

Annex 3

Technical Requirements for Pharmaceutical Products

1.1. Eligibility requirements

Only products approved by a Stringent Regulatory Authority (SRA) for sales within the country of the SRA itself, products that are approved by WHO Prequalified (PQ)/ recommended by the Expert Review Panel (ERP) and/or products that are approved by a National Regulatory Agency are eligible for this bid (as defined below by product).

Products that are subject to WHO prequalification programme; hormonal contraceptives and priority maternal health medicines (Appendix 1) will need to be supplied from a source that is either WHO prequalified or SRA approved. For ease of reference, these products are highlighted in a specific column in the Annex 9. Technical Information and Price Bid Form or for Lot 2 Annex 9a. Technical Information and Price Bid Form for Lot 2).

Bidders shall disclose (part of the Annex 9. Technical Information and Price Bid Form or for Lot 2 Annex 9a. Technical Information and Price Bid Form for Lot 2) whether it or the manufacturer has been involved with product recall or in litigation and arbitration, or whether any FDA 483 warning letters have been issued against the company in the past five years.

These requirements apply to Pharmaceutical Products procured either as stand-alone items or as part of a kit.

1.2. Specifications of Pharmaceutical Products

Specifications of Pharmaceutical Products are listed in the Annex 9. Technical Information and Price Bid Form or for Lot 2 Annex 9a. Technical Information and Price Bid Form for Lot 2).

Wherever items offered are not in compliance with specifications indicated by UNFPA, it is the supplier's responsibility to provide full descriptive specifications and documentation of such items. In such instances the item or items must be clearly marked as not being in compliance with specifications. A field for comments is included to explain variations from the UNFPA specifications.

1.3. Quality assurance system

Bidders are requested to submit a Quality Manual explaining the quality system of the supplier and should include the quality policy in relation to the various activities undertaken by the supplier. The quality system should be in line with the WHO's-Good Storage and Distribution Practices for Medical Products, Annex 7, Technical Report Series 1025, 2020.

Activities to be covered in the QM should also include the following:

- Vendor/supplier/manufacturer pre-qualification;
- Product pre-qualification;
- Storage;
- Distribution of pharmaceutical products including thermo-labile products.

Prequalification of pharmaceuticals and manufacturers/suppliers of pharmaceuticals should be consistent with WHO's current "A Model Quality Assurance System for Procurement Agencies," Annex 3, Technical Series 986, 2014.

1.4. Product information

1.4.1. Product quality assurance

The pharmaceutical products proposed under this bid shall meet the following criteria:

- a. Products shall be:
 - i. WHO pre-qualified OR Expert Review Panel (ERP) recommended; or
 - ii. In compliance with the ICH regulatory standards with authorization to market the products in the ICH/Stringent Regulatory Agency countries and not just for export only; or
 - iii. In compliance with National Regulatory Standards of the country of manufacture.
- b. Products specifications shall comply with or be superior to International Pharmacopoeia (Ph.Int), United States Pharmacopoeia (USP), British Pharmacopoeia (BP), European Pharmacopoeia (Ph.Eur) - using not more than one year old Pharmacopoeia specifications.

1.4.2. Manufacturing sites

A manufacturing site is where any aspect of manufacture of any of the components of the final product occurs.

Once contracted, the supplier shall inform UNFPA of any change in the status of every GMP certificate identified in the list of manufacturing sites included in the respective bid.

UNFPA (WHO in the case the product is prequalified by WHO) must be informed of any changes to the manufacturing site(s) once the National Regulatory Agency has made a decision on the variation according to the [WHO general guidance on variations to multisource pharmaceutical products](#), Annex 10, WHO Technical Report Series 966, 2016. Failure to obtain prior approval of such changes may result in termination of the LTA and any pending orders.

In case of any manufacturing facility relocation or substitution of manufacturing facilities, the supplier shall notify UNFPA of the change and request approval to supply the contracted products from the new location. If the change is approved by UNFPA after an inquiry to WHO for GMP status of the new location, approval will be provided by means of a formal contract modification.

In case any Notice of Concern (NOC) is issued by WHO Prequalification Team in relation to a site where a product supplied is manufactured, the supplier has the responsibility of immediately informing UNFPA on the products affected. For products that are not WHO prequalified, the supplier shall follow UNFPA's change of specifications process and report the variation according to ICH and WHO variation guidelines.

1.4.3. Manufacturer conformity with quality management system standards

For the purpose of quality assurance, it is mandatory for bidders which are not the manufacturer of the products to provide the manufacturer information. Bidders which are not the manufacturer of the

products they intend to bid for must obtain information from the respective manufacturer prior to bid submission.

The pharmaceutical products shall be manufactured in conformance with current GMP (and other supporting guidelines) as recommended by the World Health Organization such as [WHO good manufacturing practices for pharmaceutical products: Main principles, Annex 2](#), [WHO good manufacturing practices for pharmaceutical products: Main principles](#) WHO Technical Report Series 986, 2014. The rest of the GMP supporting guidelines can be accessed from the following link <https://www.who.int/teams/health-product-and-policy-standards/standards-and-specifications/norms-and-standards-for-pharmaceuticals/guidelines/production>.

As part of the Pharmaceutical Product Questionnaire (Annexes 10 and 11), suppliers are requested to submit the documents as listed in the Annexures of the respective questionnaires.

Certificates submitted for quality management systems of the manufacturer shall be in English and must indicate the following:

- a. Manufacturer's name
- a. Specific facility and location
- b. Date of issue
- c. Date of expiry
- d. Scope of inspection
- e. Certifying company's name
- f. Certifying company's country

In case of supplying a copy in a different language, a certified translation into English must be submitted. Model certificate of Good Manufacturing Practices, Annex 5 - WHO Technical Report Series 908

1.4.4. Information to support quality of the Active Pharmaceutical Ingredient (API)

For products that are **NOT** WHO Prequalified, nor SRA approved nor ERP recommended an open part of the drug master file shall be submitted [WHO guidelines on submission of documentation for a multisource \(generic\) finished product: Quality part, Annex 6, WHO Technical Report Series 986, 2014](#) . Where the manufacturer of the API prefers to submit directly to UNFPA, please use the contact details stated in this bidding document.

1.4.5. Shelf life

For products with shelf life, the products shall be recently manufactured and have a minimum shelf life of 75% remaining shelf life or depending on the overall shelf life of the product shall then follow WHO guidance with the agreement of the end user.

[Guidance on setting remaining shelf life 5 for the supply and procurement of 6 Emergency Health Kits](#)
[WHO TRS 1025 Points to consider for setting the remaining shelf-life of medical products upon delivery](#).

1.4.6. Storage conditions

Particular storage conditions (temperature, pressure, humidity, etc.) shall be clearly stated, if applicable. Labelling of the product shall be according to the WHO TRS 902, Annex 9, Appendix 2 [Annex 9](#)

[Guidelines on packaging for pharmaceutical products](#) also in accordance with storage guidance according to the WHO TRS 1025, Annex 7, Appendix 1.

[Annex 7 Good storage and distribution practices for medical products](#)

Keep cool items shall be packed/stored/transported separately and in accordance with temperature requirements for such items.

1.4.7. Country of origin

Bidders shall clearly state the country of origin for each product in the Annex 9. Technical Information and Price Bid Form or for Lot 2 Annex 9a. Technical Information and Price Bid Form for Lot). Country of origin is defined as the country where at least 80% of the product is manufactured.

1.4.8. Product HS Code

Bidders shall submit HS code of each product item in Product and Product and Price Form (Section IX.7). HS Code is the Harmonized Commodity Description and Coding System Code maintained by the World Customs Organization (WCO), an independent intergovernmental organisation with over 170 member countries based in Brussels, Belgium. [WCO Harmonization system](#)

1.4.9. Stability studies

UNFPA supplies many countries with pharmaceutical products and some countries require that the long-term stability studies are performed under Zone IVB conditions. In order to ensure the product quality is maintained throughout the product shelf-life we require that all pharmaceuticals should have undergone stability studies under $30 \pm 2^{\circ}\text{C}/ 75 \pm 5\% \text{RH}$, [WHO guidelines on stability testing of active pharmaceutical ingredients and finished pharmaceutical products, Annex 10, WHO Technical Report Series 1010, 2018](#) and [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](#). Bidders may provide sound scientific justification for not performing the studies e.g. product is unstable at these temperatures. A dated and signed commitment to start and complete stability studies under $30 \pm 2^{\circ}\text{C}/ 75 \pm 5\% \text{RH}$ will be acceptable.

1.4.10. Interchangeability/bioequivalence

For medicines that are eligible for bioequivalence studies (references include to WHO TRS 937, Annex 8), a bioequivalence study protocol and report should be attached to the Inter-Agency Finished Pharmaceutical Product Questionnaire 2019. WHO guidelines on multi source (generic) pharmaceutical products: registration requirements to establish interchangeability Annex 6, WHO Technical Report Series 1003, 2017. Where the finished pharmaceutical product is eligible for a biowaiver, a comparative dissolution study as per WHO TRS 1025, Annex 12, should be attached to Inter-Agency Finished Pharmaceutical Product Questionnaire 2014.

1.4.11. Registration

Bidders shall provide a list of countries registered in the Bid for the products offered.

Once contracted, if product registration is required, the supplier shall be responsible for registration of the Goods with the relevant authorities in the Consignee's country.

1.4.12. Patient information leaflets and package inserts

For medicines, bidders shall submit Patient Information Leaflets (PILs), instructions, etc. in three languages (English, French and Spanish) for the Goods stated in the Product and Price Form (Section IX.7).

Validation of manufacturing process should be submitted for all parenteral products, suspensions, low dose products, modified release products Annex 3: WHO Good manufacturing practices: guidelines on validation . For non-sterile products please refer to the Guidelines on good manufacturing practices: validation, TRS 992, Annex 3, Appendix 7, 2019: non-sterile process validation

1.4.13. Sterilisation

Bidders shall submit validation of sterilisation methods for all sterile goods offered under this Bid. In the case of pharmaceuticals, and as part of the Finished Pharmaceutical Product questionnaire, suppliers shall submit validation of sterilisation methods for all sterile Active Pharmaceutical Ingredients and Finished Pharmaceutical Products offered under this Bid, [WHO good manufacturing practices for sterile pharmaceutical products Annex 6, WHO Technical Report Series 961, 2011](#).

1.4.14. Managing product recalls

UNFPA reserves the right to suspend procurement of products in case of identification of inferior quality and inform publicly where applicable, the NMRA and patients who may be affected.

In the event that UNFPA in co-operation with NMRA in supplied countries decides on product recall, the supplier shall organise this recall and necessary associated activities at the cost of the supplier. Any additional recall expenditure incurred by UNFPA shall be compensated by the supplier.

1.5. **Packing Information**

1.5.1. Packing of goods for international delivery

The cost of packing and the packing material cost shall be included in the bid price offered for the items.

The packing of the product(s) shall be suitably over-packed for shipment in strong triple-wall cardboard boxes¹ and in a manner that shall provide adequate protection of the goods with sufficient buffering of the equipment for carriage by air, sea, and road to final destination and subsequent in-land distribution including remote locations under adverse climatic and storage conditions, and high humidity – i.e. not less than 17kN edge crush resistance with minimum 60% remaining with 90% at a temperature of 40°C (tropical conditions).

The handling and transport of dangerous goods is subject to rules and regulations based on international transport agreements (ADR, RID, IMDG Code, IATA DGR, ICAO) in order to prevent injury to persons, damage to cargoes and living resources. Hence, should any Goods comprised in this Agreement be classified as dangerous goods, it is the supplier's responsibility to ensure that the packing of the Goods take into account any special requirements for dangerous or hazardous goods or cold chain items and are labelled correctly, transported safely and accompanied by the necessary transport certificates during shipment. The cost of packing, including export packing, is included in the price.

¹Here is an example of triple-wall cardboard box:

Outer cartons shall be numbered consecutively. No carton may contain items from more than one manufacturing batch. Cartons containing non-uniform contents must be specially marked with red at the top corners.

Case identification as requested on the order must be mentioned on all invoices.

Packaging of product shall comply with WHO GMP standards:

- Primary packaging – sterile or non-sterile as appropriate. E.g. for sterile items, transparent film to allow clear identification of the content – sachet, plastic box, peel-off sachet. For pharmaceutical products with 30 tablets/capsules or less, it shall be in blister pack. For item with more than 30 tablets/capsules, it should be in bottle;
- Secondary packaging – to protect the primary packaging – e.g. cardboard, rigid wrapping.

1.5.2. Marking and labelling for pharmaceutical products

The labelling of the product shall meet the following requirement:

- a. Primary packaging shall be imprinted with the following:
 - i. Name of manufacturer
 - ii. Address of manufacturer's manufacturing site – where there is space enough
 - iii. Article reference of the manufacturer and the supplier
 - iv. Details to identify device in English, French and Spanish; description, composition as appropriate
 - v. Batch number prefixed by the word "LOT" or equivalent harmonised symbol
 - vi. Items with limited shelf life, expiry date using the words "use before (month)/(year) or prefixed by "EXP" or equivalent harmonised symbol (month)/(year)
 - vii. Items without expiry date, the date of manufacture (year) prefixed by the harmonised symbol, unless information already incorporated into the batch number or serial number
 - viii. For single use items, the words "DO NOT RE-USE" or "FOR SINGLE USE" or equivalent harmonised symbol
 - ix. For sterile items, the word "STERILE" or equivalent harmonised symbol, plus a warning which advises to "check the integrity of the sterile packaging before use."
 - x. Name of drug;
 - xi. Pharmaceutical dosage form
 - xii. Active pharmaceutical ingredient(s); type and amount;
 - xiii. Net quantity per unit
 - xiv. Instructions/direction for use
 - xv. Storage conditions including warnings and precautions
 - xvi. If reconstitution is required, state the storage conditions after reconstitution and shelf-life;
- b. Secondary packaging for pharmaceutical products shall be imprinted with the following:
 - i. Name of manufacturer
 - ii. Address of manufacturing site
 - iii. Labelling same as on primary packaging, in addition –
 - iv. Any special storage conditions and or handling conditions
 - v. Instructions for use in English, French and Spanish.

[WHO Guidelines on packaging for pharmaceutical products, Annex 9, TRS 902, 2002](#)

A product without storage conditions will only be considered for the UNFPA catalogue under the following special circumstances:

- ***When there is proof that the product is stable at Zone IVb climatic conditions. Stability data should be submitted to support the stability of products under Zone IVb climatic conditions***
- ***Only if the product is intended to be part of a kit, and it will be stated as such in the UNFPA catalogue.***

Products intended for bulk purchase should include storage conditions, warnings and precautions as part of the labelling requirements.

- c. Summary of Product Characteristics, package inserts and Patient information leaflets. The content should be in line with WHO SPC template which may be accessed at [ANNOTATED SUMMARY OF PRODUCT \(SmPC\) CHARACTERISTICS TEMPLATE](#)

1.6. Storage and transportation of temperature sensitive pharmaceuticals

Medicines requiring controlled temperatures during storage and transportation shall be provided in accordance with the Model guidance for the storage and transport of time- and temperature-sensitive pharmaceutical products, WHO TRS 961, Annex 9, 2011.

To maintain the desired temperature during transportation containers with dry ice, reefer containers or thermal jackets may be used. Such containers should protect the product from mechanical damage and any anticipated ambient temperature range during transportation and transit; they shall be tamper proof and allow for the recipient to establish that the product has not been tampered with while in transportation and transit.

Temperature in the container(s) during transportation and transit shall be monitored using appropriately calibrated monitoring devices.

Compliance with the required temperature conditions shall be demonstrable to UNFPA and records shall be kept as per Good Distribution Practices, [WHO good storage and distribution practices for medical products](#), Annex 7, WHO Technical Report Series 1025, 2020.

Bidders are requested to submit their established procedures with regards to the storage and distribution of heat sensitive and cold storage items.

Appendix 1

Priority Maternal health medicines

Oxytocin 10 I.U./ml injection in 1ml ampoule

Tranexamic acid, injection, 100mg/ml, 10ml ampoule

Carbetocin, injection 100 microgram/ml in 1 ml

Mifepristone 200mg + 4 misoprostol 200mcg tablets

Misoprostol 200mcg, tablet

Mifepristone 200mg tablet

Ergometrine maleate 0.2mg base/ml injection

Magnesium sulphate 500mg/ml injection

Methyldopa 250mg tablet (Optional)

Hydralazine hydrochloride 50mg tablet (Optional)

Hydralazine hydrochloride 25mg tablet(Optional)

Hydralazine hydrochloride 20mg/2ml(Optional)

Appendix 2

General documentation to consider when preparing submission for pharmaceuticals

(The documents serve as a guidance to the submissions. Manufacturers and/or Suppliers should refer to the annexures of each respective questionnaire and submit the supporting documents according to the questionnaire).

1. Formulation of the product (complete qualitative and quantitative composition including active ingredient(s) and excipients)
2. Description and composition of primary packaging materials including label mockups
3. Description and composition of secondary packaging materials
4. Copy of product registration and market status– Licence No: etc
5. Certificate of pharmaceutical product (CPP) according to the WHO Certification Scheme (WHO Technical Report Series, No. 863. An earlier version is not acceptable)
6. Recent as well as historical deficiency/acceptance letters issued by PQP/SRA in relation to the specific product dossier
7. Copy of the relevant WHO Prequalification acceptance letter signed by your company
8. WHO acceptance letter for product dossier review mentioning the WHO reference number assigned by WHO for this specific product
9. Copy of primary and secondary packaging/label
10. Patient information leaflet/package insert
11. GMP certificate of the API manufacturer(s) from the country of origin
12. Copy of the internal API(s) specification(s)
13. Validated analytical methods if analytical methods for API are in-house analytical methods, different from BP, USP and Ph.Int.
14. Data on validation of the sterile aspects of the product including recent media fill validation data, as applicable
15. Copies of three certificate(s) of analysis each for the API from the API manufacturer as well as from the FPP manufacturer
16. Copy of the certificate of suitability to the European Pharmacopoeia (CEP) and its annexes
17. Attach a copy of the Technical file
18. Recent/valid GMP certificates/letter of compliance of the FPP manufacturer
19. If in-house specification is different from BP, USP and Ph.Int., attach copy of the in-house finished product specifications and also validated analytical methods
20. Copy of the certificate of analysis for the three last batches released
21. Flow diagram and brief narrative describing the manufacturing and control process of this product with relevant parameters

22. Data on validation of the sterile aspects of the product including recent media fill validation data as applicable
23. Protocol and report for accelerated and long-term stability testing
24. Declaration that stability studies have been done or are being done with all declared API sources
25. Status report of any ongoing stability studies
26. In-use stability data and storage conditions after reconstitution for oral powder for suspension, powder for injection, or injection that may be further diluted, or multidose containers
27. Summary of pharmacology, toxicology and efficacy of the product
28. Graphic/pictorial representation of summary study results
29. Copy of the report of the proof of therapeutic equivalence (BE study) comparative dissolution profile, dissolution tests, and others if any
30. Schematic representation of study design, Study protocol summary