World Health Organization

WHO's Procedure for prequalification of vaccines

(Draft for review)

The distribution of this draft document is intended to provide information on the proposed document *WHO's procedure for Prequalification of vaccines* to a broad audience and to ensure transparency of the consultation process.

Written comments proposing modifications to this text MUST be received by 10 July 2026. Feedback is through the on-line platform.

In case feedback through the online platform is not feasible please contact us through vaccprequal@who.int indicating "*Feedback PQ vaccines procedure*"

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Abbreviations and glossary

AEFI	Adverse Event Following Immunisation
AMC	Advanced Market Commitment
CHMP	Committee for Medicinal Products for Human Use
CTD	Common Technical Document
EMA	European Medicines Agency
GBT	Global Benchmarking Tool
GCP	Good Clinical Practices
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
ICH	International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
ML1/2/3/4	Maturity Level 1/2/3/4
MoU	Memorandum of Understanding
NRA	National Regulatory Authority
NRA of reference	National Regulatory Authority that has been assessed in compliance with at least Maturity level 3, has issued the Marketing Authorization and is responsible for a full regulatory oversight of the vaccines intended for prequalification.
NCL	National Control Laboratory
PQ	Prequalification
PQT	Prequalification Team
PSPQ	Programmatic Suitability of Vaccines for Prequalification
PSUR	Periodic Safety Update Reports
RPQ	Department for Regulation and Prequalification
SOP	Standard Operating Procedure
TRS	Technical Report Series
UN	United Nations
UNICEF	United Nations Children's Fund
VVM	Vaccine Vial Monitor
WHO	World Health Organisation
WLA	WHO-Listed Authority

1 Introduction

Established in 1987, the WHO Vaccine Prequalification Program advises UN procurement agencies on the quality, safety, and efficacy of vaccines. Led by the Department of RPQ, the programme ensures that vaccines purchased by UN agencies (such as UNICEF), Member States, and international organisations are consistently safe, effective, and suitable for national immunisation programmes. It also verifies alignment with recommended immunisation schedules and with the use of concomitant products.

The assessment verifies that candidate vaccines (a) meet WHO recommendations for quality, safety, and efficacy, including compliance with GMP and GCP, and (b) fulfil the operational packaging and presentation specifications of relevant procurement agencies.

The procedure was last revised in 2012 and published in WHO TRS 978 in 2013. Since then, experience from stakeholder interactions and the reorganisation of the WHO prequalification programme has highlighted the need for updates. The COVID-19 pandemic also underscored the need for adaptive, responsive regulatory processes, accelerated collaboration between NRAs and WHO, and frameworks to address emerging public health threats. Therefore, the revised procedure introduces changes to:

- Reorganising sections to reflect the logical sequence of activities, optimising resource use, and clarifying steps.
- Updating terms to reflect current organisational structures.
- Introducing specific clauses to streamline application and assessment.
- Addressing legal implications and submission formats.

These updates aim to help manufacturers plan their submission strategies more effectively, clarify their responsibilities for the lifecycle management of prequalified vaccines, and enable the WHO vaccine prequalification team to allocate expert resources more efficiently.

The updated procedure is grounded in three key principles to strengthen vaccine safety and global health access:

- Reliance on Regulatory Authorities:
  Dependence on a stable, well-functioning NRA or regional authority of the country of manufacture. The authority must meet WHO or ML3 requirements and fulfil all regulatory functions as per the WHO GBT.
- Comprehensive Assessment:

Assessment of the product and the presentations offered, production process, quality control methods, quality systems, and clinical data relevant to the target population.

- Production Consistency:
  Assurance of production consistency through compliance with GMP requirements and ongoing monitoring of continued adherence to the established specifications

WHO can advise UN agencies on whether vaccines effectively meet the Organization's recommended requirements only if the responsible NRA exercises independent and full regulatory oversight of the vaccines in question and if the vaccines have been assessed through the procedure described in this document. Since reliance on effective regulatory oversight by the NRA of reference plays a critical role in the process, manufacturers shall: (a) inform the NRA of their application to WHO for vaccine prequalification by sending the NRA a copy of the application letter sent to WHO; (b) request the NRA to participate in the process; and (c) provide the NRA with the necessary authorization to discuss the relevant information with WHO representatives.

Because vaccines purchased by UN agencies must meet WHO recommendations or guidelines (whichever are available), WHO will prioritize developing such guidelines. As soon as a draft document becomes available, it can be used to evaluate vaccines for prequalification.

The fact that certain vaccines are not included in the published list of prequalified vaccines does not imply that they do not comply with the required standards; it may be that these vaccines have not been assessed by WHO. The database of prequalified vaccines is available on the WHO website.

WHO, in consultation with UN purchasing agencies, will determine which vaccines are priorities for prequalification and will make this information publicly available. Information on priority-setting for the WHO vaccine prequalification assessment is available on the WHO website.

Priorities are redefined at regular intervals to ensure that efforts are directed toward evaluating the vaccines of highest public health importance and greatest need in developing countries.

2 Assessment process

2.1 Conditions for acceptance of applications

The conditions for accepting applications are as follows:

- The candidate vaccine is on the current list of priority products for UN procurement.
- The candidate vaccine meets the mandatory characteristics for programmatic suitability, as defined in the document Assessing the programmatic suitability of vaccine candidates for WHO prequalification (ref).

WHO encourages manufacturers to discuss any concerns about programmatic suitability characteristics for prequalification by requesting a consultation meeting with the prequalification secretariat during the development process.

- The NRA responsible for regulatory oversight of the product has been assessed by WHO as operating at least at ML3 according to the WHO Global Benchmarking Tool (GBT) and has been found to meet all critical indicators defined for prequalification.

An applicant should check with the respective NRA to confirm whether it has been assessed by WHO. WHO will not process an application until the WHO Global benchmarking assessment of the NRA is completed and the outcome is satisfactory.

- A marketing authorization has been granted by the relevant NRA, and post-marketing regulatory oversight will be exercised by the NRA that will become the NRA of reference for Prequalification (PQ) purposes. This NRA of reference should have a mechanism for ongoing monitoring of the quality, safety, and efficacy of the vaccines under its regulatory oversight. The manufacturer should provide the WHO with updated information on these vaccines.

WHO encourages manufacturers to discuss the candidate product, related programmatic suitability, and regulatory requirements with the prequalification vaccine assessment team throughout the development process.

2.2 Selection of assessment pathways

Experience gained in recent years, including but not limited to public health emergencies such as pandemics, has demonstrated the feasibility and value of relying on the regulatory oversight of authorities that meet a high level of performance and whose regulatory decisions are robust, evidence-based, and consistent with international standards.

Based on the regulatory functions exercised by WLAs and the collaboration between the Vaccine Assessment team and the relevant WLAs, the PQT will determine the assessment

pathway to be applied. This pathway will rely on the level of performance for specific regulatory functions and on whether there are Memorandum of Understanding (MoU) or similar collaboration agreements that allow for the sharing of regulatory reports, notices, or other valuable information.

2.2.1 Full assessment

PQT will conduct a full assessment when the NRA of reference has been assessed by WHO as operating at least at ML3 according to the WHO GBT and has been found to meet all critical indicators defined for prequalification purposes, but it is not yet included in the list of WLAs.

The assessment will include evaluation of quality, safety, and efficacy/effectiveness data, as well as programmatic suitability for use in low- and middle-income countries, through review of the dossier and inspections to verify compliance with GMP requirements.

All NRAs of reference that are considered ML3 or higher fulfil the regulatory functions for lot release and testing. Therefore, all lots produced are released through testing and/or review of production and control documentation. WHO will recognize the lot release testing performed by the selected WLA/NCL responsible for the regulatory oversight of the candidate vaccine. WHO will request that the NCL submit information for review, including the lot release testing strategy and data related to testing of the candidate vaccine (e.g., testing results, raw data, trends/control charts of the vaccines, reference materials, method validation, SOPs.

The manufacturer may be required to provide the SOP for the relevant tests (to be confirmed by WHO during the assessment process).

WHO may share the manufacturer's SOP with a contracted laboratory for independent testing as a post-PQ monitoring activity.

A hybrid approach may be used when the NRA of reference meets the criteria for WLAs for some, but not all, regulatory functions.

The PQT will determine the scope of the assessment based on the degree of reliance on the performance of specific regulatory functions and on whether a MoU or similar collaboration agreements are in place that allow for the sharing of regulatory or assessment reports, notices, or other valuable information.

2.2.2 Abbreviated assessment process

The Abbreviated assessment can be applied to vaccines that have been licensed by WLAs qualified for all regulatory functions and willing to share regulatory information with WHO through a collaboration agreement.

WHO will explicitly request the assistance of the WLA responsible for the regulatory oversight of the candidate vaccine and will engage in discussions to collaborate, including an understanding of each party's roles, responsibilities, and commitments.

The scope of this collaboration can be determined by both parties and may include one or more of the following (each subject to the manufacturer's agreement):

- sharing of WLA reports relevant to product quality and clinical evaluations;
- sharing of WLA/NCL test results (including raw data);
- sharing of inspection reports.

2.2.2.1 Reliance on the WLA assessment of the Quality, Safety, and Efficacy data

WHO recognizes the assessment of the marketing authorization/licensure dossier conducted by selected WLAs responsible for the regulatory oversight of the candidate vaccine as the basis for the prequalification decision.

WHO will review the WLA assessment report instead of the PQ dossier and may review relevant parts of the dossier to address specific PQ requirements. If there are questions about issues not addressed by the NRA of reference, WHO will contact the manufacturer directly and copy the WLA on any additional exchanges of information.

Typically, the responsible WLA does not focus its review on programmatic suitability aspects specific to the national immunization schedules of countries that receive vaccines through the UN.

In view of the above, a WHO review of the following aspects remains essential:

- mandatory and critical characteristics from the programmatic suitability point of view;
- confirmation that the vaccine meets WHO recommendations;
- stability data to ensure the vaccine meets the needs of immunization programs in developing countries (particularly those with weak cold-chain systems), and the assignment of a VVM category;
- clinical data to ensure the vaccine is suitable for the target population;
- recommended immunization schedules to ensure compatibility with national immunization programs;
- suitability of samples, labels, inserts, and packaging to meet the UN

- agencies' tender requirements;
- packaging for international shipment and its validation.

The applicant must provide WHO with a copy of the file submitted to the WLA (CTD Modules 2 to 5) and Module 1, in the format of the Vaccine Prequalification Dossier, to cover the information required for the items listed above.

2.2.2.2 Reliance on the WLA lot release testing

WHO will recognize the lot-release testing performed by the selected WLA/NCL responsible for regulatory oversight of the candidate vaccine. WHO will review the available information (e.g., testing results, raw data, trends, and control charts).

2.2.2.3 Reliance on the WLA assessment of GMP compliance

This procedure is based on WHO's recognition of inspections conducted by the selected WHO Listed Authorities (WLAs) responsible for regulatory oversight of the manufacturing site(s) for the candidate vaccine.

WHO inspection, whether through a desk assessment and/or an onsite inspection, will be replaced by verification of compliance with GMP guidelines, supplemented by an assessment focused on aspects related to UN tender specifications.

2.2.2.4 Other considerations

Implementing the abbreviated prequalification procedure requires both an eligible authority and its commitment to collaborate. Special consideration must be given to authorities in non-English-speaking countries, as they will incur additional work to ensure their reports are accurate and available in English. The nature and extent of this collaboration should be defined on a case-by-case basis and formalised in the agreement.

Vaccines produced exclusively for export are ineligible for the abbreviated procedure. In such cases, the vaccine PQ team will consult the relevant NRA to determine whether a hybrid assessment can be applied to streamline the process.

2.2.3 Fast-track assessment process

A fast-track assessment may be required in special circumstances. This process applies to licensed vaccines (i.e., marketing authorization available) that are part of routine immunization programs or used only in an emergency response; it does not apply to novel vaccines not yet introduced or recently introduced into routine immunization programs.

In agreement with UN purchasing agencies or other qualified or eligible partners, the fast-track procedure can be considered in the following situations:

- an acute shortage of a vaccine that puts at risk the global supply for routine immunization programs and/or an eradication effort;
- an emergency situation (i.e., an outbreak or epidemic of a disease for which no prequalified vaccine is available, or for which availability is insufficient and an additional source of the same vaccine is required);

Any of the above situations may lead to acceptance of vaccines for evaluation in parallel with submission to the NRA for marketing authorization purposes upon:

- special request from the manufacturer; and
- endorsement by WHO senior management.

When the fast-track procedure is followed, the established deadlines for submitting dossiers do not apply.

There should be maximum flexibility in this process. For example, the dossier review and the site audit will be conducted in parallel, in collaboration with the NRA of reference.

2.3 Special considerations for submissions related to products manufactured at multiple sites or in different countries

As a precondition for any vaccine submission for prequalification evaluation, the NRA responsible for regulatory oversight of the product must be assessed by a WHO team to confirm its designation at the ML3 or higher level under the WHO GBT. The NRA's ML3 or higher status must also be maintained over time.

Given the growing diversity and complexity of vaccines manufactured at multiple sites, including across different countries, the WHO must ensure that regulatory oversight is fully exercised and that responsibilities are clearly defined at all stages of production by the relevant ML3/ML4/WLAs. Certain criteria will be applied, as described here.

There are at least two possible scenarios:

a. If a company formulates and/or fills from bulks produced by different manufacturers, each final product is considered a unique product and will be prequalified separately. WHO will require evidence that the manufacturer of the finished product has authorization from the vaccine manufacturer that produced the bulk to export the final product.
b. If a company transfers technology to other companies that will produce the vaccine from seed to finished product, each finished product will be considered unique and will be prequalified separately. Comparability data are needed to accept supporting

data generated by the original vaccine manufacturer (including, but not limited to, clinical and stability data).

A long-term contract between manufacturers must be in place. The technical terms and the duration of the contract must be submitted to WHO for review as part of the assessment procedure. Whenever necessary, additional information can be requested from the manufacturers.

WHO encourages early discussions with manufacturers and their respective NRAs if they plan to embark on a project involving multiple sites or countries in the production process, to discuss the proposed scheme and the allocation of responsibilities to the NRAs.

2.4 Letter of Intent to submit an application

A Letter of Intent (Appendix 1) to submit an application must be sent to the PQT Unit Head, with attention to the Team Lead of Vaccine Prequalification, no later than six months before the intended submission date of the dossier.

The Letter of Intent includes information about the product, the licensing status, and the manufacturer, as well as clauses outlining the manufacturer's commitments to submit a complete dossier by a specific, agreed-upon submission deadline. (See Appendix A).

This will allow manufacturers to plan their application strategy, considering the agreed-upon timelines and requirements, while enabling the PQT to efficiently plan the workload and reviewer availability within the required timeframe.

2.5 Submission deadlines

WHO established three submission deadlines per year, on 31 January, 31 May, and 30 September, by which manufacturers are required to submit the Vaccine Prequalification dossier (VPQD).

2.6 Meetings between manufacturers and PQ

There are two types of meetings that manufacturers may request:

a. A consultation meeting: This meeting is requested during product development and is intended to discuss the information required to be consolidated for submission of the PQ dossier and the CTD to be presented to the NRA to obtain marketing authorization, including, but not limited to, the programmatic suitability requirements for prequalification.

b. A pre-submission meeting: This meeting is requested after the marketing authorization has been issued, and the manufacturer is ready to apply for prequalification.

2.7 Submission format

The global use of the eCTD format has increased significantly since the last revision of the vaccine prequalification procedure. Most manufacturers have a CTD-format dossier prepared for product registration in one or more countries, and many countries that import prequalified medicines require submission of a CTD-format dossier for product registration.

The Prequalification vaccine assessment team has adopted an ICH-CTD-based format for the VPQD. This should reduce the regulatory burden on companies by eliminating the need to maintain dossiers in multiple formats.

Module 1 is unique to each regulatory body and is not part of the ICH-CTD. The Prequalification vaccine assessment team has developed Module 1, which contains information not included in the other modules and is required to assess the product for prequalification.

The PQT has published a guideline that clarifies the expected information and provides general instructions for completing each section of Module 1, which is unique to the Vaccine Prequalification assessment. Modules 2 to 5 should follow the ICH Guidelines M3 (Quality), M4 (Non-clinical), and M5 (Clinical).

2.8 Screening of the dossier and payment of fees

The objective of the screening is to verify that the dossier complies with the required format and contains the necessary general content, consistent with the following:

- The procedure for assessing, in principle, the acceptability of vaccines for procurement by UN agencies.
- The CTD format requirements established by ICH.
- The mandatory characteristics for PSPQ, primarily addressed in Module 1 of the CTD.

This screening step is conducted before the formal decision to accept the application for assessment, which includes evaluation of Quality [Chemistry, Manufacturing and Controls (CMC)], Non-clinical, and Clinical data.

If the dossier does not comply with the required format and content, the manufacturer will be notified by letter. In addition, the manufacturer will be required to submit a new Letter of Intent with the new intended submission date, in accordance with the published submission deadlines.

If screening reveals that the mandatory programmatic suitability criteria are not met, the dossier will be rejected. If a deviation from the critical characteristics or a unique, novel, and innovative characteristic, as defined by WHO is identified, the PQT, in consultation with UN procurement agencies and programs, will consider the deviation on a case-by-case basis.

As soon as the screening is finalized, a letter of acceptance or rejection of the dossier will be sent to the manufacturer. If accepted, the names of the experts proposed for the evaluation, along with copies of their curricula vitae, will be provided to the applicant for confirmation of no objection. Once the list of reviewers has been agreed upon, communications with the reviewers involved in a vaccine evaluation should be conducted only through the WHO focal persons responsible for the product.

At the same time, the WHO will send an invoice requesting payment of the prequalification fees. Manufacturers will be expected to pay the fees and confirm the acceptability of the proposed experts within 2 weeks. Payment of the fees without any further communication will be considered as a de facto agreement with the proposed experts. The assessment will then be initiated. Manufacturers should consult the WHO vaccine Prequalification webpage for updates on the assessment fees and payment schedule.

2.9 Letter of agreement

Once the application is accepted, a reference number will be assigned. This number should be used for all future communications. A letter of agreement will be sent to the manufacturer. Once the letter is signed and returned to WHO with proof of payment of the prequalification fees, WHO will begin the prequalification assessment of the application.

2.10 Assessment of the dossier

WHO experts review the dossier, and a consolidated report (quality and clinical) with a list of questions (LOQ) is sent to the manufacturer.

The responses must be submitted as a single package with adequate cross-referencing to the original file. The manufacturer must attest that all responses have been submitted. If the manufacturer requests an extension for the responses, WHO will assess the request on a case-by-case basis and reserves the right to delay the assessment or terminate the process. ss.

2.11 Testing

WHO may contact the NCL during the assessment process to gather information on lot-release testing and may request that the manufacturer provide SOPs and relevant materials for independent testing by WHO-contracted laboratories.

2.12 Inspections

WHO inspections of vaccine manufacturing site(s) are an essential component of the WHO PQ process. The primary objectives of these inspections are to assess whether vaccines are manufactured in compliance with GMP guidelines, whether they meet WHO recommendations for production and quality control, and whether they comply with the UN tender specifications, which reflect the needs of national immunization programs.

Additional important elements of the inspections include, but are not limited to, verification of compliance with the PSPQ requirements and the implementation of VVMs where applicable.

WHO inspections of vaccine manufacturing site(s) may be conducted through on-site inspections, desk assessments, or a combination of both. The decision to conduct an on-site inspection and/or a desk assessment rests solely with WHO and is based on a risk-based approach that considers multiple factors, including:

- the outcomes of previous inspections conducted by WHO and/or a WLA;
- comments and conclusions from WHO's review of the product dossier;
- the complexity of the manufacturing site, processes, and product;
- the number and significance of known quality issues (e.g., complaints, recalls);
- major changes to facilities, equipment, processes, or key personnel; and
- the site's experience in manufacturing and testing the product.

Initial inspections are planned once the product dossier has been accepted for assessment and may occur concurrently with the dossier assessment. After a vaccine is prequalified, WHO conducts routine (e.g. regular surveillance) and non-routine (e.g. for-cause or follow-up) inspections of manufacturing site(s) throughout the product's lifecycle to verify continued compliance with prequalification requirements. Routine inspections are scheduled at intervals determined by WHO using a risk-based approach and are typically conducted every three years from the date of the last WHO manufacturing site inspection, unless an earlier inspection is deemed necessary. Non-routine inspections are scheduled as needed, with timing and scope determined on a case-by-case basis.

Each manufacturing site inspection is conducted by the WHO through an appointed inspection team. The team generally comprises a WHO staff inspector and external experts (also referred to as "co-inspectors") selected by WHO. External experts must have appropriate qualifications, competence and experience in relevant fields and must comply with WHO confidentiality and conflict-of-interest requirements. The NRA of the manufacturing country, or the NRA with regulatory oversight of the product, is invited to designate one or two inspectors to participate as observers in the WHO inspection.

At the conclusion of the inspection, findings and recommendations are communicated verbally to the manufacturer during the closing meeting, allowing for discussion, clarification, and questions. Following the inspection, WHO issues a final inspection report to the manufacturer detailing any identified deficiencies or nonconformities. If corrective and preventive actions (CAPA) are required, WHO will defer final inspection conclusions and related recommendations to UN agencies until the CAPA have been adequately implemented and verified, as deemed necessary by WHO.

Failure by the manufacturer to implement agreed CAPA within established timelines may result in termination of the prequalification process for initial inspections, or in suspension or delisting of the vaccine from the WHO list of prequalified vaccines for routine or for-cause inspections. Similarly, failure or refusal by a manufacturer to participate in or permit a routine or non-routine WHO manufacturing site inspection may lead to suspension or delisting of the product from the WHO prequalification list.

WHO reserves the right, as appropriate, to issue Notices of Concern (NOCs) to inform relevant stakeholders, users, and the public of significant adverse outcomes arising from routine or non-routine prequalification inspections.

3 Outcome of the assessment

3.1 Prequalification

Once the assessment outcome is satisfactory, a letter will be send to the manufacturer outlining the conditions and post-PQ commitments (see Section N). The manufacturer must provide official confirmation of agreement to comply with the post-PQ commitments.

The Organization will then send a letter to the UN agencies and other procurement agencies, as applicable, advising on: (a) the vaccine's compliance with both the WHO requirements and the specifications of the relevant UN agency; and (b) the role of the NRA in certifying this.

The vaccine will be included in the WHO list of prequalified vaccines immediately after the letter is sent to the UN agencies. A page providing the basis for the acceptance of the prequalification of the specific vaccine will also be included in the list.

The current list may be consulted on the WHO website.

The prequalified status of a vaccine will remain valid unless WHO – through post-PQ monitoring activities – identifies that the quality, safety, and/or efficacy of the vaccine is compromised or the PQ holder decides to withdraw their vaccine from the PQ list.

WHO reserves the right to revoke the prequalification status if fraud by the manufacturer becomes evident.

3.2 Termination of the assessment process

WHO reserves the right to terminate the assessment process for the prequalification of a specific vaccine if the manufacturer is unable to provide, within the timeframe agreed by WHO and the manufacturer, any of the following:

- the required responses to the List of Questions or additional information requested by the WHO experts during the dossier assessment
- satisfactory implementation of all corrective actions resulting from the inspection in a reasonable timeframe.

In the event of termination of the assessment process, the manufacturer will need to discuss a resubmission plan with the PQ team.

During the assessment of quality, safety, and efficacy data, and of compliance with GMP, WHO may identify deviations that may trigger a re-benchmarking or performance evaluation of the regulatory system.

4 Post PQ commitments

The manufacturer must provide to the WHO:

- Reports of serious adverse events following immunization as soon as possible and no later than within 15 days of receipt of the report.
- Reports of quality complaints from the field for batches supplied to UN agencies or procured directly, as soon as possible and no later than within 15 days of the applicant receiving any such complaint or report.
- Information on any variations related to facilities, formulation, presentation, manufacturing methods, quality-control specifications, labelling, international shipment packaging configurations, Vaccine Vial Monitor (VVM) category, or any other changes that could affect the vaccine's safety and/or efficacy or alter the basis for regulatory approval by the NRA. (Please refer to the current Guidance on Variations to a Prequalified Vaccine for further information, which outlines the types of variations requiring prior WHO approval.)
- Notification of any problems or constraints in production or quality control that might affect the international supply of this vaccine, both in volume and/or lead time.

In addition, the PQT has implemented an annual reporting system for prequalified vaccines. The Guideline for the submission of an annual report for prequalified vaccines has been published (GUIDELINE ON THE SUBMISSION OF PREQUALIFIED VACCINES ANNUAL REPORT[1]).

The purpose of the Prequalified Vaccine Annual Report (PQVAR) is to ensure that each prequalified vaccine continues to meet the quality, safety, and efficacy requirements for maintaining WHO Prequalification status. Under the current vaccine PQ procedure, PQ holders must submit an annual report for each prequalified vaccine.

The guideline outlines the process for submitting annual reports via the electronic Prequalification System (ePQS) Portal, including but not limited to the following:

- A summary of changes or variations to the product(s) implemented since the previous annual report
- Test results from the ongoing stability program since the previous annual report
- Production and distribution data
- GMP inspections
- A summary update on the implementation of post-prequalification commitments
- The periodic safety update report should be provided (electronic data only).

The first annual report submission is due one year after the prequalification date and should be submitted on one of the following dates: 31 January, 31 May, or 30 September, whichever is applicable. Subsequent submissions are required annually on the same date. If submissions are delayed, a proper justification should be provided.

After reviewing the annual report, WHO may request supporting data.

The manufacturer may provide the latest annual report submitted to the NRA if it contains the relevant information.

5 Post-PQ monitoring and compliance management

5.1 Targeted testing

WHO-contracted laboratories will, upon request from WHO, test final product samples of vaccines supplied to UN agencies at least annually. WHO will select three to five batches from the supply list and request an appropriate number of samples for each vaccine type and presentation. Manufacturers must provide lot summary protocols and, where

[1] Prequalified Vaccine Annual Report (PQVAR) | WHO

applicable, NRA or NCL release certificates for review; accordingly, they must retain sufficient samples to support this programme.

In the event that specifications are not met, WHO will promptly contact the manufacturer to initiate follow-up actions. Should the vaccine ultimately fail to comply with the established criteria, the WHO will conduct an investigation and provide the relevant UN agency with a written report detailing the actions to be taken, and copies will be sent to the manufacturer and the responsible NRA.

5.2 Monitoring of quality complaints and AEFIs

5.2.1 Complaints

Upon receipt of a quality complaint, WHO will initiate an investigation and may request independent testing, as appropriate. This process involves reviewing relevant documentation, including temperature monitoring data, test results, and batch records.

For complaints submitted by NCLs in receiving countries, WHO requires the complainant laboratory to provide its test results and supporting documentation (including validation reports, SOPs, and control charts) for review prior to arbitration testing.

5.2.2 AEFIs

This investigation of the AEFI will be conducted to determine whether the cause is related to any programmatic issues/deficiencies in the field.
Lot testing will be initiated only if:

- Clinical or epidemiological data suggest a potential quality issue; AND
- A review of manufacturing and control documentation including batch records warrants further analysis.

If testing is needed, the sample size will be calculated to ensure statistical representativeness. WHO will coordinate with a contracted laboratory to specify the number of vials required and to manage logistics with national authorities.

5.3 Recommendations for action in case of non-compliance

Depending on the nature and severity of the non-compliance identified, WHO may recommend one or all of the following actions:

- Enhanced Monitoring: Implement stricter oversight of the manufacturer’s production, QC and Quality system during a probationary period.

- Suspension of Purchase: Recommendation to suspend procurement by UN agencies pending the investigation and resolution of the issue.
- Delisting

Significant gaps in the manufacturer's quality or manufacturing systems may necessitate a full reassessment of the vaccine. WHO will formally notify the responsible NRA of any field problems or failures to meet established criteria.

6 Delisting

The prequalification status of a vaccine remains in effect until the WHO revokes it. WHO will apply quality risk management principles to determine the actions required to decide whether to revoke the prequalification status.

WHO reserves the right to take appropriate measures, including suspending supply or withdrawing from the list, in the event of noncompliance with post-prequalification commitments and/or misconduct.

Alternatively, the vaccine manufacturer can request delisting of the prequalified vaccine when manufacturing is discontinued or when the Marketing Authorization holder changes and the new MA holder is not interested in continuing the PQ listing.

7 Appendices

Appendix 1- Letter of Intent

APPENDIX 1

LETTER OF INTENT

Dear Vaccine Assessment Team

We are writing to notify you of our intention to submit an application for the Prequalification of the XXXXX Vaccine.

We confirm that this product has received a Marketing Authorization by (name of the NRA) and the CTD/eCTD dossier will be submitted according to the last version approved by the NRA. Submission Details:

- Intended Submission Date: [Date]
- Format: PQ dossier

Contact Information:

Name: [Contact Person]

Email: [Email]

Sincerely,

[Signature]

[Company]

We acknowledge that we have read and accept the clauses of this Letter of Intent to submit an application for PQ

Clauses

The applicant understands and agrees with the following:

a) The letter of Intent must be submitted not later than 6 months before the intended submission date (established submission dates) to allow the PQ team to secure the availability of expert resources to screen and review the dossier upon its acceptance
b) the commitment to submit at the chosen submission date means that all modules of the dossier are complete (i.e. there are no results pending for clinical trials, regulatory inspections, etc) as rolling submission is not accepted
c) The PQ team will establish a maximum number of applications that can be submitted in each submission period based on existing resources and ongoing assessments. Therefore, even if the applicant submits before in the submission date, it is possible that the quota for the following submission date is reached and the applicant will need to wait for a later deadline for submissions.