ANNEX B – MANDATORY TECHNICAL REQUIREMENTS

1. COMPLIANCE WITH TECHNICAL SPECIFICATIONS AND WHO REQUIREMENTS

1.1 The products offered must meet all the World Health Organization (WHO) requirements currently in force. It should be understood that if WHO requirements are changed during the period of validity of the Long Term Agreement(s) (LTA) resulting from this Request For Proposal (RFP), the corresponding supplier(s) will be required to implement such changes per agreed upon timeline.

1.2 UNICEF reserves the right to reject any product which does not conform to the required specifications, as per the terms contained in "Delivery not Acceptance: Consequences of Delayed Delivery and Non-Conforming Goods" under the UNICEF General Terms and Conditions (GTC) which are annexed to and constitute an integral part of the present RFP and any resulting LTA(s) and Purchase Order(s).

2. WHO RECOMMENDATION

In accordance with its mandate to provide guidance to Member States on health policy matters, WHO issues a series of regularly updated position papers on vaccines and biologicals against diseases that have an international public health impact.

Papers summarizes essential background information on diseases and vaccines/biologicals and conclude with the current WHO position on the use of vaccines/biologicals worldwide.

In 2018 WHO position on rabies vaccines was updated, to replace the 2010 paper. It presents new evidence in the field of rabies and the use of rabies vaccines, focusing on programmatic feasibility, vaccination schedules and improved cost-effectiveness. The recommendations concern the two main immunization strategies, namely vaccination for post-exposure prophylaxis and vaccination for pre-exposure prophylaxis. In the context of post-exposure prophylaxis, recommendations are also provided on the use of **rabies immunoglobulins (**WER9316-201-219.pdf**)**

3. PRODUCTION AND TESTING

3.1 The products offered will be produced and tested in conformity with the requirements of national legislation and the following recommendations (but not limited to) established by the World Health Organization (WHO), or any subsequent revisions: https://www.who.int/teams/health-product-policy-and-standards/standards-and-specifications/norms-and-standards/vaccine-standardization

(a) Good Manufacturing Practices for Sterile Pharmaceutical Products (Annex 2. WHO Technical Report Series No. 1044, 2022)
(b) Good Manufacturing Practices: guideline on validation (Annex 3. WHO Technical Report Series No. 1019, 2019)
(c) Good Manufacturing Practices for Biological Products (Annex 2. WHO Technical Report Series No. 999, 2016)

(d) Good Manufacturing Practices for Pharmaceutical Products: Main principles (Annex 2. WHO Technical Report Series No. 986, 2014)
(e) Good Manufacturing Practices for Pharmaceutical Products (WHO Technical Report Series No.961, 2013)
(f) Good manufacturing practices for blood establishments (Annex 4. WHO Technical Report Series No. 961, 2011)
(g) Good Manufacturing Practices. Water for pharmaceutical use (WHO Technical Report Series No. 970, annex 2 (2012)
(h) Guidelines on viral inactivation and removal procedures intended to assure the viral safety of human blood plasma products (Annex 4. WHO Technical Report Series No. 924, 2004)
(i) Report of a WHO Consultation on Medicinal and other Products in relation to Human and Animal Transmissible Spongiform Encephalopathies (WHO/BLG/97.2)

Other relevant documents:

(j) Guide for Inspection of Manufacturers of Biological Products (WHO/VSQ/97.03)
(k) Guideline for National Authorities on Quality Assurance for Biological Products (WHO Technical Report Series No. 822, 1992)
(l) Recommendations and guidelines for biological substances used in medicine and other documents (Annex 6. WHO Technical Report Series No. 924, 2004)
(m) Good Manufacturing Practices: Requirements for sampling of starting materials (WHO Technical Report Series No. 929, 2005. Annex 2)
(n) Basic elements of Good Manufacturing Practices in Pharmaceutical Production (WHO Technical Report Series No.902, 2002. Annex 5)
(o) Regulation and Licensing of Biological Products in Countries with Newly Developing Regulatory Authorities (WHO Technical Report Series No. 858, 1995)
(p) Guidelines for National Authorities on Quality Assurance for Biological Products (WHO Technical Report Series No. No 822, 1992)

4. ANTISERA/IMMUNOGLOBULINS

Products must meet all the WHO recommended requirements and recommendations currently in force.

a) WHO Expert Committee on Biological Standardization, Forty-fourth report (TRS 848, WHO, 1994).
b) WHO Technical report series 822. WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION. (World Health Organization, 2010)
c) WHO Technical report series 982. WHO expert consultation on Rabies. (World Health Organization, 2013).
d) WHO laboratory techniques in rabies. Fifth edition. Department of control of neglected tropical diseases. Volume 2. February 2019.
e) WHO Guidelines for the Production, Control and Regulation of Snake Antivenom Immunoglobulins. Annex 5. WHO TRS 1004. 2018.
f) Rabies products: WHO position paper – April 2018. Weekly Epidemiological Record.

g) WHO Expert Consultation on Rabies: WHO TRS No1012. Third report. 2018.
h) Rabies products and immunoglobulins: WHO position. Summary of 2017 updates. January 2018.
i) The Immunological Basis for Immunization Series. Module 17: Rabies. WHO November March 2017 (update).
j) WHO Guidelines on management of blood and blood components as essential medicines. Annex 3, WHO TRS 1004. 2017.
k) Rabies product stockpile: fixing the supply chain. WHO. September 2016.
l) WHO good manufacturing practices for biological products. Annex 2, TRS 999, 2016.
m) WHO – World Organization for Animal health. Human and dog rabies products and immunoglobulins. Report of a meeting. Geneva, 12−13 October 2015.
n) WHO Expert Consultation on Rabies: WHO TRS No982. Second report. 2013
o) Recommendations for the Production, control and regulation of human plasma for fractionation. Annex 4, WHO TRS 941. 2007.
p) WHO Requirements for the collection, processing and quality control of blood, blood components and plasma derivatives. Annex 2, TRS 840, 1994.
q) WHO Information Sheet. Ensuring the quality and safety of plasma derived medicinal products (https://www.who.int/publications/m/item/Infosheet-plasma-derived-medicinal-product)
r) WHO AIDE MEMOIRE. Quality and safety of blood products and related substances (https://www.who.int/publications/m/item/aide-memoire-blood-products-and-related-biologicals).

5. NATIONAL REQUIREMENTS

5.1 It is recognized that, because of the special needs for products for the developing countries, the specifications prepared for UNICEF by WHO may be more detailed than those given in the WHO Requirements, although they are not in conflict with them.

5.2 In those aspects where WHO GMP requirements are not detailed enough, other international guidelines will be followed by the manufacturer – e.g., those of the European Union (EudraLex – Volume 4), United States FDA (21 CFR) and International Council for Harmonisation (ICH Q7) – and appropriate justification for the choice will be provided. In such cases WHO will assess against the standard used.

6. CHANGES IN FORMULATION, METHODS OR PROCESSES

6.1 Products meeting all the WHO recommended requirements currently in force are preferred. It should be understood that if WHO requirements, which impact on the products being supplied, are changed during the period of validity of the Offer, manufacturers will be required to implement such changes per agreed upon timeline following notification by WHO via UNICEF.

UNICEF reserves the right to reject any material which does not conform to the required specifications and the awarded Supplier shall forthwith at its own expense make good any material which has been rejected.

7. ACCESS TO FACILITIES

7.1 Under an eventual LTA, the awarded Supplier will be expected to permit UNICEF and WHO, or their representatives as may be designated under notice to the Supplier, to have access to its manufacturing and warehouse facilities at all reasonable times to assess (or periodically reassess) the production and capacity, testing, packaging and storage of the goods, and will provide reasonable assistance for such assessment including the access to information necessary for review of manufacturing protocols, lot production records, test results or quality control reports.

8. LABELS AND PACKAGE INSERTS

8.1 The labels on product primary containers will be those approved by WHO and will be affixed with water-resistant adhesive so that the labels do not become loose or fall off. Labels should state the name of product, name of manufacturer, lot number, dose and mode of administration, expiry date, storage temperature, and number of doses per primary container. Expiry date and lot number will be printed on each primary container in indelible ink. Adsorbed products as well as others known to be freeze sensitive will have the warning "DO NOT FREEZE".

8.2 The package insert will be printed at least in English, French, Portuguese and Russian. Spanish and Arabic are optional. Separate inserts in the language appropriate for the country of destination will be welcome.

9. CLOSURES

Products in vial presentations will be fitted with closures that conform to ISO standards 8362 (parts 2 through 7, as applicable). The container/closure system must be the same as that submitted to or assessed by the WHO-Prequalification Team.

10. RETENTION OF SAMPLES AND TESTING

10.1 Samples of each batch of product supplied under the LTA(s) resulting from this RFP will be retained by the corresponding supplier until their expiry date. These samples will be provided, upon request, to WHO PQT for testing.

11. SHELF LIFE

11.1 The products supplied under the LTA(s) and purchase orders resulting from this RFP will be supplied with the maximum shelf life possible consistent with current product production technology and stability data. Unless separately authorized by UNICEF, the remaining shelf life at the time of dispatch will not be less than the ones stated below:

Product	Remaining shelf life at the time of dispatch
Rabies Immunoglobulin	18 months

12. ADVERSE EVENTS AND RECALLS

In the execution of LTA(s) and purchase orders resulting from this RFP, the corresponding supplier shall in case of:

12.1 Adverse Events

The Supplier shall comply with all applicable laws, regulations and requirements. This includes monitoring, reporting and any consequent modification of product information regarding product safety required under national laws and regulations in the country of manufacture, in any other country in which the product receives marketing authorisation and also as required to fulfil the conditions of WHO prequalification. The terms used surrounding adverse experiences shall have the meanings set forth in the International Conference on Harmonization (ICH) of Technical Requirements of Pharmaceuticals for Human Use E2A Clinical Safety Data Management: Definitions and Standards for Expedited Reporting and the WHO Global Manual on Surveillance of Adverse Events Following Immunization.

The Supplier shall promptly inform WHO RPQ and UNICEF of serious issues (actual or alleged) regarding product safety and shall provide them with information sufficient to consider such issues. UNICEF shall promptly notify the supplier of serious adverse events involving the supplier's product of which they become aware.

12.2 Quality complaints and recalls

The Supplier shall notify UNICEF of any quality complaints that it becomes aware of related to the product delivered to UNICEF. If any circumstance or event may require or make reasonably appropriate any recall or withdrawal of the product or any field alert regarding the product, the supplier shall immediately notify WHO/RPQ and UNICEF and other appropriate entities. When a recall, withdrawal or field alert is required or appropriate, the Supplier shall take all appropriate actions and shall bear all associated expenses.

13. PACKING AND SHIPPING

The product shall conform to international standards for product packaging and labelling. Detailed instructions regarding shipping and requirements for invoice and shipping documents shall be provided to the awarded Supplier as part of each Purchase Order.

The cost of such packaging, packing, and all temperature monitoring devices must be included in the offered price.

All containers, invoices and shipping documents are to bear the expiry dates of the product and appropriate storage temperatures.

14. PACKING, PACKAGING, PACKING LIST, LABELLING AND DANGEROUS GOODS INSTRUCTIONS

14.1 Under the LTA, the supplier will be required to comply with the requirements for packing, packaging, packing list, and labelling Goods set out in the specifications for the Goods, the

Mandatory Technical Requirements and the relevant Purchase Order. This includes those requirements that apply to dangerous goods. The classification of Goods (including packaging) as "Dangerous Goods" is a Supplier responsibility and must be communicated to UNICEF when submitting the Proposal. For any Goods (including packaging) classified as Dangerous Goods, Bidders must submit all relevant Material Safety Data Sheets indicating accurate classification for transport purposes, storage, labelling and shipping requirements when submitting the Proposal.

14.2 The Supplier will also be required to comply with the instructions for markings of the Goods set out in the specifications for such Goods and the relevant Purchase Order.

14.3 The Supplier's costs of complying with the requirements of this Section 18 will be the sole responsibility of the Supplier.

15. BAR CODES AND DATA UPLOAD TO TRACEABILITY AND VERIFICATION SYSTEM (TRVST)

15.1 Mandatory requirement – GS1 barcode

Bar codes are required on all packaging levels used by manufacturers for supply to UNICEF, with the exception of primary packaging. This holds both for the products and their respective diluents if relevant and packed separately. Bar codes shall conform to GS1 standards, allowing through a unique company prefix to identify products available in the global supply chain from each manufacturer. The bar codes shall include Global Trade Item Number (GTIN), lot number and expiry date.

15.2 Preferred requirement – barcode serialization, data aggregation and data availability

On top of the mandatory requirement for barcodes, preference is given to barcodes on all packaging levels, with the exception of primary packaging, conform GS1 standards that:

i) include a serial number,
ii) are aggregated, and
iii) their respective data is uploaded to the Traceability and Verification System (TRVST) upon shipment. Please refer to "Annex C - UNICEF Specifications for Products Barcodes and data upload to Traceability and Verification System (TRVST)" for further information

16. GROSS WEIGHT AND VOLUME

Bidders are required to state the total estimated gross weight and volume of the products offered as part of the PACKING DETAILS SHEET in their TECHNICAL PROPOSAL.

17. TRANSPORT AND STORAGE

All shipments of products on behalf of UNICEF will be arranged through UNICEF designated freight forwarders, unless otherwise specified. The awarded Supplier will contact and provide assistance and all documents to the UNICEF designated freight forwarder well in advance of the scheduled delivery date. Any expected delay in delivery of the shipment will be communicated to UNICEF and the UNICEF designated freight forwarder without delay.

18. STANDARD DOCUMENTS

In the execution of LTA(s) and PO(s) resulting from this RFP, the Supplier will submit to the UNICEF Freight Forwarder the following documentation:

a. Invoice;
b. Packing list; the Packing List must clearly indicate the Purchase Order item number(s) contained in each package, a description of the Goods, their value, quantity, gross weight, volume in cubic meters, dimensions and markings, expiry date of the product, and appropriate storage temperature;
c. Release certificate issued by the National Regulatory Authority of the country of manufacture for each lot of product supplied;
d. If applicable, hazardous Goods documents, such as in the case of use of dry ice;
e. Any other documents as specified in each Purchase Order.

19. TIME TEMPERATURE MONITORING DEVICE

In order to monitor the cold-chain during international transit to Government central stores, manufacturers are requested to include WHO PQS prequalified electronic shipping indicators. These devices should, at a minimum, meet the specifications outlined in PQS performance specification for electronic shipping indicators, E006/TR07.4 https://extranet.who.int/prequal/key-resources/documents/pqs-performance-specification-e006tr074-electronic-shipping-indicators-0 or any updated version of the same specification, in each and every shipping carton. These devices meeting WHO requirements for international shipments can be found at the following site: https://extranet.who.int/prequal/key-resources/documents/pqs-performance-specification-e006tr074-electronic-shipping-indicators-0

Use of temperature monitoring devices powered by lithium batteries other than coin cells should be avoided (IATA 2017 Lithium Battery Guidance Document) as this would require shipments to be labelled as Dangerous Goods.

20. DELIVERY PREPARATION LEAD-TIME

Bidders will indicate, as part of their COMMERCIAL PROPOSAL, the delivery preparation lead-time for each product and presentation after receipt of an order. Delivery preparation lead-time includes time to complete administrative arrangements, including documentation, packing and marking.