ANNEX B – MANDATORY TECHNICAL REQUIREMENTS

1. COMPLIANCE WITH TECHNICAL SPECIFICATIONS AND WHO REQUIREMENTS

1.1 The vaccines 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 vaccine 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 PRE-QUALIFICATION

Only vaccines which are pre-qualified by WHO will be procured by UNICEF.

3. PRODUCTION AND TESTING

3.1 The vaccines 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 pharmaceutical products: main principles (WHO Technical Reports Series No. 986 Annex 2, 2014)
b) Good manufacturing practices for sterile pharmaceutical products (WHO Technical Report Series No.961, 2011. Annex, 6)
c) Good Manufacturing Practices for Biological Products (WHO Technical Report Series No. 999, Annex 2, 2016)
d) Good Manufacturing Practices. Water for pharmaceutical use (WHO Technical Report Series No. 970, annex 2 (2012)
e) WHO good practices for pharmaceutical quality control laboratories (WHO Technical Report Series No. 957 Annex 1)
f) Guidance on good data and record management practices (WHO Technical Report Series, No. 996, Annex 5 (2016))
g) WHO guidelines on quality risk management. WHO Technical Report Series, No. 981), Annex 2, 2013
h) Good Manufacturing Practices: Requirements for sampling of starting materials (WHO Technical Report Series No. 929, 2005. Annex 2)
i) Supplementary guidelines on good manufacturing practices: validation. WHO Technical Report Series, No. 937), Annex 4, 2006

j) General Requirements for the Sterility of Biological Substances (WHO Technical Report Series No. 530, Annex 4, 1973), Amendment 1995 (WHO Technical Report Series No. 872, Annex 3, 1998)
k) Recommendations for the evaluation of animal cell cultures as substrates for the manufacture of biological medicinal products and for the characterization of cell banks (WHO Technical Report Series No. 978, annex 3, 2013)
l) WHO Guidelines on Nonclinical Evaluation of Vaccines (WHO Technical Report Series No. 927, Annex 1, 2005)
m) Guidelines on the nonclinical evaluation of vaccine adjuvants and adjuvanted vaccines (WHO Technical Report Series No. 987, annex 2, 2014)
n) Guidelines on Clinical Evaluation of Vaccines: Regulatory Expectations (WHO Technical Report Series No. TRS 1004, Annex 9, 2017)
o) Guidelines on stability evaluation of vaccines (WHO Technical Report Series No. 962, Annex 3, 2011)
p) Guidelines on procedures and data requirements for changes to approved vaccines (WHO Technical Report Series No. 993, Annex 4, 2015)
q) Guidance on Variations to a Prequalified Vaccine, July 2015 https://extranet.who.int/prequal/sites/default/files/document_files/PQ_VXA_Variations_V7.pdf
r) Report of a WHO Consultation on Medicinal and other Products in relation to Human and Animal Transmissible Spongiform Encephalopathies (WHO/BLG/97.2), Geneva, March 1997
s) WHO Guidelines on Transmissible Spongiform Encephalopathies in relation to Biological and Pharmaceutical Products, Geneva, 2003
t) WHO good practices for pharmaceutical microbiology laboratories. WHO Technical Report Series, No. 961), Annex 2
u) WHO guidelines for drafting a site master file. (WHO Technical Report Series, No. 961), Annex 14, 2011
v) Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. WHO Technical Report Series, No. 961), Annex 9
w) WHO Guidelines for independent lot release of vaccines by regulatory authorities. WHO TRS 978, Annex 2.
x) Guidelines on the stability evaluation of vaccines for use under extended controlled temperature conditions (WHO Technical Report Series No. 999, Annex 5, 2016)
y) WHO Infection Control Guidelines for Transmissible Spongiform Encephalopathies. WHO/CDS/CSR/APH/2000.3. Geneva March 1999
z) WHO Guidelines on Tissue Infectivity Distribution in Transmissible Spongiform Encephalopathies. WHO, 2006. https://apps.who.int/iris/bitstream/handle/10665/43498/9789241547017-eng.pdf
aa) Assessing the programmatic suitability of vaccine candidates for WHO prequalification. WHO/IVB/14.10. WHO 2014.
bb) Guidelines on the quality, safety and efficacy of plasmid DNA vaccines, Annex 2, TRS No 1028 Replacement of Annex 1 of WHO Technical Report Series No. 941 10 March 2021: https://www.who.int/publications/m/item/plasmid-dna-vaccines-annex-2-trs-no-1028
cc) Guidelines on the quality, safety and efficacy of biotherapeutic protein products prepared by recombinant DNA technology. WHO TRS No. 987 Annex 4, 2014

dd) WHO Recommendations, Guidelines and other documents related to the manufacture and quality control of biological substances used in medicine. WHO TRS No. 999 Annex 1, 2016

ee) Regulatory assessment of approved rDNA-derived biotherapeutics. WHO TRS No. 999 Annex 3, 2016

ff) Evaluation of the quality, safety and efficacy of messenger RNA vaccines for the prevention of infectious diseases: regulatory considerations (WHO/BS/2021.2402 under final review)

4. VACCINES

4.1. The offered vaccines must meet all the WHO requirements and recommendations currently in force: DT Based Combined Vaccines.

4.2. In case the Supplier has agreed with WHO that any supplementary material is to be provided together with the vaccine, UNICEF requests to receive samples of such material as well and they should also be available to be supplied to WHO on request.

5. NATIONAL REQUIREMENTS

5.1 It is recognized that, because of the special needs for vaccines 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. PROGRAMMATICALLY PREFERRED VACCINE CHARACTERISTICS

Some vaccine characteristics have been identified as programmatic preferences, although they are not currently mandatory for acceptance for prequalification evaluation. These characteristics are described in WHO's guideline "*Assessing the programmatic suitability of vaccines considered for WHO prequalification" (WHO/IVB/14.10)*. The below preferred characteristics will in particular be considered by UNICEF:

6.1 Labelling

6.1.1 Labelling is included in WHO's guideline "Assessing the programmatic suitability of vaccines considered for WHO prequalification" as preferred vaccine characteristics.

6.1.2 Programmatic preference for Labels are:

- Primary and secondary containers should be labelled according to the principles set out in TRS 996, Annex 2 and Annex 3.

7. CHANGES IN FORMULATION, METHODS OR PROCESSES

7.1 For WHO prequalified vaccines, changes introduced in formulation, in methods of manufacturing in facilities or in any other aspects of production which might result in a change of safety and/or efficacy of the vaccines, or which change the licensing agreement between the manufacturer and the National Regulatory Authority should be notified to the WHO Regulation and Prequalification Department (RPQ), WHO's Prequalification Team (hereafter WHO PQT) in accordance with the WHO agreed timeframe. If the regulations of the country of manufacture do not require approval of the changes by the NRA, then the WHO RPQ Department (WHO PQT) in Geneva should be consulted in a timely manner before the changes are introduced.
Refer to WHO Guidance on Variations to a Prequalified Vaccine July 2015:
https://extranet.who.int/prequal/sites/default/files/document_files/PQ_VXA_Variations_V7.pdf

7.2 Such changes may require additional activities by WHO to assure continued compliance with WHO requirements.

8. ACCESS TO FACILITIES

8.1 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.

9. LABELS AND PACKAGE INSERTS

9.1 The labels on vaccine primary containers will be those approved by WHO as part of the prequalification process 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 vaccine, 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 vaccines as well as others known to be freeze sensitive will have the warning "DO NOT FREEZE".

9.2 The package insert will be that approved by WHO during prequalification or as revised and accepted by WHO, in correspondence with WHO recommendations (e.g. position papers if available) and 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 desirable. In all inserts the following should be inserted under "Description of vaccines". "The vaccine fulfils WHO requirements for….. (Name of vaccine)".

10. CLOSURES

Vaccines 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.

11. VACCINE VIAL MONITORS (VVM)

11.1. UNICEF requests vaccines with Vaccine Vial Monitors.

11.2. Vaccine vials should be fitted with Vaccine Vial Monitors (VVMs). VVMs should comply with WHO PQS Performance Specification (WHO/PQS/E006/IN05.3) or such updated version and in the PQS independent type-testing protocol (WHO/PQS/E006/IN05.VP.3). More information about VVM can be found here:
https://extranet.who.int/prequal/key-resources/documents/pqs-performance-specification-e006in054-vaccine-vial-monitor
https://extranet.who.int/prequal/key-resources/documents/pqs-independent-type-testing-protocol-e006in05-vp4-vaccine-vial-monitor

12. RELEASE CERTIFICATION

12.1. Final acceptance of vaccines will be subject to lot release by the National Regulatory Authority (NRA) of the country of manufacture or the NRA of Record agreed to with WHO during review for prequalification. Lot release certificates must be based as a minimum on review of the lot summary protocols.

12.2. The lot release certificate issued by the NRA of Record stating that the vaccine lots supplied meet the relevant national and WHO requirements, should accompany each shipment. Copies should be provided, upon request, to WHO PQT.

12.3. Lot release certificates and Production and Control Summary Lot Protocols (according to WHO guidelines) will be provided, upon request, to consignees, UNICEF or WHO.

13. RETENTION OF SAMPLES AND TESTING

13.1 Samples of each batch of vaccine supplied under the LTA(s) resulting from this RFP will be retained by the corresponding Supplier until their expiry date, in line with the post-prequalification requirements set out in the "*Procedure for assessing the acceptability, in principle, of vaccine for purchase by United Nations agencies*" (WHO TRS 978 annex 6) and further specified in the conditions of the WHO prequalification decision letter, as well as per GMP requirements (WHO TRS 999 annex 2). These samples will be provided, upon request, to WHO PQT for testing.

14. SHELF LIFE

14.1 The vaccines supplied under the LTA(s) and purchase orders resulting from this RFP will be supplied with the maximum shelf life possible consistent with current vaccine

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:

Vaccine	Remaining shelf life at the time of dispatch
DTwP-HepB-Hib	18 months
DTwP-HepB-Hib-IPV	18 months

15. PROPOSALS OF VACCINES NOT YET WHO PRE-QUALIFIED

If the Bidder offers a vaccine that is not WHO pre-qualified, the Proposal must include a detailed plan on the timeline to obtain WHO pre-qualification. The timeline should include information regarding the vaccine and plans for manufacturing and licensing:

- Vaccine Development: Status and plans, including source of bulk antigens to be used;
- Clinical Trials: Trials conducted so far and planned, with timelines;
- National Regulatory Registration: Status and plans for registration, including NRA that would be responsible for release of the finished vaccine and planned vaccine presentations; and
- File submission to WHO: Status and plans.

If the Bidder's Proposal was deemed of interest to UNICEF, UNICEF will advise the bidder of such and will request that UNICEF be kept informed about the progress of the submitted timeline.

If the offered vaccine obtains WHO pre-qualification during the award period and upon confirmation that the mandatory requirements of this RFP are met, UNICEF would consider awarding a quantity to the Bidder under one or more of the following conditions:

- UNICEF is facing a monopoly situation or a near monopoly situation;
- Lack of performance of current supplier(s);
- Insufficient supply from current supplier(s);
- If it meets the specific objectives of the tender; or
- To meet unallocated demand quantities.

The quantities considered for award would be those not met under established contracts or quantities that could be reallocated from existing LTA(s) after negotiation with the corresponding suppliers.

16. ADVERSE EVENTS AND RECALLS

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

16.1 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 vaccine safety required under national laws and regulations in the country of manufacture, in any other country in which the vaccine 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 vaccine 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 vaccine of which they become aware.

16.2 Quality complaints and recalls

The Supplier shall notify UNICEF of any quality complaints that it becomes aware of related to the vaccine delivered to UNICEF. If any circumstance or event may require or make reasonably appropriate any recall or withdrawal of the vaccine or any field alert regarding the vaccine, 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.

17. PACKING AND SHIPPING

Packaging/Shipping arrangements will be in accordance with the WHO Guidelines on the International Packaging and Shipping of Vaccines, Seventh Edition: https://www.who.int/publications/i/item/9789240109544 or any subsequent revisions.

Detailed instructions regarding shipping and requirements for invoice and shipping documents will be provided to the awarded Supplier as part of each Purchase Order.

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

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

18.1 Under the LTA, the Supplier will be required to comply with the requirements (as updated from time to time) for packing, packaging, packing list, and labelling goods set out in the WHO Guidelines on the International Packaging and Shipping of Vaccines, Sixth Edition, (or any subsequent revisions to such Guidelines) and the additional requirements (if any) 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, labeling and

shipping requirements when submitting the Proposal.

18.2 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.

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

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

20.1 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 vaccines and their respective diluents if relevant and packed separately. Bar codes shall conform to GS1 standards, allowing through a unique company prefix to identify vaccines available in the global supply chain from each manufacturer. The bar codes shall include Global Trade Item Number (GTIN), lot number and expiry date (written as MM.YYYY, see WHO Guidelines on the International Packaging and Shipping of Vaccines, Sixth Edition, (or any subsequent revisions to such Guidelines).

20.2 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 Vaccine Barcodes and data upload to Traceability and Verification System (TRVST)" for further information

21. GROSS WEIGHT AND VOLUME

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

22. TRANSPORT AND STORAGE

All shipments of vaccines 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.

23. 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 vaccine, and appropriate storage temperature;
c. Manufacturer's Summary Lot Protocol and release certificate issued by the National Regulatory Authority of the country of manufacture for each lot of vaccine 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.

24. TIME TEMPERATURE MONITORING DEVICE

In order to monitor the cold-chain during international transit to Government central stores of vaccines 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.

25. DELIVERY PREPARATION LEAD-TIME

Bidders will indicate, as part of their COMMERCIAL PROPOSAL, the delivery preparation lead-time for each vaccine and presentation after receipt of an order. Delivery preparation lead-time includes time to complete administrative arrangements, including documentation, packing and marking. The maximum lead time should not exceed 30 days.