# Annex D – 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 and recommendations currently in force. It should be understood that if WHO requirements are changed during the period of validity of the LTA(s) resulting from this 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 and PAHO General Terms and Conditions (Goods) included as annex [Annex A and Annex B] which constitutes an integral part of the present RFP and any resulting Long Term Arrangements (LTAs) and Purchase Order(s).

## 2. WHO PREQUALIFICATION/EMERGENCY USE LISTING

Only vaccines which are recommended under the WHO Prequalification program (prequalified or EUL) will be procured by UNICEF and PAHO.

If WHO Prequalified and/or EUL vaccines are or become insufficient to meet the public health needs, UNICEF and PAHO may, as an exceptional measure, consider procuring vaccines that comply with certain criteria such as marketing authorization granted, and oversight by an Stringent Regulatory Authority (SRA) which will be considered the National Regulatory Authority of Record (refer to section 11). Self-Financing Self-Procuring COVAX economies may exceptionally decide to procure a vaccine based on SRA approval for which an APC is established.

## 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 established by the World Health Organization (WHO), or any subsequent revisions
https://www.who.int/medicines/regulation/tsn/en/
https://www.who.int/immunization_standards/vaccine_regulation/en/:

(a) Guidelines on clinical evaluation of vaccines: regulatory expectations. WHO TRS No. 1004 Annex 9, 2017.
(b) Good Manufacturing Practices for biological products. WHO TRS No. 999 Annex 2, 2016.
(c) Regulatory assessment of approved rDNA-derived biotherapeutics. WHO TRS No. 999 Annex 3, 2016.

(d) Points to Consider for assuring the quality, safety and efficacy of RNA vaccines"7 (currently under development).
(e) Guidance on good data and record management practices. WHO TRS No. 996 Annex 5, 2016.
(f) 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.
(g) Guidelines on procedures and data requirements for changes to approved vaccines. WHO TRS No. 993 Annex 4, 2015.
(h) Good Manufacturing Practices for pharmaceutical products: main principles. WHO TRS No. 986 Annex 2, 2014.
(i) Guidelines on the quality, safety and efficacy of biotherapeutic protein products prepared by recombinant DNA technology. WHO TRS No. 987 Annex 4, 2014.
(j) Guidelines for assuring the quality, safety, and efficacy of plasmid DNA vaccines" adopted by the Seventy-first Meeting of the World Health Organization Expert Committee on Biological Standardization, 24–28August 2020.
(k) Guidelines on the nonclinical evaluation of vaccine adjuvants and adjuvanted vaccines. WHO TRS No. 987 Annex 2, 2014.
(l) WHO guidelines on quality risk management. WHO TRS No. 981 Annex 2, 2013.
(m) 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 TRS No. 978 Annex 3, 2013.
(n) Good Manufacturing Practices: water for pharmaceutical use. WHO TRS No. 970 Annex 2, 2012.
(o) Assessing the programmatic suitability of vaccine candidates for WHO prequalification. WHO/IVB/12.10. WHO 2012.
(p) Good Manufacturing Practices for sterile pharmaceutical products. WHO TRS No. 961 Annex 6, 2011.
(q) WHO guidelines for drafting a site master file. WHO TRS No. 961 Annex 14, 2011.
(r) Guidelines on stability evaluation of vaccines. WHO TRS No. 962 Annex 3, 2011.
(s) Good Practices for pharmaceutical quality control laboratories. WHO TRS No. 957 Annex 1, 2010.
(t) Supplementary Guidelines on Good Manufacturing Practices: validation. WHO TRS No. 937 Annex 4, 2006.
(u) WHO Guidelines on Tissue Infectivity Distribution in Transmissible Spongiform Encephalopathies. WHO, 2006.
(v) Good Manufacturing Practices: requirements for sampling of starting materials. WHO TRS No. 929 Annex 2, 2005.
(w) Guidelines on the international packaging and shipping of vaccines. WHO/V&B/05.23
(x) WHO guidelines on nonclinical evaluation of vaccines. WHO TRS No. 927 Annex 1, 2005.
(y) WHO Guidelines on Transmissible Spongiform Encephalopathies in relation to Biological and Pharmaceutical Products. Geneva, 2003.
(z) WHO Infection Control Guidelines for Transmissible Spongiform Encephalopathies. WHO/CDS/CSR/APH/2000.3. Geneva March 1999.

(aa) General Requirements for the sterility of biological substances. WHO TRS 872 Annex 3, 1998.
(bb) Guidance on Variations to a Prequalified Vaccine. (http://www.who.int/immunization_standards/vaccine_quality/).
(cc) 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

## 4. VACCINES

(a) WHO Target Product Profile for COVID-19 Vaccines https://www.who.int/publications/m/item/who-target-product-profiles-for-covid-19-vaccines
(b) Considerations for the Assessment of COVID-19 Vaccines for Listing by WHO, DRAFT document for consultation: https://www.who.int/medicines/regulation/prequalification/prequal-vaccines/WHO_Evaluation_Covid_Vaccine.pdf?ua=1
(c) Relevant WHO documents for SARS-CoV-2 vaccines and other biologicals https://www.who.int/biologicals/Relevant_WHO_documents_for_SARS-CoV-2_vaccines_and_other_biologicals.TZ.IK.7_Apr_2020.pdf?ua=1

## 5. PROGRAMMATICALLY PREFERRED VACCINE CHARACTERISTICS

In the context of the ongoing global pandemic, WHO is currently developing its position with regards to addressing challenges related to i) labeling and package inserts; ii) barcodes/QR codes; and iii) shelf life. As additional information become available, this will be provided without delay.

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 also be considered by UNICEF:

5.1 Labelling and package inserts

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

5.1.2 Programmatic preference for labels:

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

5.1.3 The labels on vaccine primary containers will be those accepted by WHO as part of the EUL or 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".

5.1.4 The package insert will be that accepted by WHO during prequalification or EUL 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 and Portuguese. Spanish and Arabic are optional. Separate inserts in the language appropriate for the country of destination would be desirable. In all inserts the following should be inserted under "Description of vaccines". "The vaccine fulfils WHO requirements for….. (Name of vaccine)".

5.1.5 The labels for diluent's primary container will be affixed with water-resistant adhesive so that the labels do not become loose or fall off. They must be labelled with the same information as the label of the vaccine primary container, except that "Diluent for…. vaccine" should replace the name of the vaccine. Since diluents are not intended to be administered as a standalone product, information on dose and mode of administration is not included in their labelling.

## 6. CLOSURES

Vaccines in vial presentations will be fitted with closures g conform to ISO standards 8362 (parts 2 through 7, as applicable). As for other vaccine characteristics, the container/closure system must be the same as that submitted to or assessed by the WHO Prequalification.

## 7. VACCINE VIAL MONITORS (VVM)

In line with WHO's guidelines (WHO/IVB/14.10), UNICEF prefers vaccines with Vaccine Vial Monitors.

Vaccine vials should be fitted with Vaccine Vial Monitors (VVMs). VVMs should comply with WHO PQS Performance Specification (WHO/PQS/E06/IN05.2) or such updated version and in the PQS independent type-testing protocol (WHO/PQS/E06/IN05.VP.1). More information about VVM can be found here:
http://www.who.int/immunization_standards/vaccine_quality/vvm_10years_index/en/
or https://apps.who.int/immunization_standards/vaccine_quality/pqs_catalogue/

In the current pandemic phase, VVMs are preferred characteristics but not mandatory, in line with the Target Product Profile listed under section 4 (a) above.

## 8. BAR CODING

WHO is currently developing its position with regards to barcodes/QR codes in the current

pandemic situation. As additional information become available, this will be provided without
delay.

With implementation latest 31st December 2021, bar codes are required on all packaging levels used by manufacturers for supply to UNICEF, with the exception of primary packaging. 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. In support of the general efforts to improve traceability systems for health products in the supply chain, for this tender bar codes are included as a preferred characteristic with specifications included in Annex E

## 9. RELEASE CERTIFICATION

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 or EUL. Lot release certificates must be based as a minimum on review of the lot summary protocols.

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.

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

## 10. SHELF LIFE

WHO is currently developing its position with regards to shelf life with the aim to ensure access
to vaccines in the current pandemic situation. As additional information become available, this
will be provided without delay.

The vaccines supplied under the LTAs 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. Deviations of the agreed remaining shelf-life may be separately authorized by UNICEF in time.

## 11. PROPOSALS OF VACCINES NOT YET APPROVED UNDER THE WHO EUL OR PREQUALIFICATION PROCEDURE

If the Bidder offers a vaccine that is not yet recommended by WHO under the EUL or prequalification process, the Proposal must include a detailed plan on the timeline to obtain

WHO prequalification. 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 approval: Status and plans for approval, including NRA that would be responsible for release of the finished vaccine and planned vaccine presentations; and
- EUL/Prequalification dossier 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.

In case the offer of WHO EUL/prequalified vaccines are or becomes insufficient to meet the public health needs, UNICEF and PAHO may, as an exceptional measure, consider procuring licensed vaccines which comply with certain criteria such as oversight by an SRA.

This may be the case in the following situations:
If the offered quantity of WHO recommended vaccines under EUL or prequalification does not meet the specific objectives of the tender (fully), e.g.:

1) There are unallocated demand quantities;
2) There are exceptional emergency situations (increased demand and/or changed requirements) that requires additional supply for emergency response;
3) Insufficient supply from current Supplier(s);
4) Lack of performance of current Supplier(s);
5) UNICEF is facing a monopoly situation or a near monopoly situation.

UNICEF and PAHO may procure vaccines which are not Prequalified or approved under the EUL procedure by the WHO. Should UNICEF and PAHO decide to procure such vaccines, procurement will be subject to specific contracting terms. The process will be based on additional criteria and technical information which will be used for determining a potential award as detailed below:

i. The vaccine shall be licensed by the NRA in the Country of Manufacture, and this NRA must be considered a Stringent Regulatory Authority (as assessed by WHO Regulatory Systems Strengthening) which takes responsibility for the regulatory oversight of the vaccine, including issuing lot release certificates for supplied vaccines, under the guidance of WHO.
ii. Manufacturers that have obtained WHO pre-qualification for at least one (1) vaccine product will be preferred.
iii. Manufacturers should provide the plans to ensure the active data collection and the analysis of information on the safety and effectiveness of the product.

iv. The vaccine dossier (as per CTD, following ICH format) and summary of the assessment report issued by the SRA of record shall be provided.

v. Procurement of the offered vaccine is conditional to country acceptance, including the capacity to meet post deployment monitoring requirements. PAHO reserves the right to share with any interested Member State all relevant information to facilitate country decision.

## 12. ADVERSE EVENTS AND RECALLS

In the execution of LTAs 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 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 Prequalification 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.

12.2 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 Prequalification and UNICEF and other entities, as required. 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. CHANGES IN FORMULATION, METHODS OR PROCESSES

13.1 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 NRA should be notified to the, WHO's Prequalification Team (hereafter WHO PQT) in accordance with current WHO guidance document and the agreed timeframe. If the regulations of the country of manufacture do not require approval

of the changes by the NRA, then the WHO PQT should be consulted in a timely manner before the changes are introduced.

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

## 14. PACKING AND SHIPPING

Packaging/Shipping arrangements will be in accordance with the WHO "Guidelines on the International Packaging and Shipping of Vaccines", (WHO/IVB/05.23, http://apps.who.int/iris/bitstream/10665/69368/1/WHO_IVB_05.23_eng.pdf) 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.

Proposers should be informed that WHO is currently revising the “Guidelines on the International Packaging and Shipment of Vaccines". The revision is being conducted by WHO in consultation with industry. Any changes in requirements in the Guidelines will be implemented within a reasonable timeline.

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

## 15. PACKING, PACKAGING, PACKING LIST, LABELLING AND DANGEROUS GOODS INSTRUCTIONS

15.1 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 "Guidelines on the International Packaging and Shipping of Vaccines", (WHO/IVB/05.23) (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, Proposers must submit all relevant Material Safety Data Sheets indicating accurate classification for transport purposes, storage, labeling and shipping requirements when submitting the Proposal.

15.2 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.

15.3 The Supplier’s costs of complying with the requirements of this Section 16 will be the sole responsibility of the Supplier.

## 16. UNICEF TRANSPORT, STORAGE AND STANDARD DOCUMENTS

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. In case of non-standard transportation requirements, alternative offers can be provided for delivery to the port of entry in the receiving country.

In the execution of LTA(s) and Purchase Orders 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) Release certificate issued by the NRA of the country of manufacture for each lot of vaccine supplied;

d) If marketing authorization have been granted for the COVID-19 vaccine offered, a Certificate of Pharmaceutical Product or Free Sale Certificate must be required;

e) Summary Protocol of Manufacturing and Control for each batch of the vaccine supplied;

f) Certificate of analysis for each batch of the vaccine supplied and diluent (if applicable);

g) If applicable, hazardous Goods documents, such as in the case of use of dry ice;

h) Any other documents as specified in each Purchase Order.

## 17. PAHO TRANSPORT, STORAGE AND STANDARD DOCUMENTS

All shipments of vaccines on behalf of PAHO are to be booked well in advance and flight details shall be furnished to PAHO by e-mail only, no less than five business days prior to the date of arrival of the product. Unless otherwise specified by PAHO, the notification of flight details shall include:

1. Purchase Order number.
2. Type of product, batch number, type of WHO prequalified shipping indicator(s) and number of doses.
3. Number of cartons, gross and net weights in kilos.