2010 - WHO Expert committee on specifications for pharmaceutical preparations, chapter 11. Miscellaneous, page 62.*
5. The **route of administration** must be specified e.g., oral, IM, IV, SC, topical, rectal.
6. In addition to a **batch formula** that should be provided, certain excipients known to have some action or effect should be specified qualitatively and quantitatively in the labels, patient information leaflets and section 2 of the Summary of Product characteristics (SmPC) – Qualitative and quantitative composition. *See excipients included in the European Medicines Agency guideline Annex to the European Commission guideline on ‘Excipients in the labelling and package leaflet of medicinal products for human use.’* However, if the FPP is parenteral, topical, ophthalmological or if used for inhalation, all excipients must be stated. The FPP manufacturers should ensure that during audits of excipients’ manufacturers involved in production, control, storage and distribution of excipients for pharmaceutical use have

established, document, implement and maintain a comprehensively designed and clearly defined quality management system².

7. State whether a product is a fixed-dose combination (FDC) (co-pack or co-formulated as two or more active components in fixed proportions in a single dosage form).

Regarding drug-device combinations, please refer to primarily EU's Medicinal Products Framework (refer to [Medical Device Regulation \(EU\) 2017/745 \(MDR\)](#)). Key guidance includes the [Guideline on quality documentation for medicinal products when used with a medical device](#), which requires detailed documentation on device quality, safety, and performance for both integral (e.g., pre-filled pens) and non-integral (e.g., co-packaged needles) devices

1.1.1 Biologicals

The requirements are to be addressed under *Annex 2h Interagency finished pharmaceutical product questionnaire for BTPs and SBPs*

Biological therapeutics (Biologicals) and biosimilars are quite different in their nature and how they are produced, regulated, tested, and controlled than other medicines. Small molecule biological products are assessed by UNICEF or by WHO through WHO ERP process upon submission of IAFPPQ for biologicals. For large biological molecules, because of their complexity, currently UNICEF accepts only products registered by SRA/WLA or those that are WHO Prequalified.

² WHO Technical report Series No 1060 of 2025, Annex 3 WHO good manufacturing practices for excipients used in pharmaceutical products

1.1.2 Packaging

For details on packaging refer to 3.6 Container-closure systems

1.2 Regulatory Compliance

1.2.1 Regulatory (Licensing) status

The requirements are to be addressed under section 1.6 of the IAFPPQ and supporting documents must be submitted in *Annex D* and *E*.

Evidence should be provided for all Finished Pharmaceutical Products that the product(s) is/are registered/licensed and marketed in the country of manufacture/origin. In exceptional circumstances, UNICEF may consider for assessment products registered for EXPORT ONLY. For EXPORT ONLY pharmaceuticals are products approved only exclusively for supply outside the country of manufacture "Country of origin".

Bidders must provide a list of all countries where the product is registered, together with the registration reference numbers, registration date and registration validity period.

Bidders must submit a Certificate of Pharmaceutical Product (CoPP or CPP) for each FPP (can be for any country) according to the WHO Certification Scheme, or an equivalent, issued by the NRA in the country of manufacture/origin. *Recommended CPP format is specified in the relevant WHO Technical Report Series 863, 1996 – Annex 10: Guidelines for implementation of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce, page 163 (earlier versions not acceptable)*. Note that this is for assessment purposes only. Specific country CPPs may be required and requested during the procurement process.

1.2.2 Pharmacopoeial standards

The following requirements concern sections 2 and 3 of the IAFPPQ.

UNICEF accepts the following pharmacopoeias with reference to specifications, qualitative and quantitative composition, quality standards, identification, and compliance test methods for APIs, FPPs and excipients.

1. British Pharmacopoeia (BP);
2. European Pharmacopoeia (Ph.Eur.);
3. International Pharmacopoeia (Ph.Int.);
4. Japanese Pharmacopoeia (JP);
5. United States Pharmacopoeia (USP);

Whenever referenced, the specific edition and year of publishing must be stated.

In general, Ph. Eur. does not include FPP monographs. Any references to the European pharmacopoeia must be clarified.

Each FPP should comply with the specific monograph (if it exists) and the general requirements for dosage forms in pharmacopoeial reference. Where a monograph exists in any of the acceptable pharmacopoeia, the bidder should follow the monograph methods. The suitability of Pharmacopoeia methods should be verified under actual conditions of use for the specified API or FPP and the results of verification studies must be submitted.

The control of degradation products should be clearly defined in the control of the FPP quality.

It should be noted that reference to any other pharmacopoeial standard shall be reviewed as inhouse standard.

1.2.3 Analytical methods-In house methods

The following requirements concern sections 2.1 and 3.2 of the IAFPPQ and supporting documents must be submitted in *Annex M and T*.

Where an official acceptable monograph exists, the use of in-house methods is discouraged.

In-house methods are not acceptable, except:

- a) Where no official monograph exists in the acceptable pharmacopoeias listed above. Reference to other pharmacopoeia not listed above shall be treated as in-house.

- b) In instances where the method can be demonstrated to depend largely on the product as formulated by the manufacturer, even when a monograph exists in any of the acceptable pharmacopoeia above, an inhouse method would be acceptable. For example, dissolution method, including dissolution test acceptance limits. In all cases, where a monograph exists in any of the above listed pharmacopoeia, the use of in-house specifications and methods MUST be accompanied by a suitable scientific justification, explanation, together with a table comparing pharmacopoeial monograph and in-house methods side by side. Such justifications could include but not limited to, the inhouse method could be superior to the pharmacopeial standard method, for instance. in terms of specificity and sensitivity, sustainability (e.g. short run times and less use of organic solvents).

Generally, any in-house method/specification should not be inferior to the official monographs in the acceptable Pharmacopoeia.

All in-house specifications and methods must be described in sufficient detail to enable all procedures to be repeated, including biological and microbiological analysis where relevant. The results of validation studies, including comments on the choice of routine tests and standards, must be submitted too.

When referencing Pharmacopoeia, all tests included in the product specification should comply with the claimed Pharmacopoeial standards, e.g. BP or BP and USP. For example, as per BP, *"a drug product to be compliant with a BP monograph: 1. The monograph that was in force at the date of product manufacture should be applied, 2. All ingredients (drug substances and excipients) that are used to make the product should comply with the published BP or Ph.Eur. monograph for those substances, 3. The product should comply with the relevant general monographs, 4. The product should comply with the requirements of the monograph for the formulated preparation"*.

2. Active pharmaceutical ingredients (s), intermediates and excipients

APIs and excipients should comply with the current requirements of the acceptable Pharmacopoeia listed above. API specification from FPP manufacturers, Certificates of Analysis (CoAs) from API and FPP manufacturers should be submitted. If not described in a pharmacopoeia, or manufacturer has additional specifications to those in the pharmacopoeia, a copy of the manufacturer's specification, the certificate of analysis and a

description of the analytical methods with limits for results and analytical validation data must be submitted.

Special attention should be given to pharmaceutical products that have raw materials and/or excipients derived from animal sources (e.g., gelatine). If used, BSE-Free Certificate (BSE - Bovine Spongiform Encephalopathy) should be provided. A BSE-Free Certificate declares that the product does not contain any prohibited materials and that the manufacturing process and packaging are equally free of contaminationⁱ. Halal certification should be provided, where available.

2.1 Active Pharmaceutical Ingredients

The following requirements concern sections 2.1, 2.2, 2.4, and 2.5 of the IAFPPQ. Additionally, *Annexes N, O, P and Q* of the IAFPPQ

1. **Active Pharmaceutical Ingredient specification(s):** must include the chemical form (INN), reference standard (Pharmacopoeial and/or In-house), all critical tests and test acceptance for description, identification, assay, control of purity, physical and chemical characteristics. Biological substances shall follow similar requirements. Active pharmaceutical Ingredient specification(s) from the finished product manufacturer must be submitted in *Annex L*.
2. **Analytical testing validation data:** If analytical methods are in-house, the detailed method and the validation report must be submitted as *Annex M*. Please refer to section 1.3 of this document for additional guidance.
3. **Manufacturing site(s) and processes:** All manufacturing sites involved in the production of the active pharmaceutical ingredient must be listed, and each stage of the process—from starting materials to the final active substance (e.g., biological production, extraction, purification, and intermediates) must be described (in DMF) when using non accredited API source.
4. **GMP compliance and certification:** Last GMP audit conducted by SRA, NRA, PIC/S or other competent authorities must be indicated and the cGMP certificate issued by the SRA/NRA must be submitted as *Annex K* of the *IAFPPQ*.

Exceptionally, GMP certificate issued by an accredited third-party auditor or auditing body may be considered, subject to strong justification as to why a GMP certificate from an SRA, NRA, or other competent authority cannot be provided. Additionally, in such cases it is recommended that finished product manufacturers conduct

comprehensive on-site audit(s) in accordance with their own documented supplier-evaluation procedure.

5. **Certificates of Analysis (CoA):** A copy of the most recent CoA from the active ingredient manufacturer as well as the product manufacturer must be submitted in *Annex Q* of the IAFPPQ. The CoA must clearly indicate the laboratory address and accreditation.
6. For the Active Pharmaceutical Ingredient(s) it should be clear which base, salt, ester or pro-drug compound was used and the information should be consistent throughout the documents submitted. Special attention should be given to **isomerism and polymorphism**, and it should be clearly indicated which form is used and documents/tests should demonstrate justification for use of the certain form. Use of the same API from different manufacturers should be supported with documents demonstrating that APIs from different manufacturers have the same characteristics.
7. For **sterile API(s)** the data on validation of the sterile aspects including recent media fill validation data and method and description of sterilization used should be submitted. Sterile API(s) should have a Certificate of Suitability (CEP) or SRA/WLA approval or WHO Prequalified. Non-sterile APIs, it is preferred to have CEP or SRA/WLA approval or WHO Prequalified.
8. Where there is no **CEP, SRA/WLA approval or WHO Prequalified APIs**, bidder shall submit the **Open part of the drug master file (DMF) for the API**, registered in the country of origin. As characteristics of API/s are especially important for the quality and safety of the FPP, UNICEF may request more information about the APIs that could be found in the DMF, like API stability, use of potentially hazardous solvents and reagents in the manufacture of API (documents about those should be submitted if DMF is not available).
9. UNICEF requires FPP manufacturers to appropriately qualify their API suppliers, including API manufacturing site(s) audits for GMP, and to submit a declaration confirming API supplier's qualification. An **API declaration form (annex 2e)** should be duly filled in, signed by the FPP Qualified Person (QP)³ and submitted together with the IAFPPQ Annex 2C any time a new API source is introduced/changed.

³ A qualified person as defined by European Commission Directives OR Equivalent

10. All **API manufacturing processes and sites** should be identified/specified: manufacture of active substance by chemical synthesis, extraction of active substance from natural sources, manufacture of active substance using biological processes, intermediates. If necessary, a flow-chart should be provided to illustrate the role of all the different sites involved.
11. In case of several API suppliers, **equivalency information** should be provided in comparative tabular format e.g. showing the particle size distribution (for polymorphic APIs of BCS class II & IV) and method of synthesis.

Refer to:

WHO Technical Report Series No. 957, 2010 – Annex 2: WHO good manufacturing practices for active pharmaceutical ingredients (bulk drug substances)

WHO Technical Report Series No. 885, 1999 – Annex 5: WHO good manufacturing practices for the manufacture of pharmaceutical excipients

2.1.1 Active Pharmaceutical Ingredient comparability across multiple sources

The following requirements concern section 2.5 of the IAFPPQ and the supporting documents must be submitted in *Annex R*.

In the case of introducing a new API source that is not supported by data already submitted, manufacturers should provide a document, as a minimum proof, showing that the new API can replace the old one. For example, provide a table showing comparability of both methods of synthesis, particle size, etc. In addition, a minimum of 6 months accelerated stability data and 12 months long-term stability data for FPP with the new API source is required. Less stability data with a commitment of ongoing stability data of FPP with the new API source may be acceptable in certain circumstances. Introduction of new API source or change of pre-approved API source is considered a major variation and should not be initiated in relation to specific purchase orders.

Regarding API, due attention should be given to impurities and residual solvents that can affect the safety of FPP. Organic impurities as well as solvents, reagents, and catalysts may pose a risk. The control of degradation products should be clearly defined in the control of the FPP quality.

Manufacturers should prioritize quality risk assessment for APIs and FPPs based on factors such as API polymorphism, isomerism, biopharmaceutical classification, therapeutic index, maximum daily dose, and duration of treatment.

2.2 Excipients

Excipients known to have a recognized action or effect, so-called “excipients of concern,” should be avoided whenever possible, especially in products for children. UNICEF does not recommend the use of preservatives in FPPs unless justified. Sterile single use parenteral products that can undergo terminal sterilization must not contain preservatives. Evidence must be provided that any colouring agents, taste masking and flavouring agents and coating excipients are required and are not interacting with the actives. Use of sugars should be carefully thought through because of the limitations and possible complications they can cause for some patient groups. The EU guideline (Annex Sante 2017-11688)ⁱⁱ lists excipients with safety related issues as label warning. Refer to Annex to the European Commission guideline on ‘Excipients in the labelling and package leaflet of medicinal products for human use’ (SANTE-2017-11668). Certificates of Analysis/es (CoAs) for novel excipients and polyethylene glycol demonstrating control of diethylene glycol/ethylene glycol should be submitted.

Refer to WHO TRS 1060 Annex 3 WHO good manufacturing practices for excipients used in pharmaceutical products

The following documents must be submitted:

1. Specification with pharmacopeial standard referenced
2. Certificate of Analysis(s) for all excipients
3. Material Safety Data Sheet (MSDS), for novel excipients

2.3 Nitrosamines

The requirements concern *Annex Y* (Risk assessment on Nitrosamines) of IAFPPQ.

In order to ensure that the medicines are of good quality, efficacy and safety, the suppliers through the marketing authorization holders and manufacturers are requested to provide risk assessment reports regarding nitrosamines including control of nitrosamines, in line with ICH M7(R2) for assessing DNA-reactive impurities (for mutagenic nitrosamines) or ICH

Q3A (R2) and ICH Q3B (R2) for non-mutagenic nitrosamines in drug substances and finished pharmaceutical products, respectively.

Risk assessment and appropriate actions should be undertaken to reduce or prevent the **presence of nitrosamine impurities in APIs, excipients and FPPsⁱⁱⁱ**. The acceptance limits should be set in line with ICH M7 (R2), ICHQ6A (R2) or official monograph requirements.

Please see:

- *FDA, 2020 – Control of Nitrosamine Impurities in Human Drugs*
- *ICH Q9 Quality risk management “Current revision”*
- *Nitrosamine impurities: guidance for marketing authorisation holders | European Medicines Agency (EMA)*
- *Information about Nitrosamine Impurities in Medications | FDA*
- *US FDA September 2024 Pharmaceutical Quality/ Manufacturing Standards (CGMP) Revision 2; Control of Nitrosamine Impurities in Human Drugs Guidance for Industry.*
- *ICH 2023: ICH M7 Assessment and control of DNA reactive (mutagenic) impurities in pharmaceuticals to limit potential carcinogenic risk - Scientific guideline*
- *WHO TRS 1060 Annex 2 WHO good practice considerations for the prevention and control of nitrosamines in pharmaceutical products*

3. Finished Pharmaceutical Product (FPP)

The following requirements concern section 3 of the IAFPPQ.

3.1 General requirements for dosage forms

At the minimum, all dosage forms must be packed:

- To facilitate course-of-therapy usage, unless specified otherwise.
- Together with dose measurement and delivery devices, as applicable (for oral liquids).
- In tamper-evident packaging.
- In functional secondary/tertiary packaging strong enough to resist crushing and damage during transportation and storage. For more information about the packaging, refer to chapter 3.6 Container-closure systems. Appropriate Patient Information Leaflet (PIL)/Instructions for the user or equivalent.

3.2 Manufacturing site(s) GMDP status

The following requirements concern section 3.1 and annex S of the IAFPPQ.

The manufacturing site(s) including contracted sites, where any aspect of manufacture occurs, must be fully stated. This includes production, packaging, quality control, wholesaling, and distribution. All manufacturing sites, including contract sites and any changes in manufacturing site(s) at any time during the validity period of a Long-Term Arrangement must be approved by UNICEF.

Both APIs and FPPs must be manufactured as per the current Good Manufacturing Practice (GMP)^v and distributed as per the current Good Distribution Practice (GDP) guidelines and any related current guidelines established by WHO^{vi}. The bidder must submit a copy of the valid GMP certificates for the sites where the API(s), intermediates (as applicable) and FPP dosage forms are manufactured, as issued by the relevant authorities in the country of manufacture/origin and (where applicable) foreign regulatory authorities, such as, WLAs or Pharmaceutical Inspection Cooperation Scheme (PICs), stating the products and dosage

forms authorized for manufacture at the respective site. In addition, the bidder should submit a copy of their valid Manufacturing and/or Wholesale and/or Distribution license as applicable.

WHO Technical Report Series 986, 2014 - Annex 2: WHO good manufacturing practices for pharmaceutical products: Main principles^{vii}

WHO Technical Report Series 1044, 2022 - Annex 2: WHO good manufacturing practices for sterile pharmaceutical products^{viii}

WHO Technical Report Series 1025, 2020 – Annex 7: WHO good storage and distribution practices for medical products^{ix}

WHO Technical Report Series 961, 2011 – Annex 14: WHO guidelines for drafting a site master file^x

3.2.1 Contract manufacturing

Bidder(s) should state all details about contracting out part or all processes and relations to other companies, UNICEF must approve the site(s) of contract manufacturer(s) and any changes thereof.

3.2.2 Inspection

Vendor(s) shall ensure that UNICEF or any other representative as may be designated by UNICEF, has access to all manufacturing facilities, including contract sites at all reasonable times to perform an inspection. The vendor and/or manufacturer shall provide reasonable assistance to UNICEF or any other representative including providing copies of any documentation as may be necessary. The inspection may be carried out in conjunction with the relevant National Regulatory Authority. Vendor should also note that UNICEF may, upon request, share the inspection report generated on a confidential basis with Partners under the Interagency Pharmacists Group (IAPG)- inclusive of the International Committee of the Red Cross (ICRC), Médecins Sans Frontières (MSF), World Health Organization (WHO), The Global Fund, Stop TB Partnership The Global Drug Facility, United Nations Family Planning Agency (UNFPA) and United Nations Children’s Fund (UNICEF), the Pharmaceutical Inspection Co-operation Scheme (PIC/S) inspection authorities, regulatory authorities and

other partners carrying out capacity building for regulatory or manufacturing functions. The vendor will be notified in case such request is received.

Inspection reports of contract research organizations (CROs) from the relevant regulatory authorities should be provided as proof of therapeutic equivalence through clinical trials, such as, Bioequivalence for poorly soluble APIs in certain dosage forms. Refer to: ICH Guideline M13A on bioequivalence for immediate-release solid oral dosage forms - Scientific guideline. The inspection of CROs to assess compliance to Good clinical Practice (GCP), regulatory requirements and data integrity to assure that the clinical trials data is credible. Refer to: ICH E6 Good clinical practice - Scientific guideline.

3.3 Manufacturing process and process validation

The following requirements concern Section 1.1.4 and 3.4 of the IAFPPQ and relates to *Annexes W and X* of IAFPPQ

Submit a flow diagram and a brief narrative describing the manufacturing process and controls of critical steps (tests and acceptance criteria). Description of the manufacturing method/process validation, including documentation and report for three consecutive commercial scale batches (protocol for prospective validation if not yet validated) should also be provided. For products that meet criteria of an established multisource product, a product quality review as outlined in *WHO Technical Report Series 970, 2012 - Annex 4 Guidelines on submission of documentation for a multisource (generic) finished pharmaceutical product for the WHO Prequalification of Medicines Programme: quality part, Appendix 2 Product quality review requirements for established multisource products* may be submitted in lieu of the information above.

Refer to:

EMA, 2016 - Guideline on process validation for finished products - information and data to be provided in regulatory submissions^{xi}

WHO Technical Report Series 1044, 2022 - Annex 2: WHO good manufacturing practices for sterile pharmaceutical products^{xii}

FDA, 2011 - Process Validation: General Principles and Practices^{xiii}

WHO Technical Report Series 970, 212 – Annex 3: Pharmaceutical development of multisource (generic) finished pharmaceutical products: points to consider^{xiv}

Copies of the executed production documents should be provided for the batches used in the comparative bioavailability i.e., bioequivalence studies^{xv} or biowaiver^{xvi} studies^{xvii}.

It is particularly important to include batch size in the Certificate of Analysis (CoA) and stability reports and to give justification if it differs from the validated batch size. Any variance of the batch size should be within tenfold of the validated batch size.

In case of sterile products, data on validation on the sterile aspects of the product including media fill validation data or sterility assurance where applicable, and detailed description of method(s) of sterilization should be provided with justification for choice of sterilization method.

EMA, 2019 - Guideline on the sterilisation of the medicinal product, active substance, excipient and primary container

Manufacturers should provide supportive documents for products manufactured by continuous model of manufacture as per *ICH Q13 Continuous manufacturing of drug substances and drug products*.

Antimicrobial product manufacturers, including antibiotics, antivirals, antifungals and antiparasitics, should ensure systems are in place to mitigate/prevent the potential spread of antimicrobial resistance. Application of the requirements outlined in the below mentioned WHO GMP guideline shall be verified during onsite GMP inspections.

WHO Technical Report Series, No. 1025, 2020 - Annex 6: Points to consider for manufacturers and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance^{xviii}.

A UNICEF Guidance Note on Antimicrobial Resistance (AMR)

3.3.1 Batch formula

Requirements under *Annex A* of IAFPPQ

Provide the product formulation; complete qualitative and quantitative composition including active ingredient(s), overages, and excipients, indicating the reference standard/monograph for each ingredient (e.g., BP, USP, in-house) and its functionality. Mention specifically if the product is a fixed-dose combination (FDC) or co-packaged.

WHO Technical Report Series 970, 2011 – Annex 5: Development of paediatric medicines: points to consider in formulation. Please refer to the latest version which is currently under review.

3.4 Specifications of Finished Pharmaceutical Product (FPP)

The following requirements concern sections 3.2 and 3.3 of the IAFPPQ and supporting documents must be submitted in *Annex T* and *U*.

Bidder/manufacturer must provide a copy of the FPP specification(s) dated and signed by authorized personnel (i.e., the person in charge of the quality control or quality assurance department). Two separate sets of specifications at release and at the end of shelf-life should be provided. Any differences between release and shelf-life tests and acceptance criteria should be clearly indicated and justified. Note that such differences for parameters such as dissolution are not accepted.

Indicate if the product refers to any recognized pharmacopoeia as listed in this document.

For setting out the specifications refer to *ICH's Q6A guideline Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances*

Functionality of relevant attributes to pharmaceutical dosage forms such as functionally scored, dispersible, enteric coated, bi-layered, film coated, sugar coated, release mechanism (immediate or modified) tablets should be supported with analytical data.

3.4.1 Analytical procedures used for testing the FPP and their validation

Analytical methods for testing FPP should be provided. If analytical methods are pharmacopeial, analytical method verification is required. Copies of the validation protocol and reports for the in-house analytical procedures proposed for routine testing should be

provided. Whenever a pharmacopoeial standard is claimed, and inhouse analytical method is used, proof of equivalency with the pharmacopoeial method should be provided.

Compendial method(s) should be shown suitable for controlling the proposed FPP, so a method verification report should be provided. For officially recognized compendial FPP assay methods, verification should include a demonstration of specificity, accuracy and repeatability (method precision). substances. If an officially recognized compendial method is used to control related substances not specified in the monograph, full validation of the method is expected for those related substances. In instances, where the applicant claims an official standard and the analytical method is in-house standard, evidence of method equivalency should be provided in line with the allowable method deviation from the pharmacopoeial method.

WHO Technical Report Series 1019, 2019 - Annex 3: Good manufacturing practices: guidelines on validation^{xix}

3.4.2 Certificates of Analysis

Requirements relate to *Annex U* of the IAFPPQ

A Certificate of Analysis (CoA) is issued following full qualitative and quantitative analysis of all relevant aspects of the product and in compliance with its marketing authorization and release specification.

For all FPPs, certified copies of certificates of analysis for the last three production batches are required for submission with tenders as per *WHO Technical Report Series 1010, 2018 – Annex 4: WHO model certificate of analysis*.

Certificates of analysis must also accompany products when they are delivered to UNICEF or designated UNICEF consignees. In addition, a copy of the certificate of analysis should be sent via e-mail as follows:

- For shipments to UNICEF Supply Division warehouse in Copenhagen, the certificate of analysis should be sent to danpackinglists@unicef.org together with a copy of the packing list and other related shipping documents prior to the delivery estimated time of arrival.

- For direct shipments, the certificate of analysis should be sent to dangainspections@unicef.org together with a copy of the packing list and other related shipping documents prior to the estimated delivery time of arrival.

Where applicable, a batch specific CoA may be required for non-finished medicinal products such as intermediates, bulk or partially packed products.

The vendor should ensure that the batch number indicated on the CoA is identical to that on the product labels.

The CoA should state the manufacturing site/unit and address where the final product was manufactured.

In the case of a co-pack, CoAs of all components should be submitted, with all necessary information included to ensure traceability.

The CoA should state the specifications with limits, the results and the conclusion of the testing. The CoA should include info on FPP's pack size and type, API name(s) and API source(s) used and batch size. Batch size should be expressed in the same unit as in the Manufacturing Process Validation report.

The CoA should be numbered in such a way that it is possible to identify the current page and the total number of pages in the CoA e.g., page x of y.

For all CoA quantitative specifications, numerical values of results must be stated. The word "complies" or "conforms" is NOT acceptable in place of numerical values. Theoretical test results are not acceptable. If tests are not performed, it should be justified and in line with approvals from UNICEF, and there should be a footnote in the CoA (e.g., rotation/skip testing).

3.5 Stability

The stability requirements concern section 3.6 of the IAFPPQ. The stability study protocol and consequent report must be submitted in *Annex Z, AA and AB*.

Supplier must demonstrate stability of the FPP throughout its intended shelf-life under the climatic conditions prevalent in UNICEF target countries. Most countries to which UNICEF supplies pharmaceutical products are in WHO climatic zones III, IVa and IVb^{xx}.

For consistency and ease of planning, UNICEF requires that all products supplied to or through UNICEF are suitable for transport and storage at Climatic zone IVb (30°C±2°C/75% RH ±5% RH) and with total shelf-life of 36 months or longer. Exceptions may apply only in situations where API/Active Moiety characteristics typically do not support zone IVb conditions and/or longer shelf-lives.

The FPP batch used for stability study should be the same as the FPP commercial batch to be supplied to UNICEF with respect to product formula, all declared API sources, manufacturing site and packaging materials. The vendor must declare which API sources have been used in the FPP under stability studies and commit to conduct stability studies for FPP using all declared API sources.

FPP stability data generated with a new API source should be provided. Less stability data with a commitment of ongoing stability data of FPP with new API source may be acceptable in certain circumstances.

1. Stability studies under the conditions defined for climatic zone IVb (30°C±2°C/75% RH ±5% RH) should be performed on each individual strength, dosage form, pack type and size and batch size of the FPP in line with CH Q1A(R2) Stability testing of new drug substances and drug products, under ICH Climatic Zone IVb conditions (30°C ± 2°C / 75% ± 5% RH). Reduced designs of bracketing or matrixing may be applied, in line with ICH Q1D (R2) bracketing and matrixing designs for stability testing of drug substances and drug products - Scientific guideline.
2. Stability testing should cover chemical, physical, biological and microbiological attributes, including preservative content. Tests should be conducted on those attributes that are susceptible to change during storage and transport and that can influence the safety, efficacy and quality of the product.
3. Stability report should be for the FPP product from the site/unit where it is manufactured. The exact address of the site/unit where the FPP was manufactured should be clearly stated in the stability report.

4. Stability studies should be carried out on at least three primary FPP batches⁴ and for every declared API source to be used in the FPP. As indicated in the WHO TRS 953 “the primary batches should be of the same formulation and packaged in the same container-closure system as proposed for marketing. The manufacturing process used for primary batches should simulate that to be applied to full-scale production batches and should provide product of the same quality and meeting the same specification as that intended for *marketing*.”
 - a. In the case of conventional dosage forms with APIs that are known to be stable, data from at least two primary batches should be provided.
 - b. Two of the three batches should be at least pilot-scale batches⁵ (pilot-scale batch should be manufactured by a procedure fully representative of and simulating that to be applied to a full production-scale batch correspond to at least 10% of future/planned full-scale production batch size or 100,000 units, whichever is larger) and the third one can be smaller. This is compulsory for FDC products and new APIs⁶.
 - c. Where possible, batches of the FPP should be manufactured using different batches of the API(s) (declared). When there is more than one API source declared, stability study should be conducted for FPPs manufactured with various sources.
 - d. Preference will be given to products with acceptable real-time stability data from full-scale production batch sizes that cover the assigned shelf-life.
5. In some circumstances results of six months accelerated stability studies and at least 12 months real time stability studies could be acceptable with commitment for continuing stability studies for the duration of full shelf-life. Shelf-life extrapolation is acceptable in line with ICH Q1E Evaluation of stability data - Scientific guideline. Stability studies should be continued for a period sufficient to cover the entire shelf-life as allocated to the FPP.
6. The specifications and methods used during stability studies must be described in the stability protocol and report. If this is identical to a methodology described

⁴ A batch of a drug substance or drug product used in a formal stability study, from which stability data are submitted in a registration application for the purpose of establishing a retest period or shelf-life, respectively. A primary batch of a drug substance should be at least a pilot-scale batch. A primary batch may be a production batch.

⁵ Pilot-scale batch: A batch of a drug substance or drug product manufactured by a procedure fully representative of and simulating that to be applied to a full production-scale batch. For solid oral dosage forms, a pilot-scale is generally, at a minimum, one-tenth that of a full production-scale or 100,000 tablets or capsules, whichever is larger.

elsewhere in the data set, a cross-reference will suffice. If a different methodology was used, the test procedures applied to the stability tests on the FPP should be validated or verified, and the accuracy as well as the precision (standard deviations) should be recorded. In general, specific methods, such as high-performance liquid chromatography (HPLC), thin layer chromatography (TLC) or gas chromatography (GC), must be used for the assay and determination of degradation products.

7. For all stability studies, numerical values of results must be stated, the word “complies” or “conforms” will not be acceptable in place of numerical values.
8. A full stability report, including trend graphs of all relevant parameters and analyses and discussion of results, should be presented. Shelf-life conclusions should be drawn therein.
 - a. Each stability report should also include information about the type, size, and material of the pack, clearly stated stability conditions, FPP manufacturing site address, API source(s) and batch size(s).
 - b. **IN-USE stability:** Where the product is to be reconstituted and/or diluted before use, such as powder or concentrate for injection or a powder for oral suspension “in-use” stability data must be submitted to support the recommended in-use storage conditions and duration.
 - c. UNICEF takes note that some FPPs, e.g., those with marketing authorization in countries with SRA may not necessarily be labelled for zone III and IV, even when supportive stability data exists⁷.
 - UNICEF requires that products for supply to countries that have conditions of zones III and IV be supported by stability data generated at $30^{\circ}\text{C} \pm 2^{\circ}\text{C} / 75\% \text{RH} \pm 5\% \text{RH}$ (zone IVb) on the primary or production batches of the product in the same packaging as approved for marketing of the FPP by the reference regulatory authority/country/region. For products packaged in semi permeable containers, stability data should be carried out at $40^{\circ}\text{C} \pm 2^{\circ}\text{C} / 25\% \pm 5\% \text{RH}$ (for accelerated stability studies) and at $30^{\circ}\text{C} \pm 2^{\circ}\text{C} / 35\% \pm 5\% \text{RH}$ (for long term stability studies).

⁵ UNICEF recognizes that the requirement for zone IVb labelling may result in a change to regulatory approved product information. For a limited time period, UNICEF may accept product with labelling other than zone IVb, together with acceptable stability data for zone IVb for the entire labelled shelf-life. This determination will be based on the ability of target countries to handle such product/information logistically, only if other products with zone IVb stability cannot be accessed at that time. It is therefore in the interest of the supplier to obtain the necessary regulatory approvals for change in labelled storage conditions and shelf life at the earliest opportunity

- If an FPP does not have zone IVb labelling, UNICEF requires that the vendor reviews stability data that the marketing authorization holder submitted for approval of the label storage conditions and shelf-life to the reference regulatory authority to determine suitability of supply to zone IVb climatic conditions. The vendor should submit to UNICEF the report of this review, along with the relevant stability data.
- If zone IVb stability data is not available, the vendor should ensure that the manufacturer initiates full long-term stability testing at zone IVb conditions in the same packaging as approved by the reference regulatory authority. A minimum of 12 months long-term stability data is required. Considerations to accept a product without acceptable zone IVb stability data and labelling will be on a case-by-case basis, driven largely by target country capacity to handle such a product.

WHO Technical Report Series 1010, 2018 - Annex 10: Stability testing of active pharmaceutical ingredients and finished pharmaceutical products^{xxi}

3.5.1 Shelf-life and storage requirements

1. Shelf-life should be established based on complete long-term data at 30°C ±2°C/75% RH ±5% RH (zone IVb).
UNICEF prefers products with a shelf life of ≥36 months where they are scientifically feasible. Products with a shorter shelf life may be considered when justified by the inherent properties of the API or dosage form and supported by adequate stability data generated under Zone IVb (30°C/75% RH) conditions.
2. The manufacture and expiry date that reflects the assigned shelf-life and recommended temperature storage conditions MUST be written on FPP labels and should be included in package inserts/patient information leaflets.
 - a. Manufacture and expiry dates and the storage conditions must be consistent on the primary, secondary labels. The summary of product characteristics and package insert/patient Information leaflets.
 - b. Statements such as “Store at room temperature” or “This product does not have special storage requirements” are not acceptable; The ACTUAL numerical temperature storage conditions MUST be specified e.g. Store below 25°C. It is

preferable to include minimum temperature the product can be stored at. Thus, include a statement, such as, “store between 15°C to 25°C”.

- c. The recommended storage statements for use based on stability studies are provided in WHO stability guidelines *WHO Technical Report Series 1010, 2018 - Annex 10: Stability testing of active pharmaceutical ingredients and finished pharmaceutical products*.
3. In-use shelf-life: manufacturer MUST indicate storage conditions and shelf-life after reconstitution/dilution/opening, where applicable, such as powder for oral liquid, and powders for injection after reconstitution or injections that might be further diluted or multi dose containers such as ear/eye products. The specific solvents used for reconstitution/dilution must be specified/indicated together with specific storage conditions supported by in-use stability data.
4. Vendor is responsible to include additional labelling requirements such as “Do not freeze,” “Protect from light,” “Store and transport in dry conditions” on FPP and all external packaging. UNICEF prefers fresh production to the extent possible. The remaining shelf-life shall be reviewed at procurement on a case-by-case basis.

3.5.2 Stability requirements when considering long shipment of intermediates

In case a supplier has a co-manufacturing agreement with another manufacturer/packer, where-in bulk oral dosage forms such as coated tablets are shipped to another site for final packaging, the tablet manufacturer must conduct hold-time stability study when the time for transport, storage and final packaging takes more than 30 days.

Hold-time stability study must simulate transport and storage conditions expected and be undertaken for the estimated duration, considering worst case scenarios. Ideally, the hold-time duration would be less than 3 months and no more than 6 months.

The product manufacturer, in this case responsible for final packaging, must test the intermediate bulk product, at receiving, for critical quality and safety parameters as per acceptance criteria set for product release.

For guidance on hold-time stability studies refer to:

WHO Technical Report Series, No. 992 – Annex 4: General guidance on hold-time studies.

3.6 Container-closure systems

The following requirements concern section 1.3 of the IAFPPQ.

Container-closure systems are defined by UNICEF as the sum of functional packaging components that together contain and protect the dosage form^{xxii}. This includes primary packaging and secondary packaging components if the latter is intended to provide additional protection (e.g., light barrier) to the drug product. Or contain dosing devices and use instructions.

A container closure system (CCS) for medicines is:

The complete packaging system that contains and protects a pharmaceutical product, consisting of the container (e.g., vial, bottle, ampoule, blister) and the closure (e.g., stopper, cap, seal), together forming a secure barrier that maintains the product's identity, strength, quality, sterility (where required), and stability throughout its shelf life and use.

A properly designed CCS must:

1. Protect the product

- From contamination (microbial, particulate, chemical)
- From moisture, oxygen, and light
- From loss of solvent or volatile components

2. Maintain quality and stability

- Prevent degradation
- Maintain potency and purity
- Ensure sterility for sterile products

3. Ensure compatibility

- No harmful interaction between product and packaging
- No leachables/extractables affecting safety or quality

4. Allow safe use

- Maintain integrity during storage and transport
- Support correct dosing and administration
- Provide tamper evidence where required

Container-closure systems/packaging must preserve the stability and quality of the FPP during transport and storage for the duration of the shelf-life, including in-use shelf-life, where applicable. In some cases, child-resistant container-closure systems may be required as an enhanced safety feature.

Vendors must demonstrate the suitability of the container-closure system used for the storage, transportation (shipping) and use of the FPP such as compatibility of the materials used for packaging with the dosage form, including sorption to container and leaching. Description, specifications and CoAs of packaging materials should be provided.

Container-closure systems must be tamper-evident i.e., it should be possible to know if the product has been altered or falsified.

Please refer to WHO Technical Report Series No. 902, 2002 – Annex 9: Guidelines on packaging for pharmaceutical products.

3.6.1 Primary Packaging

The primary packaging specification must be submitted in *Annex B*.

1. Materials used for primary packaging must conform to the relevant edition of the BP, USP, Ph.Eur. or Ph.Int. with reference to the specific API and FPP; must be safe for use with the dosage form for the intended route of administration^{xxiii}; and be suitable for shipment, storage and worldwide use at extreme temperatures and humidity.⁸
2. The size of the container must be proportional to its content with the addition of appropriate padding to prevent damage to the product during handling and transport.
3. Glass containers will not be accepted above a maximum of 250 ml. Glass bottles must be separated by crisscross box dividers or box partitions or be packed individually in cartons.

⁸ this refers to placing and sealing of the medicinal product within the finished product packaging material which is in direct contact with the product.

4. For glass ampoules, single ended, break-off necks are required. Non-glass packaging such as from “blow-fill-seal (BFS) are acceptable provided that all necessary compatibility and stability studies are acceptable.

3.6.2 Secondary packaging ⁹

The secondary packaging specification must be submitted in *Annex C*.

Secondary packaging is a pack component that is normally not in direct contact with the product.

UNICEF accepts secondary packaging that is functional i.e., adds protection to that provided by the immediate primary pack, against:

1. Excessive moisture and reactive gases, e.g., fibre drums, HDPE bottles for products which are immediately packaged with LDPE bag.
2. Secondary packaging for large volume parenterals, including additional plastic sheath, is key in making sure that FPP in primary packaging is well protected and adequately labelled.
3. Light, e.g., opaque carton outside PVC/Alu blister.
4. Microbial contamination.
5. Rough handling during transport and storage.

Secondary packaging may also be acceptable if they provide a means to contain summary of product characteristics/patient information leaflets and/or dosing devices.

Information related to the functionality of the secondary packaging must be provided in the dossier submission.

1.1.2.1 Dose measurement and dose delivery devices

⁹ this refers to placing the medicinal product, which is already sealed within its primary packaging material within an outer packaging material. This also includes labelling operations or the assembly of other components which are specified in the Marketing Authorisation to form the finished product pack.

1. A dose measurement and dose delivery device is required to be included with the container-closure system for administration of oral liquids or solids that are converted into liquid prior to oral administration, whenever the package provides for multiple doses.
2. Dose measuring devices must be graduated in intervals to allow accurate measurement of all the doses approved for that medicine.
3. The dosage scales/volumes embossed on dose measurement devices must be in METRIC units. For liquids preparations supplier is required to submit study results that confirm the suitability of the container-closure system contact materials, and this should also include extraction studies and interaction studies (migration/sorption)¹⁰.
4. For a dose measuring device accompanying a multi-dose container, the results of a study should be provided demonstrating the reproducibility of the device (e.g., consistent delivery of the intended volume).
5. A description of the container-closure systems should also be provided, including the identity of materials of construction of each primary packaging component (including those used for drug delivery) and its specification. Information on the identity of secondary packaging should be included if secondary packaging is functional.
6. Droppers should be provided with certain pharmaceutical dosage forms (e.g., eye drops, ear drops)
7. An applicator device MUST be included with vaginal tablets/pessaries.
8. All dose measurement and delivery devices should be adequately packed with a product or fixed to a product in such a way as to avoid losing it, damaging it and causing unhygienic conditions.

1.1.2.2 Packaging to improve Supply Logistics efficiency and for sustainability

In addition to protecting FPP and providing information to support FPP usage, packaging should:

1. Improve supply planning and operational efficiency at minimal costs.
2. Ensure user-friendliness and support patient compliance.

¹⁰ Container closure system suitability should include but not limited to functionality, protection and prevention of contaminants through studies such as leaching.

3. Maintain safety and minimize medication errors.
4. Be tamper-evident and/or tamper proof.
5. In line with sustainable procurement efforts, vendors are asked to consider eliminating non-functional secondary/tertiary packaging WITHOUT compromising the integrity of the FPP and while still ensuring that sufficient product information to health professionals and patients is available together with the product.

For more information on packaging including requirement on shipper carton strength tests (including bursting strength and edgewise crush resistance) waterproofing capabilities, follow the Updated specifications for packing, packaging and labelling (to be enforced from 2 October 2023) [Updated specifications for packing, packaging and labelling \(to be enforced from 2 October 2023\)](#) | UNICEF Supply Division

3.7 Labels

The following requirements concern sections 1.7.2 and 1.7.3 of the IAFPPQ.

A copy of the primary packaging label with artwork and secondary packaging label with artwork must be submitted in *Annex H and I*, respectively.

Labels must be indelible and self-adhesive e.g., pharmaceutical defibred paper (80gsm), that is film coated or UV treated for protection against humidity and firmly affixed to be tamper proof and to prevent detachment in tropical climates.

Language English and/or French are the standard language/s for labels and pack inserts. Additional label language in UN official languages may be required from time to time e.g. Arabic, Spanish, Chinese and Russian. Such language translations of labels and pack inserts are to be shared in electronic formats or a cloud-based repository, with the link provided to UNICEF to be shared with requesters upon request. Other local languages specific to the recipient country may be requested with specific tenders and/or purchase orders.

Type Preferably by lithography directly on container/packaging in font size 6 point for readability, directly on container/packaging.

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

For consistency and ease of logistical handling, it is recommended that manufacturers apply the same artwork and minimum labelling requirements, on all primary, secondary and/or tertiary packaging.

The supplier should agree to updating the label, as per UNICEF's and/or importing country's applicable regulatory requirements.

3.7.1 Minimum Labelling Requirements

Labels must have adequate information to permit identification, safe transport, storage and use of the product throughout its shelf-life. In certain instances, labelling and patient information in Braille or AUDIO may be required.

At the minimum, the FPP label must include the following: -

1. **Name of the medicine:** The International Non-proprietary Name (INN), pharmaceutical dosage form and strength should be written in a bold, clearly visible, large font size. For large volume parenterals, the INN name of the medicine should be readable in both the upright and upside down (inverted) positions.
2. **List of Active Pharmaceutical Ingredients:**
 - a) If an International Non-proprietary Name (INN) (also referred to as the generic name) recommended by the World Health Organization exists for the active moiety, the English version of the name should be used exactly as published without omissions or abbreviations.
 - b) If a Modified INN (INN_M) recommended by the World Health Organization has been published for active moiety, it should be used within the name of the medicinal product exactly as published without omissions or abbreviations.
 - c) Where the active moiety is an unpublished INN_M, the name of the medicinal product should be that as agreed by users of INNs (Pharmacopoeias, regulatory bodies, stakeholders), in accordance with the *WHO International Nonproprietary Names Modified*.
 - d) If an INN or INN_M does not exist, other common names, such as the British Approved Name (BAN) are acceptable. Information on INN names and stems is available from *WHO Health products policy and standards – INN& Medicines classification*.
 - e) The expression of the amount or percentage of API or active moiety per dosage unit, unit of volume or unit of weight should be in metric units.

3. **Excipients:** Names and amounts of excipients known to have a recognized action or effect i.e., excipients of concern, e.g., “contains 10% ethanol”, “contains lactose” must be clearly stated as minimum on the secondary pack label and PIL. If the pharmaceutical product is parenteral, topical, inhalational or an eye preparation, all excipients must be stated.
4. **Route of administration:** List the route of administration (e.g. oral) and any preparation needed prior to use (e.g. for oral suspensions)
5. **Posology and directions for use for the intended target group(s):** Provide the intended dose or serving size and any specific instructions such as “do not chew” or “take after a meal”.
6. **Pharmacopoeia reference used for the FPP, where applicable:** Pharmacopoeia reference should only be included in the name of the product where ALL standards and analytical methods for the product refer to that pharmacopoeia. It should not be used where in-house standards and methods are used or where more than one pharmacopoeia reference is used.
7. **Net quantity per unit pack** labelled on that unit pack (primary, secondary, tertiary) in metric units in a visible manner.
8. **Storage and handling conditions:** The following storage and handling conditions should be listed when applicable.
 - a. Recommended temperature (numerical °Celsius) requirements during transport and storage
 - b. Special storage and handling instructions, including warnings and precautions, use of solvents for reconstitution
 - c. If a product has a limited shelf-life after the primary package is opened and manipulated, the **in-use period and storage conditions** should be indicated on the label
9. **Manufacturing details:** The following information regarding the manufacture of the finished product should be included on the product label.
 - a. **Batch identification.** Please note that batch numbers can only consist of 10 digits due to limitations in the SAP system utilized by UNICEF.
 - b. **Manufacturing date** in a format that can be easily understood. The required format is DD/MM/YYYY. To avoid confusion, the year of manufacture should be 4 digits.
 - c. **Expiry date** in a format that can be easily understood. The required format is DD/MM/YYYY. The year of expiry must be 4 digits.

d. **Name and address of manufacturer and marketing authorization holder.**

For contract manufacture, indicate as: manufactured by company X for company Y.

The label information on manufacturing dates, expiry dates and batch numbers should be dynamically printed. All label information and specially manufacturing and expiry dates should be written in the same format and consistent on primary, secondary and tertiary/shipping packaging as well as in the PIL, to avoid confusion.

10. **GS1 system should be used for barcodes:** All information provided in the barcodes of one product should be consistent in all packaging levels (primary, secondary, tertiary).
11. In exceptional cases e.g. secondary packaging for Large Volume Parenterals (LVP), **a product label must be applied to the secondary packaging** with information related to product name, batch number, manufacturing date and expiry date that are consistent with a primary label, also in cases where the unit of measure is equivalent to the shipper box.
12. **Co-packs-** (Drug-Device co-pack, Drug+Diluent Co-pack, Co-packed Medicines) e.g. Volume Parenterals packed with giving sets, or any other co-pack, secondary/shipper package label should include the manufacturing and expiry dates that are the same format as manufacturing and expiry dates on the primary label/s (DD/MM/YYYY). It is recommended to assign a **new batch number for a co-pack** to enable tracing and use the individual product's expiry date with **the shortest shelf life**. The manufacturer should ensure that the **remaining shelf life** is higher or aligned with the individual product. Recommendations for minimum additional information to be provided on the combined product label:
 - a. Co-pack name "Product Name"
 - b. A description of its pharmaceutical form, strength and, where applicable, method of application
 - c. New assigned batch number for the Co-pack.
 - d. The pack size
 - e. Storage conditions (more stringent between two or more components)
 - f. **Expiry date (of the component with the shortest expiry date;** format in line with the UNICEF
 - g. packing specifications DD/MM/YYYY)
 - h. Name of the MAH (Marketing Authorization Holder) or the manufacturer

Best practices on label formats and style (non-binding requirements)

1. Information 1-4 listed above should appear clearly on the front face of the label AND in the same field of view, without any additional information or logos or background texts or graphics.
2. The strength of the API (or active moiety) should always appear next to the name of the API (or active moiety), e.g., Artemether 20mg + Lumefantrine 120mg;
3. Components in fixed dose combination FPPs (FDCs) and co-packs should be written in ascending alphabetical order with reference to the first letter of the INN e.g., Artemether 20mg + Lumefantrine 120mg;
4. Co-formulated FDC products, should be denoted with a "+" or "/" sign e.g. Artemether 20mg + Lumefantrine 120mg, while co-packaged FDCs should be denoted with an "&" sign e.g., Amodiaquine 153mg & Artesunate 50mg;
5. Where another name such as British Approved Names is used, e.g., Co-Amoxiclav the INN names of the two active moieties should be stated with their full INN names i.e., Amoxicillin 500mg + Clavulanic Acid 125mg;
6. The design of the secondary packaging label, and where applicable, the primary packaging label, must allow for the writing of dispensing information or addition of dispensing labels without covering valuable information on the manufacturer label.

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

3.7.2 Summary of product characteristics, pack inserts/patient information leaflets

A Patient Information Leaflet (PIL) and/or Summary of Product Characteristics (SmPC) must be submitted as *Annex J*.

The summary of product characteristics (SmPC)^{xxiv} as well as a detailed pack insert/PIL as per standards and norms for each FPP must be submitted for any solicitation process and they should have consistent information included.

It is MANDATORY to include a package insert and/or a patient information leaflet with each FPP either within the secondary packaging or as part of the label (label booklet) or attached to top of the primary package. Additionally, electronic means of providing product

information i.e. PIL and/or Summary of Product Characteristics, such as QR codes are encouraged. Please refer to: *Key principles outlining a harmonised approach to develop and use electronic product information (ePI) for human medicines across the European Union*.

The PIL should include all the necessary information according to the *Directive 2001/83/EC Labelling and package leaflet, articles 54 and 59* or any other WLA/SRA regulation on PIL. The following list indicates the most important info that should be included in the PIL:

- 1. Name of the Medicinal Product** – product name, strength, pharmaceutical form.
- 2. Qualitative and Quantitative Composition** – active substances and important excipients.
- 3. Pharmaceutical Form and Presentation** – dosage form, content (weight/volume/units), packaging description.
- 4. Therapeutic Indications**
- 5. Before You Take This Medicine**
 - 5.1. Contraindications
 - 5.2. Special warnings and precautions, including hypersensitivity or allergenic reactions
 - 5.3. Interactions (with food/medicines)
 - 5.4. Use in special populations (children, elderly, pregnant/lactating, specific conditions)
 - 5.5. Effects on ability to drive or operate machinery
 - 5.6. Notable excipients requiring patient awareness
- 6. Dosage and Method of Administration** – dose, route, frequency, duration, instructions for special populations, overdose management.
- 7. Possible Side Effects** – adverse reactions and necessary actions.
- 8. How to Store the Product** – expiry date, storage conditions, special warnings on appearance/handling.
- 9. Marketing Authorization Holder** – name and address.
- 10. Manufacturer(s)**
- 11. Date of Last Revision**

3.8 Safety, efficacy and/or therapeutic equivalence

The requirements relate to *Annexes AC, AD, AE, AF, AG and AH* of the IAFPPQ

The report of the proof of therapeutic equivalence (bioequivalence or multimedia comparative in vitro dissolution profiles or any other method), should be submitted as outlined in the Interagency Finished Pharmaceutical Product Questionnaire or its equivalent. Additionally, contract research organization (CRO) inspection reports, preferably the most recent by the reference NRA or WHO, should accompany technical offers alongside the Bioequivalence study protocol and reports.

The product used in the therapeutic equivalence study should be the same as the one that will be supplied i.e., same APIs/ excipients from the same manufacturers, same formula, and same manufacturing method(s).

Submission of such a report of proof of therapeutic equivalence may not be required for FPPs that are WHO prequalified or approved by an WLA/SRA that requires proof of therapeutic equivalence to be submitted as part of their dossier assessment for marketing authorization/product registration, as long as bidder attests this to be the case.

For innovator products, a summary report on pharmacology, toxicology and efficacy of the product should be submitted.

3.9 Suitability of invented/brand names or registered trade names

UNICEF prefers that ONLY the International Non-proprietary Name (INN) is written on all labels and pack inserts. Where proprietary, brand or registered trade names are used, the International Non-proprietary Name (INN) must be more prominent e.g., in bigger font than the proprietary, brand or registered trade name.

In accordance with *World Health Assembly (WHA) resolution 46.19*, an invented/brand name should not be derived from its own INN or INN stem.

If used, the invented/brand name, strength and pharmaceutical dosage form

1. Should preferably be the same as that registered and in the summary of product characteristics (SmPC).
2. Should not cause confusion with the INN name of this medicine or name of another medicine in print, handwriting or pronunciation.
3. Should not be misleading with respect to therapeutic effect, composition, or safety of the product. Words in the brand name such as “forte,” “strong,” “fast-acting,” “extra,” “double strength,” should not be used UNLESS supported by evidence/data in the SmPC and relevant to the indications approved for the product.
4. Must not be so prominent as to mask the appearance and readability of the INN.

3.10 Samples

Samples should be submitted for each solicitation activity when requested. Label artwork (primary & secondary packaging), SmPC and PIL should be submitted in any case.

Photos are part of the technical submission (as *Annex G* of the updated IAFPPQ) AND are mandatory once the product is accepted for procurement by UNICEF. All photos should clearly show the FPP (tablet, capsule, ampoule, vial, tube etc.), all sides of the primary and secondary packaging, labels as well as other relevant components e.g., delivery devices like dose measuring devices.

NOTE: UNICEF Supply Division¹¹ regularly requests and receives samples from a variety of vendors. It is VERY IMPORTANT for the vendor to ensure that packages containing samples are addressed correctly with the correct reference to make sure they are delivered in time to the right person and physical location within UNICEF Supply Division.

In cases where samples submitted are NOT commercial samples, i.e. mock samples, they MUST be labelled as NON-COMMERCIAL SAMPLE. A justification on why a commercial sample cannot be submitted must be included with the submitted sample.

3.11 Track and Trace

1. Make product handling easier, efficient and more automated by using the standard GS1 system for barcodes - GS1 General Specifications Standard, placed so that it can easily be read. The tertiary packaging and pallets shall be labelled with the required information in both writing and encoded in barcodes as per encoding type GS1-128. Other smart codes such as QR codes are acceptable but must be consistent with other information on primary, secondary and tertiary labels.
2. Enable traceability and supply chain safety e.g., incorporate Track-and-Trace systems that assure chain of custody and/or anti-counterfeiting measures.

3.12 Transport and transit storage requirements^{xxv}

Suppliers shall comply or ensure compliance with UNICEF transportation requirements in accordance with WHO or internationally recognized guidance for good transportation, storage, and distribution practices applicable to their products. Suppliers are responsible for providing transport and storage temperature (and humidity – where relevant) information on shipping documents. Regardless of the mode of transport, it should be possible to demonstrate that the product has not been exposed to conditions that may compromise their quality and integrity. A risk-based approach should be used when planning transportation.

1. The vendor is responsible to SPECIFICALLY NOTIFY UNICEF about
 - a) Any special transport and storage requirements such as cold chain transport;
 - b) Any specific temperature requirements during transport and transit storage that are different from the conditions indicated on the product label.

¹¹ <https://www.unicef.org/supply>

2. The vendor MUST ensure that transport and transit storage temperature/humidity information and any other special handling conditions are clearly visible on shipping documents accompanying the product during transport.
3. The transport and storage temperature and any other special handling conditions (e.g., DO NOT FREEZE) MUST be visibly indicated on external packaging such as shippers and pallets.

The IATA (International Air Transport Association) Time and Temperature Sensitive Label (below) is a shipment label specific to the healthcare industry. It, or an equivalent should be affixed to all shipments that are time and temperature sensitive (have a temperature requirement and shelf-life) indicating the external transportation temperature range of the shipment. IATA equivalent labels must also be affixed to products to be transported via other modes of transport such as sea/water and land.



4. Depending on the storage conditions of the FPP, the temperature indicated on the lower half of the IATA label or equivalent must match the approved transportation temperature range, e.g., +15°C to +25°C, 0°C to +8°C. Permissible temperature excursions and special transport conditions should be stated as part of technical offer submission.
5. The vendor is responsible for informing the freight forwarder or any consignee accordingly and ensuring that product temperature conditions are maintained within specified acceptable limits during transport and transit.

3.12.1 Temperature monitoring during transport and transit

1. Temperature and humidity MUST be controlled and monitored during transport, preferably by electronic data loggers with alarm settings to prevent exposure to unacceptable conditions and that can be used as proof that a product is safely transported within the transport temperature profile defined for that product. Considering that temperature excursions may occur outside the specified temperature range, Bidders are required to provide risk assessment for both the lower and higher acceptable temperature limits outside the specified range; the permissible excursion limits should be stated. These should be justified by providing risk assessment study protocols and reports, for instance, freeze thaw studies, thermal cycling studies or stress studies. In addition, the data logger should have alarm settings and acceptable excursion period based on the risk assessment, as applicable. Any deviations from the specified temperature ranges must be investigated in line with GDP/GMP standards.

For the products that require cold-chain transportation, products should be packed in such a way that the cold chain is maintained during transport

2. Temperature monitoring devices must be included appropriately with every shipment.

They are necessary to provide evidence that a product is transported within the transport temperature profile defined for that product. The data loggers should be placed on the surface of a shipper carton or pallet where it would be easy to scan but close to the material being monitored; the shipper carton or pallet with the data logger should be clearly labelled. Information on the number of data loggers, their serial numbers, where they are placed should be included in the shipping documentation. The number of data loggers requirement per reefer container is to be determined through a risk based approach; for minimum requirements on data logger specifications and the minimum number of data logger required please refer to Guidance for temperature monitoring devices for pharmaceuticals: [Data-Logger-Specifications-for-Pharmaceuticals.pdf](#)

3. The Manufacturer should ensure there is validated cold chain packing and transportation of temperature sensitive products to ensure their quality and safety

from the point of origin to the end user. Transport validation studies and/or hold-time studies should be provided.

WHO Technical Report Series 1025, 2020 Annex 7: Good distribution practices for medical products^{xxvi}

3.13 Reporting of Complaints/Adverse events

If UNICEF becomes aware of any Complaint/Adverse event associated with the product(s) supplied to UNICEF , it shall be recorded and reported to the manufacturer/LTA holder, preferably within one (1) business day but not later than what is stated in the supplier contract with UNICEF, after UNICEF becomes aware of such an event through its reporting mechanisms.

Contact person in UNICEF Supply Division for complaint and adverse events:

Senior Quality Assurance Manager Francisco Blanco

Email: fblanco@unicef.org and rapidalerts@unicef.org

For the avoidance of doubt, UNICEF will have no obligation to report Adverse Events about which it is not made aware, nor shall it be required to place its Local Implementing Partners under any obligation to inform UNICEF as the Local Implementing Partners are supposed to follow national legislation/requirements.

UNICEF SD can be a part of pharmacovigilance only as a conveyor of information.

3.14 Emergencies

Upon the declaration of public health emergency of international concern (PHEIC) by WHO, UNICEF may procure products for use in emergencies that have:

- Been accepted in line with emergency use assessment and Listing procedures by WHO
- Emergency use Authorized/approved by SRA or WLA

3.15 Periodic Safety Update Reports

The bidder may be required to provide periodic safety reports. Requirements relate to *Annex AI* of the IAFPPQ, whenever applicable.

Pharmacovigilance is post-authorization activities for reporting new adverse effects (normally not picked in clinical trials) upon marketing of the product and arising due to extensive use in large population, for long periods and with possible drug interaction with other drugs.

Pharmacovigilance reports normally include the following:

- Individual case reports (ICSRs); for individual patients
- Periodic Safety update reports (PSURs)- regular reports summarizing safety updates
- Follow up reports-additional information that may be requested by the regulatory authorities or entities.

UNICEF does not require the submission of pharmacovigilance documentation; however, an application in review of product information or applicable regulatory document is expected whenever such reports are available.

Please note that PSURs apply for both innovator and generic products. Whenever, PSURs are published by the WHO, the Industry or National regulatory Authorities, or supplier's (Marketing Authorization holder's) own received reports from healthcare professionals or patients, the supplier is expected to ensure that the information is reviewed for applicable products and thus used for updates of patient information including the Summary of product characteristics (SmPC), PIL and product label, as applicable. Further actions, including but not limited to changes to API or FPP specifications, may apply.

Reference can be made to WHO's Uppsala monitoring Centre database or Europe's Eudravigilance database.

Further reference to a CIOMS (Council for International Organizations of Medical Sciences) case report (specifically the CIOMS I form) is a standardized, international document used in pharmacovigilance to report adverse drug reactions (ADRs). [Fillable-Form CIOMS-to-E2B.pdf](#)

4. Sustainability

Suppliers should consider all aspects of sustainable procurement, with special emphasis on environmental, social, and economic aspects. Over time, our procurement criteria for sustainability will be more stringent.

Currently, suppliers need to fill in the form on UNGM and also any annex to UNICEF tender documents related to sustainability. UNGM - Sustainable procurement indicators [Sustainable Procurement Indicators \(ungm.org\)](https://ungm.org/sustainable-procurement-indicators)

As a technical team, for now, we put a special emphasis on and evaluate manufacturer's practice with waste management, chemicals and toxic impact. GMP inspectors will review site waste management as part of the GMP inspections.

Related to resources depletion, implementation of *ISO14001 – Environmental management* will be preferred during our evaluation, for both FPP and API manufacturers. Existence of medicines take-back programmes and system/protocol for destruction of medicines will be evaluated.

To support action in substituting toxic chemicals in products and manufacturing operations with safer alternatives, we will evaluate use and management of chemicals used throughout the life cycle of the product.

The following solvents used in manufacturing active pharmaceutical ingredients (APIs) should be avoided: 1,2-dichloroethane (DCE); 1,4-dioxane; benzene; carbon tetrachloride (CCl₄); chloroform; diethyl ether; Di isopropyl ether; dimethylacetamide (DMAc); dimethyl ether (DME); dimethylformamide (DMF); hexane; methoxy ethanol; n-methyl-2- pyrrolidone (NMP); nitromethane; pentane; or triethylamine (TEA).

Hazardous and highly hazardous solvents should be reduced.

Persistent, Bio accumulative, and Toxic (PBT) substances should be avoided, and all substances used for the product should be evaluated for their environmental attributes, including persistence, bioaccumulation, toxicity, and environmental risk.

See UNDP (United Nations Development Programme), 2021 - Sustainable Procurement Index for Health (SPIH) ^{xxvii}

In line with sustainable procurement efforts and to eliminate waste, vendors are asked to consider eliminating non-functional secondary/tertiary packaging WITHOUT compromising the integrity of the FPP and while still ensuring that sufficient product information to health professionals and patients is available together with the product.

Where necessary, vendors should use sustainable packaging against sustainability standards.

See UNICEF Sustainable procurement procedure [Sustainable procurement procedure / UNICEF Supply Division](#)

5. COMMITMENT

Vendors must fulfil commitments they have made at any time and report back to UNICEF e.g., carrying through stability studies, process validation of batch sizes.

Vendors must fill, duly sign and submit the UNICEF commitment declaration form where required.

For all products on LTA or contract with UNICEF, vendors shall inform UNICEF immediately about

1. Any serious quality and/or safety concerns about their manufacture, control or use;
2. Suspension or cancellation of marketing authorizations;
3. Any statement of GMP non-compliance issued by a regulatory authority or international organization such as World Health organization;
4. Suspicion and/or confirmation of falsification.

The vendor pledges to work with UNICEF to minimize potential public health risks by actively organizing product recalls of defective products and either replacing the defective product or covering the direct and related costs related to replacing the defective product within defined timelines as specified in the contractual requirements.

The manufacturer will investigate any non-compliance of the product, provide a report, and take appropriate actions to ensure quality risk reduction for potential future supplies.

NOTE – All reference documents should be provided in italic, with a full title and source. Links are not acceptable because of numerous and frequent changes of links.

Requirements for Suppliers/Bidders

For this guidance, the supplier of products is mainly the manufacturer of the product. However, Wholesaler/Distributor are also eligible for supplies. A potential supplier should meet the following:

- a) abide by the UN Supplier Code of Conduct 21;
- b) accept the terms of the relevant procurement solicitation documents (RFP, RFQ or otherwise specified);

- c) be registered in the United Nations Global Marketplace (UNGM);
- d) Comply with the requirements of this guidance, as applicable and
- e) Fill in and submit the relevant questionnaires.

Appendix 1: Technical Instructions, Questionnaires and Annexes

Annex 1 UNICEF Technical Requirements for Pharmaceutical & Nutrition Products 7th Edition March 2026

Annex 2 Instructions for Technical Proposals and Offers

Annex 3 Instructions for uploading Technical Documents to SharePoint

Annex 2a UNICEF Technical questionnaire for pharmaceutical manufacturers

Annex 2b UNICEF Technical Questionnaire for pharmaceutical wholesalers

Annex 2c Interagency Finished Pharmaceutical Product Questionnaire (IAFPPQ)- Version 21 October 2024

Annex 2d IAFPPQ Commitment and signature - Section 5

Annex 2e UNICEF API Declaration form (to be filled in by FPP manufacturer)

Annex 2f UNICEF Technical Offer form

Annex 2g UNICEF Technical commitment declaration form

Annex 2h - Interagency finished pharmaceutical product questionnaire for BTPs and SBP

Annex 2i Letter of Authorization permitting UNICEF access to information from WHO, ERP, MSF etc.

Annex 2k Declaration of Equivalence (if applicable)

Section 6	Section 6: Checklists for Annexes and attachments under Annex 2C
Annex A	Formulation of the product (complete qualitative and quantitative composition including active ingredient(s), justification in case of overages, and excipients)
Annex B	Description, composition and specifications (including reference to standards-monographs/inhouse) of primary packaging
Annex C	Description, composition and specifications (including reference to standards-monographs/inhouse) of secondary packaging
Annex D	Certificate of Pharmaceutical Product (CoPP)
Annex E	Copy of latest Marketing Authorization (MA)

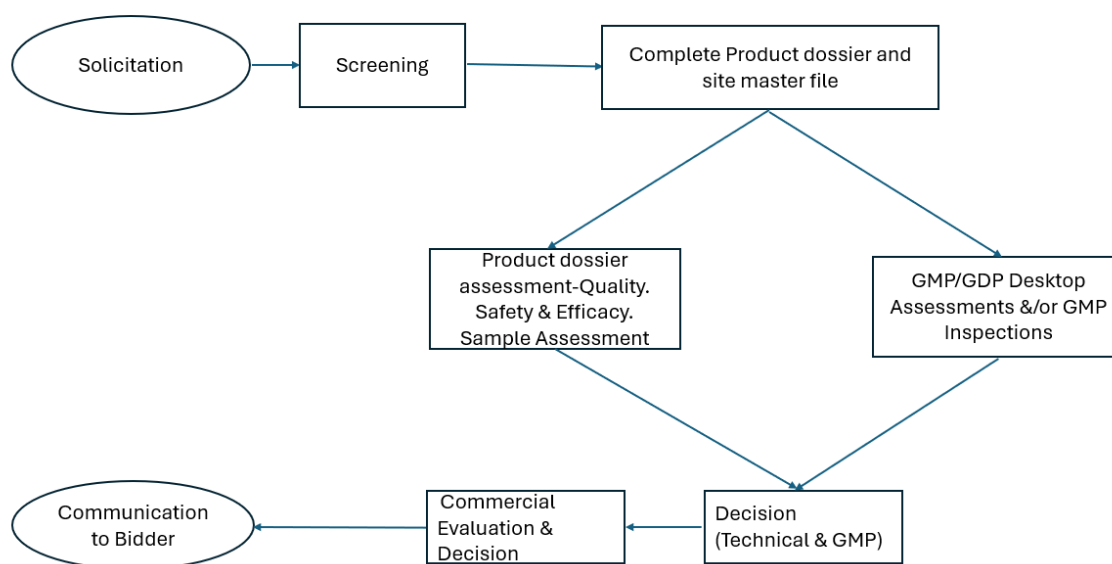
Annex F	Copy of WHO PQ acceptance letter for product dossier including number
Annex G	High Quality Photos of the product, Primary and secondary packaging (New)
Annex H	Copy of primary packaging/label
Annex I	Copy of secondary packaging label
Annex J	PIL/Package insert & SmPC
Annex K	GMP Certificate for API site from the country of origin
Annex L	Copy of FPP manufacturer internal API specifications
Annex M	Validated analytical methods for API
Annex N	Copy of the API certification and annexes
Annex O	Copy of the open part of DMF
Annex P	Data on validation of sterile aspects of the product including recent media fill
Annex Q	Certificate of Analysis (COA) of the API from both API and FPP manufacturers
Annex R	Comparative analysis for different API sources that demonstrate they are equivalent (New)
Annex S	Recent copy of Valid GMP certificate/letter of compliance of the FPP manufacturer
Annex T	Copies of FPP release and shelf life specifications. To attach validated analytical methods if in-house specifications
Annex U	Certificates of analyses (COAs) for the last three batches released
Annex V	Manufacturing process flow diagram and narrative
Annex W	Process validation report
Annex X	Data on validation of sterile aspects of the product including recent media fill
Annex Y	Risk assessment on Nitrosamines
Annex Z	Stability studies protocol and reports for accelerated and longterm and status of report of any ongoing stability studies
Annex AA	Declaration that stability studies have been done or are being done
Annex AB	In-use stability data and storage conditions
Annex AC	Summary on pharmacology, toxicology and efficacy of the product
Annex AD	Graphic/pictorial representation of study design
Annex AE	Copy of report of proof of therapeutic equivalence (Bioequivalence (BE) and Comparative dissolution profile (CDP))

Annex AF	CRO inspection positive outcome evidence and certificate of Accreditation of clinical facility, clinical laboratory and analytical laboratory
Annex AG	Schematic representation of study design and Study protocol
Annex AH	Study protocol summary
Annex AI	Latest Periodic Safety report
Annex AJ	Copy of the power of attorney

Appendix 2: UNICEF'S Supplier Qualification Process Diagram

A simplified process flow diagram below explains UNICEF's Supplier Qualification process for Pharmaceutical Products.

Appendix 2: UNICEF'S Supplier Qualification Process Diagram



Appendix 3: Reference To UNICEF Technical Offer Submission types

Technical offer Types

While this document details ALL general technical requirements, there may be differences of type/number of documents to be submitted with each solicitation/purchase order; please refer to the table below.

1. TABLE SUMMARIZING UNICEF Technical offer requirements

Regulatory pathway	Conditions	Technical Documentation ¹	UNICEF assessment process for GMP
WHO PQ & ERP	N/A	Annex 2f, 2g and 2a	Risk-based desktop GMP assessment informs whether a GMP inspection is required or not ²
WLA/SRA	MAs Acceptable up to 3 years prior to designation as WLA except for previously SRA	Annex 2f, 2g and 2a or 2b	
ML3/ML4	MAs Acceptable from the time of listing as ML3/ML4	Annex 2c, 2d, 2e and 2a. Additional documentation under 1.2.1.3	
Other	Refer to IAFPPQ	Annex 2c, 2d, 2e and 2a.	

1) For description of Annexes, please refer to Appendix 1

2) For REOI Annexes 2a or 2b are not required at the time of tender

References

- ⁱ TRS 1060, 2025 - Annex 3: WHO good manufacturing practices for excipients used in pharmaceutical products
- ⁱⁱ EMA EMA/CHMP/302620/2017 Rev. 2 (Nov 2019): Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' (SANTE-2017-11668)
- ⁱⁱⁱ TRS 1060, 2025 - Annex 2: WHO good practice considerations for the prevention and control of nitrosamines in pharmaceutical products
- ^{iv} *FDA, 2020 – Control of Nitrosamine Impurities in Human Drugs*
- ^v More information about GMP guidelines and Quality assurance systems can be found on the WHO website under
- ^{vi} Quality assurance of pharmaceuticals: a compendium of guidelines and related materials: volume 1: Good practices and related regulatory guidance, 10th ed
- ^{vii} *WHO Technical Report Series 986, 2014 - Annex 2: WHO good manufacturing practices for pharmaceutical products: Main principles*
- ^{viii} TRS 1044, 2022 - Annex 2: WHO good manufacturing practices for sterile pharmaceutical products
- ^{ix} *WHO Technical Report Series 1025, 2020 – Annex 7: WHO good storage and distribution practices for medical products*
- ^x *WHO Technical Report Series 961, 2011 – Annex 14: WHO guidelines for drafting a site master file*
- ^{xi} *EMA, 2016 - Guideline on process validation for finished products - information and data to be provided in regulatory submissions*
- ^{xii} TRS 1044, 2022 - Annex 2: WHO good manufacturing practices for sterile pharmaceutical products
- ^{xiii} *FDA, 2011 - Process Validation: General Principles and Practices*
- ^{xiv} *WHO Technical Report Series 970, 212 – Annex 3: Pharmaceutical development of multisource (generic) finished pharmaceutical products: points to consider*
- ^{xv} WHO TRS, No. 996, 2016, Annex 9. Guidance for organizations performing in vivo bioequivalence studies (revision) (2016)
- ^{xvi} EMA M13B, 2025 Bioequivalence for Immediate-Release Solid Oral Dosage Forms: Additional Strengths Biowaiver
- ^{xvii} WHO TRS, No. 1003, 2017, Annex 5. General background notes on the list of international comparator pharmaceutical products (2017).
- ^{xviii} *WHO Technical Report Series, No. 1025, 2020 - Annex 6: Points to consider for manufacturers and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance*
- ^{xix} *WHO Technical Report Series 1019, 2019 - Annex 3: Good manufacturing practices: guidelines on validation*
- ^{xx} World Health Organisation Technical Report Series (TRS) 953, 2009, Annex 2: Stability testing of active pharmaceutical ingredients and finished pharmaceutical products.
- ^{xxi} *WHO Technical Report Series 1010, 2018 - Annex 10: Stability testing of active pharmaceutical ingredients and finished pharmaceutical products*
- ^{xxii} WHO Technical Report Series, No. 902, 2002, Annex 9: Guidelines on packaging for pharmaceutical products
- ^{xxiii} World Health Organisation, WHO Expert Committee on Specifications for Pharmaceutical Preparations, 43rd Report, Geneva, 2009, Annex 2: Stability testing of active pharmaceutical ingredients and finished pharmaceutical products
- ^{xxiv} WHO prequalification programme (PQP) 'Guidance on Patient Information Leaflet, Summary of Product Characteristics and Labelling.
<http://apps.who.int/prequal/>
- ^{xxv} http://www.who.int/medicines/areas/quality_safety/quality_assurance/ModelGuidanceForStorageTransportTRS961Annex9.pdf
- ^{xxvi} *WHO TRS 1025, 2020 Annex 7: Good distribution practices for medical products*
- ^{xxvii} UNDP (United Nations Development Programme), 2021 - Sustainable Procurement Index for Health (SPIH)