

# UNICEF Technical Requirements for Pharmaceutical Products

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## INTRODUCTION

### General information

UNICEF seeks to provide timely access to affordable medicines and nutrition products that are safe, efficacious and of good quality in both development and humanitarian emergency contexts. Our product range is designed to meet global demand for key health and nutritional interventions and can be tailored for specific country/partner needs to optimize programme success. In principle, UNICEF products are aligned with normative standards and guidelines and designed to facilitate rational use to the lowest level of health care service delivery. WHO Model of Essential Medicines List (EML) [WHO Model Lists of Essential Medicines](#) and disease specific treatment guidelines inform UNICEF product selection. UNICEF Supply Catalogue [All Products \(unicef.org\)](#) lists all standard products, that could be procured on a regular basis, primarily for UNICEF programmes. However, UNICEF undertakes procurement of additional products for special needs on behalf of governments, other UN agencies, non-governmental organizations (NGOs), philanthropic organizations and universities for their programmes and needs and those products are considered non-standard products. WHO technical guidance informs specifications and requirements for procured products, including non-standard items.

This document is intended to assist suppliers, primarily manufacturers of finished pharmaceutical products (FPP), that are participating in UNICEF tenders. Adequately prepared technical documentation/product dossier for a tender is facilitating the process and saves time and effort on both sides.

Quality assessment is done principally via technical assessment of pharmaceutical product dossiers, product samples, Good Manufacturing Practices (GMP) of manufacturers of finished pharmaceutical products (FPP) and active pharmaceutical ingredients (API) as well as their Good Distribution Practices (GDP).

Technical information required for technical assessment is compiled by the supplier/applicant (manufacturer, wholesaler, distributor, marketing license holder etc.) through the **Interagency Finished Pharmaceutical Product Questionnaire (IAFPPQ)** [Interagency finished pharmaceutical product questionnaire | UNICEF Supply Division](#) which is based on the World Health Organization (WHO) Model quality assurance system for procurement agencies (MQAS) [WHO Quality assurance policy for the procurement of essential medicines and other health products](#)

Manufacturer's GMP related information is collected through the **UNICEF Technical Questionnaire for Pharmaceutical Manufacturers** [Technical questionnaire for pharmaceutical manufacturers | UNICEF Supply Division](#) . Wholesalers and manufacturers performing distribution, should demonstrate their GDP compliance. According to the IAFPPQ, the applicant/supplier should clearly indicate their link with the product and be clear about exact address of manufacturing site(s) (and all respective activities performed there) and relation of the manufacturer with potential contractor, wholesaler, distributor, MA holder, external QC facility or other.

Based on the provided information and the history of procurement to UNICEF and/or other partner agencies, GMP/GDP audit will be performed.

This Technical Requirements document provides further explanations to 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.

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

Nutrition products in this document refer to all pharmaceutical vitamin and mineral products designed to prevent and/or treat single nutrient deficiencies, manufactured according to standards for pharmaceutical finished products.

Vendors are encouraged to carefully read this document and all documents provided in links and seek clarifications in advance of any solicitation/tender process.

While this document details ALL general technical requirements, there may be variations of type/number of documents to be submitted with each solicitation/purchase order with respect to:

1. Multisource (generic) finished pharmaceutical products (FPPs) not approved by Stringent Regulatory Authorities (SRAs) – all documents should be submitted;
2. Multisource (generic) FPPs approved by SRAs;
3. Innovator FPPs approved by SRAs;
4. WHO Prequalified products;
5. Any of the above products supplied through a wholesale or distributor or agent.

There is an abbreviated questionnaire and a list of documents required that are used for above mentioned products (2, 3, 4 and 5) and it is annexed to all requests for proposals.

Stringent Regulatory Authority is a regulatory authority which is:

- a member of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), being the European Commission, the US Food and Drug Administration and the Ministry of Health, Labour and Welfare of Japan also represented by the Pharmaceuticals and Medical Devices Agency (as before 23 October 2015) or
- an ICH observer, being the European Free Trade Association, as represented by Swissmedic, and Health Canada (as before 23 October 2015) or
- a regulatory authority associated with an ICH member through a legally-binding, mutual recognition agreement, including Australia, Iceland, Liechtenstein, and Norway (as before 23 October 2015).

The list of countries whose regulatory authorities are considered SRA can be found at [List of Stringent Regulatory Authorities \(who.int\)](#)

## SECTION 1 - GENERAL INFORMATION

### Product identification

Each FPP must be fully identified as stipulated in the most current version of the Interagency Finished Pharmaceutical Product Questionnaire, with the following additional explanations:

1. Finished pharmaceutical product(s) (FPP) should be identified by its International Non-proprietary Name(s) (INN). Generic name(s), British Approved Name(s) (BAN) or others should be stated if different from INN;
2. The Active Pharmaceutical Ingredient(s) (API) should be stated as base, salt, ester or pro-drug compound as applicable.
3. Trade (proprietary) name(s) (if any). UNICEF does not recommend use of trade names and does not approve the same. Information is collected for the record only;
4. Vendor should include relevant pharmaceutical dosage form and dosage form attributes e.g. if tablets are functionally scored, dispersible, enteric coated, bilayered, film coated, sugar coated, what release mechanism the product has (immediate or modified);
5. Specify the strength per dosage unit or the amount of active ingredient per dosage unit. Where this is given in terms of the salt, ester or pro-drug, the equivalent amount of active moiety must be specified; further described in WHO TSR 957 (page 62) 2010 - [44th report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations - TRS, No. 957](#)
6. Specify the route of administration e.g., IM, IV, SC, PO, topical, rectal.
7. 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 and Patient information leaflets. See excipients included in the guideline “Excipients in the labelling and package leaflet of medicinal products for human use” (The rules governing medicinal products in the European Union, Volume 3B) [Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' | European Medicines Agency \(europa.eu\)](#). However, if the FPP is a

parenteral, topical, ophthalmological or if used for inhalation, all excipients must be stated.

8. Mention if product is fixed-dose combination (FDC), co-pack/co-blisters, co-formulated.

## **Biologicals**

Biological therapeutics (Biologicals) and biosimilars are very different in their nature and how they are produced, regulated, tested, and controlled than other medicines. Because of their complexity, at the moment, we accept only products registered by SRA or WHO Prequalified.

## **Packaging**

See Container-closure systems

## **Regulatory (Licensing) status**

Evidence should be provided for all Finished Pharmaceutical Products that the product(s) is/are registered/licensed in the country of manufacture/origin. Where product is registered in the country of manufacture/origin, vendor must indicate whether the product is marketed in that country or registered for EXPORT ONLY.

Vendor should list other countries where the product is registered, including respective license numbers and validity periods. Registration in countries where UNICEF supplies will be sent is important. The countries can be identified from the forecasting information or as specified in the solicitation document.

Vendors must submit a Certificate of Pharmaceutical Product (CoPP or CPP) for each FPP according to the WHO Certification Scheme, or an equivalent, issued by the National Regulatory Authority in the country of manufacture/origin. Recommended CoPP/CPP format is specified in the relevant WHO Technical Report Series (WHO TRS 863, page 163, earlier versions not acceptable - [TRS 863 - 34th report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations](#) ). The CoPP required for tender technical assessment can be for any country. Specific country CoPPs may be required and requested during the procurement process. If a CPP cannot be obtained from the national medicines regulatory authority (NMRA), please state the reason and send an equivalent document if any.

## **Pharmacopoeial standards**

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

1. The British Pharmacopoeia (BP);

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

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 exist) and the general requirements for dosage forms in pharmacopoeia. Where a monograph exists in a pharmacopoeia, the vendor MUST 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. Where an official acceptable monograph exists, the use of in-house methods is discouraged.

In-house methods are considered acceptable where no official monograph exists in the acceptable pharmacopoeias listed above. Reference to “non acceptable” pharmacopoeia will be treated as in-house method.

If in-house specification is used, vendor MUST justify it by giving an explanation AND providing a table comparing monograph and in-house methods side by side. As a general rule, it is expected that 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 as well.

When referencing to Pharmacopoeia, all tests included in the product specification should comply with that Pharmacopoeia. If individual tests refer to different Pharmacopoeias, the FPP cannot refer to one Pharmacopoeia. For example, for “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” (BP)

## **SECTION 2 - ACTIVE PHARMACEUTICAL INGREDIENT(S), INTERMEDIATES AND EXCIPIENTS**

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 manufacturer should be supported with documents demonstrating that APIs from different manufacturers have the same characteristics.

APIs and excipients should comply with the current requirements of the acceptable Pharmacopoeia listed above. API specification from FPP manufacturer, 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.

For sterile API(s) the data on validation of the sterile aspects including recent media fill validation data and description of sterilization used should be submitted.

Submission of the Open part of the drug master file (DMF) for the API, registered in the country of origin, would be appreciated. Characteristics of API/s are very important for the quality and safety of the FPP. We prefer to have some more information about the API that could be found in 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).

UNICEF requires FPP manufacturers to appropriately qualify their API suppliers (including manufacturing site(s) audits for GMP) and to submit a declaration confirming API supplier's qualification. Site audit may be exempted for APIs that are WHO Prequalified [Active Pharmaceutical Ingredients | WHO - Prequalification of Medical Products \(IVDs, Medicines, Vaccines and Immunization Devices, Vector Control\)](#) or that have Certificate of Suitability (CEP) [Certificates catalogue \(edqm.eu\)](#) or where API and/or intermediates manufacturing site has been approved by WHO prequalification or Stringent Regulatory Authority (SRA). An **API declaration form** should be duly filled, signed by the FPP Qualified Person (QP) and submitted together with the Interagency Finished Pharmaceutical Product Questionnaire with every solicitation and at any time a new API source is introduced/changed. API declaration form can be found in the tender documents.

WHO good manufacturing practices for active pharmaceutical ingredients (bulk drug substances) [WHO good manufacturing practices for active pharmaceutical ingredients \(bulk drug substances\)](#)

WHO good manufacturing practices for the manufacture of pharmaceutical excipients Annex 5, WHO Technical Report Series 885, 1999 [WHO good manufacturing practices for the manufacture of pharmaceutical excipients](#)

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 different sites involved.

In the case of introducing a new API source that is not supported by data already submitted, manufacturer should provide, as a minimum proof, that the new API can replace the old one. e.g. 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.

Excipient known to have a recognized action or effect, should be avoided, especially in products for children. Special attention should be given to preservatives, we don't recommend use of preservatives in FPPs. If used, their use should be justified. Sterile parenteral products, especially for single use, must not contain preservatives. Coloring agents, taste correcting agents, coating excipients should not interact with API(s) and that must be proven. Use of sugars should be carefully thought through because of the limitations and possible complications they can cause for some patient groups. CoAs for all excipients should be submitted.

Due attention should be given to residual solvents and degradation products that can affect the quality of FPP. Recovered materials such as solvents, reagents, and catalysts may pose a risk, for example of nitrosamine impurities and risk assessments as well as appropriate actions should be undertaken to reduce or prevent the presence of nitrosamines in APIs and FPPs.

Manufacturers should prioritize quality risk assessment for APIs and FPPs based on factors such as maximum daily dose, duration of treatment, therapeutic indication, and number of patients treated.

FDA, Control of Nitrosamine Impurities in Human Drugs [Control of Nitrosamine Impurities in Human Drugs | FDA](#)

ICH Q9 Quality risk management [ICH Q9 Quality risk management | European Medicines Agency \(europa.eu\)](#)

Special attention should be given to pharmaceutical products that have raw materials (e.g. gelatin) derived from the animal source. Preferably use of those materials should be avoided. 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 contamination.

## SECTION 3 - FINISHED PHARMACEUTICAL PRODUCT

### **Manufacturing site(s) GMDP status**

The manufacturing site(s) including contracted sites, where any aspect of manufacture occurs, must be 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 Good Manufacturing Practice (GMP) and distributed as per the Good Distribution Practice (GDP) guidelines established by WHO. The vendor must submit a copy of the valid Manufacturing Licence and GMP certificates for the sites where the API(s), intermediates and different types of FPP(s) and FPP dosage forms are manufactured, as issued by the relevant authorities in the country of manufacture/origin, stating the products and dosage forms authorised for manufacture at the respective site. In addition, the vendor should submit a copy of their valid Manufacturing and/or Wholesale and/or Distribution license as applicable for distribution of the product.

WHO good manufacturing practices for pharmaceutical products: Main principles, Annex 2, WHO Technical Report Series 986, 2014 [WHO good manufacturing practices for pharmaceutical products: Main principles](#)

WHO good manufacturing practices for sterile pharmaceutical products, Annex 6, WHO Technical Report Series 961, 2011 [Forty-fifth report of the WHO Expert Committee on specifications for pharmaceutical preparations](#)

WHO good storage and distribution practices for medical products, Annex 7, WHO Technical Report Series 1025, 2020 [trs1025-annex7.pdf \(who.int\)](#)

WHO guidelines for drafting a site master file [untitled \(who.int\)](#)

Vendors may be required to submit a copy of the most recent inspection report by the National Regulatory Authority or other agencies as listed in the IAFPPQ.

### **Contract manufacture**



Vendor 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.

## **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 inclusive of the International Committee of the Red Cross (ICRC) - Geneva, Médecins Sans Frontières (MSF) - Geneva, World Health Organisation (WHO) - Geneva and the Pharmaceutical Inspection Co-operation Scheme (PIC/S) inspection authorities. The company will be notified in case such request is received.

## **Manufacturing process and process validation**

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 Appendix 2 of Annex 4 of WHO TRS 970 5<sup>th</sup> edition may be submitted in lieu of the information above. [TRS-970-pdf1.pdf0"0 \(who.int\)](#)

Guideline on process validation for finished products, EMA [Guideline on process validation for finished products - information and data to be provided in regulatory submissions \(europa.eu\)](#)

Process Validation: General Principles and Practices, FDA [Process Validation: General Principles and Practices | FDA](#)

Pharmaceutical development of multisource (generic) finished pharmaceutical products: points to consider - TRS 970 - Annex 3 [Pharmaceutical development of multisource \(generic\) finished pharmaceutical products: points to consider - TRS 970 - Annex 3 \(who.int\)](#)

Copies of the executed production documents should be provided for the batches used in the comparative bioavailability or biowaiver studies.

Copies of the FPP master production documents should be provided for each proposed strength, commercial batch size and manufacturing site.

It is very 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.

In case of sterile products, data on validation on the sterile aspects of the product including media fill validation data and detailed description of method/s of sterilisation should be provided.

We accept the products manufactured by continuous model of manufacture. Manufacturer should provide supportive documents as per ICH Q13 Continuous manufacturing of drug substances and drug products [ICH Official web site : ICH](#)

### **Batch formula**

Please provide the formulation of the product (complete qualitative and quantitative composition including active ingredient(s), overages if any and excipients). Please also indicate the standard for each ingredient (e.g. BP, USP, in-house). Mention specifically if the product is a fixed-dose combination (FDC) or co-packaged.

Development of pediatric medicines: points to consider in formulation [Development of paediatric medicines: points to consider in formulation \(who.int\)](#)

### **Specifications of Finished Pharmaceutical Product (FPP)**

Supplier/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 normally not accepted.

Indicate if the product refers to any recognized pharmacopoeia.

For setting out the specifications refer to ICH's Q6A guideline [Q6A Guideline.pdf \(ich.org\)](#)

Pharmaceutical dosage form could have certain attributes e.g. if tablets are functionally scored, dispersible, enteric coated, bilayered, film coated, sugar coated, what release mechanism the product has (immediate or modified). Functionality of relevant attributes should be supported with analytical methods.

## **The analytical procedures used for testing the FPP and their validation**

If analytical methods are in-house, different from BP, USP and Ph.Int., attach a copy of the analytical methods and analytical validation data.

Copies of the validation protocol and reports for the in-house analytical procedures proposed for routine testing should be provided.

Compendial method(s) should be demonstrated suitable for the control of the proposed FPP therefore 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). If an officially recognized compendial method is used to control related substances that are not specified in the monograph, full validation of the method is expected with respect to those related substances.

TRS 1019 - Annex 3: Good manufacturing practices: guidelines on validation [TRS 1019 - Annex 3: Good manufacturing practices: guidelines on validation \(who.int\)](#)

## **Certificates of Analysis**

A Certificate of Analysis 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 as per WHO Model Certificate of Analysis format - TRS 1010 - Annex 4, WHO Technical Report Series 1010, 2018 [WHO model certificate of analysis - TRS 1010 - Annex 4](#) for the last three production batches are required for submission with tenders.

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 send via e-mail as follows:

- For shipments to UNICEF SD warehouse in Copenhagen, the certificate of analysis should be sent to [danpack-inglists@unicef.org](mailto:danpack-inglists@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](mailto:dangainspections@unicef.org) together with a copy of the packing list and other related shipping documents prior to the delivery estimated time of arrival.

Where applicable, the 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 specifications with limits, the results and the conclusion of the testing. The CoA should include info on FPP's pack size and type, API source(s) used and batch size.

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.

## **Stability**

Supplier must demonstrate stability of the Finished Pharmaceutical Product throughout its intended shelf-life under the climatic conditions prevalent in UNICEF target countries. Majority of countries to which UNICEF supplies pharmaceutical products are in WHO climatic zones III, IVa and IVb.

For the purpose of consistency and ease of logistics, UNICEF requires that all products supplied to or through UNICEF are suitable for transport and storage at Climatic zone IVb ( $30^{\circ}\text{C} \pm 2^{\circ}\text{C}/75\% \text{ RH} \pm 5\% \text{ RH}$ ) 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 used for stability study should be the same as the FPP 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.

In the case of introducing new API sources that are not supported by data already submitted, manufacturer should provide, as a minimum proof, that the new API can replace the old one, e.g. provide a table showing comparability of both methods of synthesis, particle size etc. 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 ( $30^{\circ}\text{C} \pm 2^{\circ}\text{C}/75\% \text{ RH} \pm 5\% \text{ RH}$ ) should be performed on each individual strength, dosage form and container type and size of the FPP unless bracketing or matrixing is applied. Reduced stability study designs such as bracketing and matrixing must be justified;
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 studies should be carried out on at least three primary FPP batches 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 batches (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 APIs, if justified;
  - 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 different 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.
4. Results of six months accelerated stability studies and at least 12 months real time stability studies should be provided. Stability studies should be continued for a period of time sufficient to cover the entire shelf-life as allocated to the FPP;
5. 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 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;
6. 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;
7. 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 ICH regions may not necessarily be labelled for zone III and IV (non-ICH regions), even when supportive stability data exists;
  - i. UNICEF requires that products for supply to non-ICH zones 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;
  - ii. 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;
  - iii. 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 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 guidelines on stability testing of active pharmaceutical ingredients and finished pharmaceutical products, Annex 10, WHO Technical Report Series 1010, 2018  
[TRS1010\\_Annex10.pdf \(who.int\)](#)

Stability testing of active pharmaceutical ingredients and finished pharmaceutical products: Stability conditions for WHO Member States by Region, Appendix 1 - Annex 2, WHO Technical Report Series 953, 2018 (Update March 2021) [Stability testing of active pharmaceutical ingredients and finished pharmaceutical products: Stability conditions for WHO Member States by Region](#)

### **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). Total shelf-life of 36 months or longer is preferred.
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 label, in the package inserts/patient information leaflets and throughout the submitted documentation as well as on shipping packages and documents.
  - 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.
  - c. The recommended storage statements for use based on the stability studies are provided in WHO stability guidelines (TRS1010, Annex10 see the link above).
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.
5. UNICEF prefers fresh production to the extent possible. Total remaining shelf-life shall be reviewed at the time of procurement on a case-by-case basis.

### **Transport and transit storage requirements**

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.
2. The vendor MUST ensure that transport and transit storage temperature/humidity information and any other special handling conditions are clearly visible on 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 Time and Temperature Sensitive Label (below) is a shipment label specific for 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.
5. It is the responsibility of the vendor to inform the freight forwarder or any distributors accordingly and to ensure that product temperature conditions are maintained within acceptable limits during transport and transit. 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 or delivery routes and modes of transport should be utilized when planning transportation.
6. For the products that require cold-chain transportation, temperature monitoring devices should be included in the shipment.

WHO model guidance for the storage and transport of time - and temperature-sensitive pharmaceutical products, Annex 9, WHO Technical Report Series 961, 2011 [untitled \(who.int\)](#)



## **Kits**

Special attention should be given to transport, storage and labelling of kits that are sent to UNICEF SD or directly to countries (Interagency Emergency Health Kit and other kits). Instructions given for each specific kit should be followed, especially for the components that require special conditions (cold-chain, psychotropic substances).

## **Container-closure systems**

Container-closure systems are defined by UNICEF as the sum of packaging components that together contain and protect the dosage form. This includes primary packaging components and secondary packaging components, if the latter are intended to provide additional protection (e.g. light barrier) to the drug product.

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.

WHO guidelines on packaging for pharmaceutical products, Annex 9, WHO Technical Report Series 902, 2002 [trs902-annex9.pdf \(who.int\)](https://www.who.int/publications/m/item/trs902-annex9)

## **General requirements for dosage forms**

At the minimum, all dosage forms must be packed:

1. So as to facilitate course-of-therapy usage, unless specified otherwise;
2. Together with dose measurement and delivery devices as applicable;

3. In tamper-evident packaging;
4. In functional secondary/tertiary packaging strong enough to resist crushing and damage during transportation and storage;
5. Together with patient information leaflet or equivalent.

### **Primary Packaging**

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 active pharmaceutical ingredient (API) and FPP; must be safe for use with the dosage form for the intended route of administration; and be suitable for shipment, storage and worldwide use at extreme temperatures and humidity;
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 shipment;
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;
4. For glass ampoules, single ended, break-off necks are required. Non-glass packaging such as from “blow-fill-seal (BFS) technology (aseptic production of liquid injectables) are acceptable provided that all necessary compatibility and stability studies are adequate;
5. Primary packaging must bear appropriate labels providing content and usage information.

### **Dose measurement and dose delivery devices**

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 (e.g. solutions, emulsions, suspensions and powders or granules), whenever the package provides for multiple doses;
2. Dose measuring devices must be graduated in intervals to allow accurate measurement of all doses approved for that medicine;
3. The dosage scales/volumes embossed on dose measurement devices must be in METRIC units. The use of teaspoonful and other such measurements is not acceptable;
4. For oral liquids or powders for oral liquid, 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);
5. For a 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). 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;

6. An applicator is required to be included with vaginal pessaries.

### **Secondary packaging**

A pack component 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., fiber drums, HDPE bottles for products which are immediately packaged with LDPE bag;
2. Secondary packaging for large volume parenterals is usually the same as shipping packaging, extra care should be taken to make sure that FPP in a primary packaging is well protected and adequately labeled;
3. Light, e.g. carton outside PVC/Alu blister;
4. Microbial and dirt 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.

### **Commercial/marketing pack**

A combination of primary and secondary packaging, whether or not the latter has any overt stability maintenance function.

### **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 logistics and operational efficiency at minimal costs;
2. Ensure user-friendliness and support patient compliance;
3. Maintain safety and minimize medication errors;
4. Be tamper-proof and/or tamper-evident;

5. Make product handling easier, efficient and more automated by use of standard GS1 system for barcodes [GS1 General Specifications - Standards | GS1](#), placed in a manner 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 have to be consistent with other information available on a primary, secondary and tertiary labels.
6. Enable traceability and supply chain safety e.g. incorporate Track-and-Trace systems that assure chain of custody and/or anti-counterfeiting measures;
7. 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 patient is available together with the product.

## Labels

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

Language	English and/or French is/are the standard language/s for labels and pack inserts. Arabic, Portuguese, Russian and Spanish may be requested from time to time. Other local languages specific to recipient country may be requested with specific tenders and/or purchase orders.
Type	Preferably by lithography directly on container/packaging.
Ink/colour	The writing on primary and secondary packs must be in indelible ink, preferably in black on white.

## Information required on labels

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 contain

1. Name of the medicine; The International Non-proprietary Name (INN) name, 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
  - 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 (INNM) recommended by the World Health Organization has been published for the 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 INNM, 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 [International Nonproprietary Names Modified \(who.int\)](http://www.who.int/publications/m/item/international-nonproprietary-names-modified)
  - d. If an INN or INNM 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 \(who.int\)](http://www.who.int/publications/m/item/health-products-policy-and-standards)
  - 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.
2. Names and amounts of excipients known to have a recognized action or effect, e.g. “contains 10% ethanol”, “contains lactose”. If the pharmaceutical product is a parenteral, topical, inhalational or an eye preparation, all excipients must be stated;
  3. Pharmaceutical dosage form;
  4. Route of administration;
  5. The pharmacopoeial 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;
  6. Net quantity per unit pack labelled on that unit pack (primary, secondary, tertiary) in metric units in a visible manner;
  7. Posology and directions for use for the target group(s);
  8. Any special instructions for use e.g. “to be swallowed whole - do not chew”;
  9. Recommended temperature requirements during transport and storage;
  10. Special storage and handling instructions, including warnings and precautions, use of solvents for reconstitution;
  11. If a product has a limited shelf-life after the primary package is opened and manipulated, the in-use period and storage condition should be indicated on the label;
  12. Batch identification;
  13. Manufacture 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.

14. 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.
15. Name and address of manufacturer and marketing authorisation holder. For contract manufacture, indicate as: manufactured by company X for company Y.
16. In special 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.
17. In cases of Large 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/YYYYY). In addition, it is recommended to assign a new batch number for a combined pack to enable tracing and to use expiry date of the product with the shortest shelf life. Manufacturer should ensure that the remaining shelf life of the giving set is higher or aligned with the individual product. Recommendations for minimum information to be provided on the combined product and giving set label:
  - Product name
  - A description of its pharmaceutical form, strength and, where applicable, method of application
  - The pack size expressed in terms of the number, weight or volume of the product in the final container
  - Number of LVPs per shipper carton
  - Number of giving sets per shipper
  - New assigned batch number
  - Storage conditions (more stringent between two materials)
  - Manufacturing date (format in line with the UNICEF packing specifications DD/MM/YYYY)
  - Expiry date (format in line with the UNICEF packing specifications DD/MM/YYYY)
  - Name of distributor or manufacturer

All label information and especially 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 Patient Information Leaflet, to avoid confusion. All information provided in the barcodes of one product should be consistent in all packaging levels (primary, secondary, tertiary). GS1 system should be used for barcodes.

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

1. Information 1-7 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 at all times 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;

Where another names 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;

5. 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 labels without covering important 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 is expected to confirm that they are able to do such labelling, should their samples submitted for technical assessment be different.

### **Summary of product characteristics, pack inserts/patient information leaflets**

Directive 2001/83/EC Labelling and package leaflet, articles 54 and 59 [Microsoft Word - Human Code.doc \(europa.eu\)](#)

The summary of product characteristics (SmPC) as well as a detailed pack insert/patient information leaflet (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 patient information leaflet with each FPP either within the secondary packaging or as part of the label (label booklet) or attached on top of the package. Additionally, electronic means of providing information, such as QR codes are encouraged.

Patient information leaflet (PIL) should include all the necessary information according to the Directive 2001/83/EC (see the link above) or any other SRA regulation on PIL. The following list indicates the most important info that should be included in the PIL:

- Identification of the FPP – name, strength, dosage form, pharmaco-therapeutic group
- Indications
- Info necessary to know before taking the medicine – contra-indications, precautions, interactions with food and/or other medicines, special warnings, different categories of patients should be considered – children, pregnant or breastfeeding women, elderly, persons with specific pathological conditions, possible effects on the ability to drive or operate machinery, emphasize some excipients used that patients should be aware of to stay safe
- Instructions for use for different categories of patients – dosage, route of administration, frequency of administration, duration of treatment, overdose and actions to be taken etc.
- Adverse reactions and actions to be taken
- Expiry date, storage precautions, special warnings concerning the appearance of the product, full qualitative composition and quantitative composition of API/s, presentation of the product (packaging), pharmaceutical form and content in weight, volume or units of dosage
- The name and address of the manufacturer (MA holder)
- The date of the last revision

### **Safety, efficacy and/or therapeutic equivalence**

The report of the proof of therapeutic equivalence (bio-equivalence 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.

The product used in the therapeutic equivalence study should essentially be the same as the one that will be supplied i.e., same materials from the same suppliers, 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 SRA that requires proof of therapeutic equivalence to be submitted as part of their dossier assessment for marketing authorization/product registration.

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



### **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 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.

### **Samples**

Samples should be submitted for each tender when requested from UNICEF technical staff. Manufacturer/vendor will be informed if they need to send the sample.

Photos of the product will be requested at the time when the first purchase order is placed and to be sent prior to the shipment of the product. The photos should clearly show the FPP (tablet, capsule, ampoule, vial, tube etc.), primary and secondary packaging as well as other relevant components e.g. delivery devices like measuring cups and giving sets.

### **Sustainable procurement**

Supplier 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.

At the moment, supplier needs to fill 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 and evaluate manufacturer's practice with waste management, chemicals and toxic impact.

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 (CCl<sub>4</sub>); chloroform; diethyl ether; diisopropyl ether; dimethylacetamide (DMAc); dimethyl ether (DME); dimethylformamide (DMF); hexane; methoxyethanol; n-methyl-2- pyrrolidone (NMP); nitromethane; pentane; or triethylamine (TEA).

Hazardous and highly hazardous solvents should be reduced.

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

Sustainable Procurement Index for Health (SPIH) [Report \(savinglivesustainably.org\)](https://savinglivesustainably.org/)

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.

UNICEF Sustainable procurement procedure [Sustainable procurement procedure | UNICEF Supply Division](#)

### **Notification of changes**

UNICEF should be notified and approve of any changes in the API and/or Finished Pharmaceutical Product specifications, manufacturing site, manufacturing process or changes

to any of the aspects that have been technically evaluated and approved and can have an impact on the quality of the product.

See below links for information on what changes are important for approval:

WHO general guidance on variations to multisource pharmaceutical products

Annex 10, WHO Technical Report Series 966, 2016 [trs966-annex10.pdf \(who.int\)](#)

WHO guidelines on variations to a prequalified product, Annex 3, WHO Technical Report Series 981, 2013 [47th report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations - TRS, No. 981](#)

WHO guidelines on transfer of technology in pharmaceutical manufacturing, Annex 7, WHO Technical Report Series 961, 2011 [untitled \(who.int\)](#)

### **Reporting of Complaints/Adverse events**

In the event that UNICEF SD becomes aware of any Complaint/Adverse event associated with the product(s) supplied to UNICEF SD, it shall be recorded and reported to the manufacturer/LTA holder within one (1) business day after UNICEF SD becomes aware of such an event through its reporting mechanisms.

Contact person in UNICEF SD for complaint and adverse events:

Quality Assurance Specialist Peter Svarrer Jakobsen

Email: [pjakobsen@unicef.org](mailto:pjakobsen@unicef.org)

[rapidalerts@unicef.org](mailto: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.

## **SECTION 4 – 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 authorisations;
3. 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.