

Emergency Use Listing Procedure

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1. Introduction

The World Health Organization (WHO) developed the Emergency Use Assessment and Listing (EUAL) mechanism in response to the 2014 – 2016 Ebola Virus Disease (EVD) outbreak. The EUAL is a risk-based procedure for assessing and listing candidate in vitro diagnostics (IVDs), therapeutics and vaccines for use primarily during public health emergencies of international concern (PHEIC) but also in other public health emergencies if appropriate. The current procedure consists of three key components: 1) review of the documentation relating to the manufacture of the product, including compliance with WHO manufacturing quality norms and standards; 2) review of documentation relating to safety and efficacy/performance, especially with respect to use during the public health emergency; and, 3) where applicable for IVDs, an independent laboratory evaluation, coordinated by WHO, of the product's performance and operational characteristics.

Only two submissions for Ebola vaccines were received. Both vaccine developers and national regulators identified the need to revise and simplify the procedure, in order to improve clarity on procedure aspects, and to avoid overlap or gaps in their respective functions

Four therapeutic products were in development during the 2014-16 Ebola outbreak. None of these were submitted for EUAL. For IVDs, 25 applications were received for Ebola assays of which seven were listed, Thirty three applications were received for Zika assays of which three were listed.

Challenges encountered during the review of IVDs applications included poor quality of submissions and assay validation data, lack of international standards to guide the assessment, lack of reference preparations and panels for validating assays, missing ethical clearance related to the sourcing of these materials and concerns about the biosafety of IVDs. Manufacturers and regulators agreed that there was a need for better guidance on validation data required for IVDs in the EUAL process, as well as the availability of international reference materials and other validation materials

The WHO Informal Consultation on options to improve regulatory preparedness to address public health emergencies (Geneva, May 2017)¹ concluded that some

¹ http://www.who.int/medicines/news/2017/PHEmeeting-reportIK-EG16_Nov_2017.pdf?ua=1

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aspects of the existing WHO EUAL procedure need to be reconsidered and revised. The consensus was to reframe the process as the Emergency Use Listing (EUL) procedure. The revised procedure should be used in exceptional circumstances – primarily during a Public Health Emergency of International Concern (PHEIC). It should ensure that the use of an investigational product under the EUL framework is based on a pre-determined rationale and criteria, that the degree of reliance on NRAs for assessments is clear, and that NRAs of potentially affected countries are involved in the development and implementation of the procedure. The EUL should also ensure that pre-emergency activities are planned and executed appropriately to allow a rapid listing decision once the emergency is declared.

2. Scope and purpose of the procedure

The goal of the new procedure is to define the steps that WHO will follow to establish eligibility of products, the essential information required, and the process to be used in conducting the assessment to list a product under a limited-time listing status, while further data is being gathered and evaluated.

The Prequalification Team is the best prepared unit in WHO to assess the products for listing due to its expertise in product evaluation, and in dealing with procurement organizations and National Regulatory Authorities (NRAs) responsible for regulatory oversight of products, including NRAs of potential user countries. **However, the EUL is not equivalent or an alternative to WHO prequalification, and should not be thought of as such.** Rather, it is intended to provide time-limited listing for products in an emergency context when limited data is available and the products are not suitable for application for prequalification. **The main reason for not qualifying for PQ is that these products will, at the time of submission for EUL, not fall within the scope of prequalification program.** However, the ultimate goal is to complete the development of the product for WHO prequalification.

The EUL is a special procedure for vaccines, medicines and in vitro diagnostics in the event of a public health emergency when the community/public health authorities may be willing to tolerate less certainty about the efficacy and safety of products, given the morbidity and/or mortality of the disease and the lack or paucity of treatment or prevention options

WHO has developed the EUL process to expedite the availability of medical products needed in public health emergency situations, to assist interested UN procurement agencies and Member States on the acceptability for use of specific products in the context of a public health emergency, based on an essential set of available quality, safety, and efficacy/immunogenicity/ performance data.

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It should be noted that it is the sole prerogative of WHO Member States whether or not to allow the emergency use of a candidate vaccine/medicine/IVD in their country.

This document describes the procedure for eligibility and assessment of products for listing under the EUL. It is intended to assist manufacturers who are willing to submit applications, with the goal of obtaining a listing of their product (s) for use during public health emergencies. Participation in the procedure is voluntary.

3. Phases of the procedure

Past experiences with emergency situations have shown that a preparedness plan is key to a rapid response when the emergency is declared. The WHO Research & Development (R&D) Blueprint was established based on this principle.

As products in development are added to the pipeline for each priority disease, there are several activities that can be planned and executed during the pre-emergency phase. This strategy is intended to concentrate as much as possible all the activities that can be done in advance, thus minimizing the time required for a final decision about listing of a product for use once the public health emergency is declared.

The activities are divided into two types according to the objectives and the stakeholders involved:

1) Establishment of an assessment platform.

This includes activities that are intended to establish a platform for collaboration between WHO, external experts and national regulatory authorities responsible for the oversight and from user countries. Also included is activity to establish a roster of experts to be called upon at the different stages of the procedure.

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2) Eligibility and assessment of products

These aspects of the pre-emergency phase are related to the interactions with applicants. They include pre-submission meetings/activities, selection of products for assessment according to established eligibility criteria (See eligibility criteria below), assignment of an evaluation pathway, and assessment of submitted data (initial and updates), with reports thereon. These aspects are part of the eligibility and assessment process and use the resources of the assessment platform.

The implementation of all these pre-emergency activities is intended to accelerate the decision making process for listing when the public health emergency is declared. During the emergency phase, a recommendation for use (or non-use) will be issued and published.

The procedure also includes a post-deployment evaluation conducted by WHO on the use of the products, with continuous monitoring as the emergency unfolds.

3.1. Pre-emergency phase

3.1.1 Establishment of the assessment platform

3.1.1.1 Agreements with NRAs of record for information sharing

In order to use a fast track assessment WHO has an official agreement for information sharing with the NRA responsible for the regulatory oversight of the products. These agreements will allow WHO to rely on the assessment/inspections of quality, pre-clinical and clinical information and facilities by the NRA that issued the authorization under extraordinary circumstances such as a public health emergency. Reliance upon the NRA, originally responsible for the regulatory oversight of a product, will determine whether the assessment pathway under the EUL procedure will be based on an abridged or a full review process. An abridged pathway to EUL listing may have an impact on the time required to complete the evaluation. (See "Selection of assessment pathways" below.)

The EUL procedure will take into consideration existing agreements and the establishment of enhanced and new agreements to ensure there are provisions for those situations where alternative mechanisms are used to authorize the use of medical products under extraordinary circumstances, such as public health emergencies.

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WHO will avoid duplication of effort and reduce the time taken to assess a product by focusing on aspects where the WHO EUL assessment brings added value. WHO will review the available evidence of quality, safety and efficacy (and performance for IVDs) to determine whether the product qualifies for an abridged EUL assessment. Products that do not qualify for abridged assessment will undergo a full EUL review.

3.1.1.2 Framework for interaction with NRAs and Ethics Committees of potentially affected countries

As priority diseases are identified -in alignment with the WHO R&D Blueprint- and products are considered eligible for assessment, potentially affected countries will also be identified. Communication strategies will be established with the NRAs and Ethics Committees of potentially impacted countries, individually or through existing regulatory cooperation platforms.

In order to minimize the layers of review and timelines for authorization at the country level, a specific framework for authorization for use of those products listed under the EUL procedure will be established involving relevant authorities from potential user countries during the pre-emergency and emergency phases. An agreement with potential user countries on the essential information required to support a fast-track national approval will be key in minimizing timelines for decision-making at the country level.

3.1.1.3. Establishment of a roster of experts to support the different phases of the procedure

A roster of experts will be established through a “call and selection” process by the Regulation of Medicines and other Health Technologies (RHT?

Experts will be selected from suitably qualified members of existing ad hoc or standing advisory committees, relevant WHO expert panels, including representatives from NRAs of manufacturing countries, NRAs responsible for the regulatory oversight of products and NRAs of potentially affected countries, academia and other relevant institutions. The pool of expertise should cover all technical/scientific areas to be considered during the pre-emergency, emergency and post-emergency decisions, so that ad-hoc committees can be rapidly established when required.

The experts will complete a Declaration of Interest (DOI) and Non-Disclosure Agreement (NDA) as per WHO rules and procedures.

3.1.1.4. Committees

There are two types of Ad Hoc Committees to be established from the roster of experts:

1. Product Evaluation Committee (PEC)

This Committee will be called during the pre-emergency phase of the procedure to a) determine what sets of guidelines, requirements and scientific consensus procedures will be used to assess a product; b) evaluate applications of products that have met the EUL eligibility criteria and have passed screening.

The Chair of the PEC will consolidate recommendations made by the experts, whether consistent or not for further consideration by the Prequalification (PQ) Group Lead or the Advisory Committee on Emergency Use Listing (ACEUL) whenever the report is used for a recommendation for EUL.

The Product Evaluation Committee (PEC) will have three branches:

a- PEC-V: for vaccines and will be coordinated by the Vaccines Prequalification Group Lead.

b- PEC-M: for medicines and will be coordinated by the Medicines Prequalification Group Lead.

c- PEC-D: for IVDs and will be coordinated by the In Vitro Diagnostics Prequalification Group Lead.

The PECs will be composed of members from the established roster of experts, according to their specific area of expertise. They will perform a risk-based assessment of the scientific data for a product, including quality, safety/efficacy, and programmatic aspects. The Committee will prepare a report based on the available information, request additional information, and assess supplementary data/updates as required.

The Committee will be selected by the Prequalification teams according to criteria established in the Terms of Reference (See Annex 4).

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2. Advisory Committee on Emergency Use Listing (ACEUL): The committee will have three branches:
 - a- ACEUL-V: for Vaccines and will be coordinated by the Vaccines Prequalification Group Lead.
 - b- ACEUL-M: for Medicines and will be coordinated by the Medicines Prequalification Group Lead.
 - c: ACEUL- D for In vitro Diagnostics and will be coordinated by the In Vitro Diagnostics Prequalification Group Lead.

This committee will be established once a public health emergency has been declared, in order to make a decision on the listing of a specific product based on the recommendations of the Product Evaluation Committee. Additional information may be requested at this level.

Committees will be led by the Leaders of the Prequalification Team Groups. Their deliberations and recommendations may take place during face to face meetings or via other means of communication.

See Terms of Reference for Committees in Annex 4.

3.1.1.5. Regulatory consensus on essential requirements on quality, safety, efficacy/immunogenicity/performance and lot release (when applicable) for specific products

It is very likely that when the assessment of a product under the EUL procedure starts, there will not be WHO written standards or regulatory guidelines available that are fully applicable for a specific product. The priority list for development of written and physical standards may not be aligned with the priority list of diseases as per R&D Blueprint.

However, some guidelines that are of a more general nature (i.e. for vaccines for cell substrates, virus inactivation and others) may be used for the assessment of products that are in development and for which there are no product-specific published WHO or NRA guidelines. The use of existing guidelines, either from WHO or NRAs, will be considered and discussed by the Product Evaluation Committee in order to decide which ones will be used to assess a specific product, and what are the scientific and/or regulatory criteria that will be applied when no written standards and/or guidelines are available.

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3.1.2 Eligibility and assessment of products

3.1.2.1 Eligibility of candidate products

The three product streams have requirements for products to be eligible for evaluation.

In order to qualify for an EUL, the use of the product must meet the following criteria:

- The disease for which the product is intended has been declared by the WHO Director-General to be a Public Health Emergency of International Concern (PHEIC). The Director-General may authorize use of this procedure for a public health emergency that does not meet the criteria of a PHEIC if s/he determines that this is in the best interest of public health.
- The disease for which the product is intended is serious or immediately life threatening, causing an outbreak, epidemic or pandemic and there is no licensed product for this disease
- Based on the contingencies of the specific public health emergency, it is reasonable to consider the product for EUL assessment e.g., there are no licensed therapies for the indication or for a critical subpopulation (e.g., children).
- The product is manufactured in compliance with current Good Manufacturing Practices (GMP) in the case of medicines and vaccines and under a functional Quality Management System (QMS) in the case of IVDs
- The applicant attests that it intends to complete the development of the product (validation and verification of the product in the case of IVDs) and apply for WHO prequalification. In the ideal situation, the remaining clinical trials and other requisite testing will already be underway at the time of the application for an EUL.²

WHO may consider reviewing a candidate product for EUL that does not meet all of the requirements. In such situations, the application letter and documentation provided to WHO should justify the application of the product although it does not meet all eligibility requirements.

² A future prequalification application should incorporate all information submitted for the EUL plus any other information needed to complete a prequalification application

3.1.2.2. Pre-submission activities/ meetings

If considered necessary or desirable by the applicant and WHO, a discussion may be held between the applicant and WHO before the actual evaluation process starts. These pre-submission exchanges may be done via a chosen method of communication, including face to face meetings. Pre-submission meetings should be scheduled as early as possible, with a predefined agenda addressing questions sent to WHO in advance by the applicant. Such meetings are important for discussing availability of essential data required for specific products, expected timelines for submission and updates, monitoring of safety and effectiveness after deployment, and other relevant information. Additional meetings may be held during the assessment process, as required.

The procedural aspects of a pre-submission meeting are detailed in Annex 2

3.1.2.3 Assignment of Assessment pathway

Some national regulatory authorities have implemented pathways to assess submissions for products that are still in clinical development and authorize their use under extraordinary circumstances like a public health emergency. Where products submitted for WHO EUL have undergone a previous assessment and/or obtained such an extraordinary authorization by an NRA, it is not the intent of WHO to undertake duplicative work, if the review of the other emergency mechanism is deemed to be of a satisfactory standard.

The criteria for assessment of each type of product according to reliance on the NRA responsible for the regulatory oversight of the product and other parameters for Vaccines and Medicines are detailed in Annex 8

In the case of IVDs, when considering whether a product qualifies for an abridged assessment procedure, WHO takes into account two factors: whether the product has been approved through another emergency mechanism, and whether the regulatory version of the product submitted for prequalification is the same regulatory version that was approved through another emergency mechanism.

3.1.2.4. Assessment of initial information received

Once the product has been considered eligible for assessment under the EUL procedure, the PQT Group Lead of each product stream will designate a focal person for the EUL assessment of a specific product (or group of products).

The focal person will perform the screening of the submission to ensure that there is substantial information for the assessment based on the essential data requirements.

In addition to the EUL dossier review process, the PQT inspection team will conduct a desk review of available inspection reports. As appropriate, the inspection team may also undertake on-site inspection of manufacturing and clinical sites, depending on the

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outcomes and recommendations of the PEC and desk review of the available inspection reports.

The focal person will coordinate the distribution of the submitted data package to the members of the PEC, provide specific instructions for the review as appropriate, and manage communications between the committee and the applicant.

A consolidated report will indicate whether the information received is considered sufficient for a recommendation, or if additional information is needed prior to giving a recommendation. If the applicant has provided a timeline for additional results according to the product development plan, this will be indicated in the consolidated report.

The objective of this report is to ensure that if/when a public health emergency is declared, the Committee responsible for a final recommendation on listing (ACEUL) has an opinion from the PEC based on currently available data, as well as an indication of how soon additional data may be received for assessment. (See TORs of the PEC in Annex 4)

The PEC review report should follow the templates in Annex 3

3.1.2.5. Submissions updates

After the initial submission of the application with all the required information for initial assessment, applicants should submit any additional information on the development of the product, particularly if it may affect the product's benefit/risk assessment.

The applicant should – as much as possible- provide tentative timelines for submission of additional/supplementary information based on the expected dates of completion/planned interim analyses of studies currently ongoing/or being initiated soon.

Submission of updates/additional data should clearly follow the section numbering system of the initial submission (see Essential Data Requirements in Annex 1).

3.2 Emergency phase activities

3.2.1. Ad hoc Committees

The ad-hoc Advisory Committee for Emergency Use and Listing (ACEUL) will be established upon declaration of public health emergency. Members of the Committee will be selected from the established roster of experts. The focal point designated by the Group Lead of each PQ product stream will provide members with the report prepared by the relevant PEC and any other information considered critical for the deliberations and decisions.

(See Terms of Reference of the ACEUL in Annex 4)

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3.2.2. WHO decision on emergency use listing

The procedure includes provisions to concentrate most of the activities related to submission and assessment of available data during the pre-emergency phase. Therefore, optimally the ACEUL will have all the necessary information to deliberate and issue a recommendation for listing and conditions for use in a short period of time. The report from the relevant PEC should include an indication if and when any new data is expected, as stated above. However, the ACEUL may request further information from the applicant before making a recommendation. The recommendation is the output of the ACEUL that will be used by WHO to issue the Emergency Use Listing for the product.

3.2.3 Publication of review outcomes and communications

Upon making a decision to grant an emergency use listing, WHO will publish information about the product in a public report available on a dedicated portal of the WHO website. The validity of an emergency use listing in the context of a public health emergency will generally be for 12 months. All decisions to grant an emergency use listing will be reassessed at 12 months (or sooner, if further data become available that could alter the original opinion). When deemed necessary, the emergency use listing can be extended. Products may be taken off the EUL list earlier if new data become available that change the benefit-risk balance of the product or immediately upon declaration by the WHO Director-General that there no longer is a PHE. Manufacturers must supply any new information/data to WHO as soon as it is available.

3.3 Activities after the products have been deployed and used

3.3.1 Post deployment monitoring

For products listed and used under the EUL, appropriate post-EUL monitoring mechanisms should be established to allow for the timely evaluation of adverse events (AE) and notification to WHO and the relevant NRAs. This includes ensuring the existence of a spontaneous Adverse Events Following Immunization (AEFI)/AE reporting system, and the possibility of conducting active surveillance studies in order to investigate specific concerns, either because they were identified as signals during the product clinical evaluation or due to other considerations.

Appropriate post-EUL monitoring mechanisms must be in place to allow for the timely evaluation of adverse events and notification to WHO and the relevant NRAs. The Prequalification Team will coordinate with Regional Offices of WHO and relevant authorities in potential user countries to develop mechanisms to support the post-EUL monitoring. Information related to the product will be sent to WHO through relevant safety notice platforms.

WHO will ensure that any necessary corrective action is implemented and that users are informed through a safety notice. WHO reserves the right to issue an information notice for users, if at any time, WHO deems that the EUL holder is not responding to a post-listing quality/safety issue in a timely and scientifically sound manner.

If a quality/safety/efficacy issue cannot be resolved to WHO's satisfaction, WHO reserves the right to restrict or revoke the emergency use listing of the product.

3.3.2. Post EUL changes

Once the product has been listed under the EUL procedure, the development of the product continues to completion for prequalification, whenever possible.

Changes to the product that the manufacturer intends to introduce must be submitted to WHO for review. Additional details on the review process are described in 3.1.2.4

Changes to the product proposed after the product has been listed in the EUL or when it has been taken off the list should be submitted to the PQT. Changes to products listed based on an abridged procedure must have been accepted by the original NRA responsible for the oversight of the product, and WHO must be notified of the accepted changes.

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Table 1: list of activities during the three phases of the EUL

Activity	Pre-emergency phase	Emergency phase	Post deployment
Agreements with NRAs	✓		
Roster of experts	✓		
Eligibility of specific products	✓		
Consensus on requirements	✓		
Assignment of assessment pathway	✓		
Establishment of ad hoc committees	✓	✓	
Assessment of submission	✓		
Decision on listing		✓	
Adverse event monitoring			✓
Extension of listing			✓
Post EUL changes			

Annex 1: Essential data requirements for EUL for vaccines, medicines and in vitro diagnostics

Since the expectation is that the development of the product submitted for EUL will continue to completion and ultimately submitted for prequalification, the submission for EUL of medicines and vaccines should follow the ICH CTD format. In the CTD dossier, sections for which no information is available at the time of the initial submission should be indicated as “data or information not available”, “study ongoing” or “not applicable” as the case may be.

For IVDs, the dossier structure to be used for the submissions has been developed by the IVD PQT. Applicants should follow the dossier structure requirements laid down in documents *PQDx_018 Instructions for compilation of a product dossier* and *PQDx_049 Product dossier checklist*. The instructions for compilation of a product dossier and the product dossier checklist can be found on the PQ website: http://www.who.int/diagnostics_laboratory/evaluations/PQDxInfo/en/

Clarification of specific data requirements may require discussion between the applicant and WHO. Applicants are highly encouraged to contact WHO as early as possible to discuss specifics of their application (See Pre-submission meetings).

Vaccines

Manufacturing Quality Data:

- (1) Full characterization of cell banks according to WHO TRS 978, and any subsequent updates.
- (2) Full characterization of master and working seed organism(s), based on reference to the most appropriate WHO TRS.

Process validation and demonstration of consistency of production at the production scale used for the lots to be distributed. If deemed appropriate, data on clinical batches with a commitment to complete validation on production batches and to submit the data as part of lot release review may be considered.

N.B., if full characterisation is not possible at the time of submission, adequate justification must be submitted as to why not, and a plan must be presented to address the data gaps.

- (3) Justified specifications for starting material, intermediates, and final products,
- (4) Validation of potency test (or initial interim data as available),
- (5) Stability data for the vaccine produced at the scale to be supplied in the field. For vaccines being assessed for emergency use, WHO and the Ad Hoc Committee for the Emergency Use Listing (ACEUL-V – see below), when convened, will consider programmatic suitability and may consider candidate vaccines with characteristics that would not be accepted for prequalification.

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- a. Vaccines requiring storage at less than -20°C are generally not accepted for prequalification. However, under this emergency provision, such vaccines can be considered. Upon receipt of such an application, other parts of the WHO Emergency Response Group such as those responsible for vaccine deployment will be informed by the WHO EUAL team. The Emergency Response Group should evaluate and consider assistance for recipient countries with regards to infrastructure for vaccine storage and distribution at required temperatures.
 - b. Routinely, if the vaccine presented for prequalification requires storage below $+2^{\circ}\text{C}$ during its shelf-life period, it should have a minimum period of storage between $+2^{\circ}\text{C}$ and $+8^{\circ}\text{C}$ of 6 months. Under this emergency provision, vaccines with a shelf life at $+2$ to $+8^{\circ}\text{C}$ of less than 6 months can be considered. The application should include stability data at $+2$ to $+8^{\circ}\text{C}$ to determine the minimum acceptable storage period at $+2$ to $+8^{\circ}\text{C}$. Upon receipt of such an application, other parts of the Emergency Response Group at WHO will be informed by the WHO EUAL team. The Emergency Response Group should evaluate and consider assistance for recipient countries with regards to infrastructure for vaccine storage and distribution at required temperatures
 - c. Routinely, multi-dose vaccines for prequalification should contain adequate preservative, unless they are live-attenuated vaccines (where the preservative may have an adverse effect on the viability of the microbe). However, if a multi-dose vaccine submitted under this emergency provision does not contain a preservative, information/plans on how such a vaccine could be safely managed in the field should be submitted.
- (6) Inspection report(s) from the responsible NRA or from the WHO prequalification team showing compliance with the GMP requirements needed for the extenuating public health emergency, and
- (7) Process changes: by the time of submission, it is likely that the manufacturing process is not finalized and that numerous changes will have to be applied after the first listing. The normal regulatory process for assessment and listing of those variations should be applied but in an expedited manner

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Non-clinical and Clinical Data:

- (1) Non-clinical data demonstrating acceptable safety, immunogenicity, and efficacy in the most appropriate animal model. The applicant must justify the choice of animal model. If the non-clinical package is not complete at the time of submission, the applicant must submit adequate justification for the lack of complete data and a plan and timeline for submitting those data.
- (2) Clinical data demonstrating the appropriate dose to be used and initial acceptable safety and immunogenicity in the population in which the vaccine will be used in the context of the public health emergency
- (3) Preliminary data showing some efficacy– if available. If preliminary human data showing some efficacy are not available for the vaccine under consideration and if not imminently available for other vaccines being concurrently developed, WHO will consider whether the preponderance of evidence from the non-clinical, and early human studies justifies considering the immunogenicity data as a potential surrogate that is thought to be reasonably predictive of clinical efficacy. In such cases, the emergency use listing can proceed provided there are trials underway that will ultimately provide validation data for the surrogate. Safety and immunogenicity data from other vaccines made by the manufacturer using the same product platform may be considered as supportive data for review.

Plan for monitoring and reporting of adverse events

Once the vaccine is deployed and used, since the vaccines listed under the EUL procedure have not been licensed for use in routine immunization settings, post marketing data would not be available at the time of application, Therefore, the manufacturer may discuss with WHO in pre-submission meetings, the plans to ensure the collection and analysis of information on the safety and effectiveness of the EUL product during the period when the authorization is in effect and for a reasonable time following such period. WHO encourages applicants to discuss proposals for active data collection and follow-up mechanisms to capture adverse event information under the EUL, during the pre-submission meetings.

Labelling:

- Summary of product characteristic (information for healthcare provider)
- Patient information leaflet
- Container labeling
- Any other instructional materials provided to the user.
- A plan to help assure that prospective recipients and healthcare providers are adequately informed about the uncertainties regarding both the potential benefits and risks.

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Note: When the product is listed, the labeling should include a statement regarding risk assessment and clearly indicate that that product is for emergency use only.

Medicines

Clarification of specific data requirements will require discussion between the applicant and WHO. Applicants are highly encouraged to contact WHO as early as possible to discuss specifics of their application.

1. Manufacturing and Quality Data:

(1) Information on the active ingredient(s) and finished product, including characterization (including known and potential impurities), composition, preparation, controls (specifications, analytical methods and their validation).

(2) A list of intended changes for scale up, if any, along with a discussion on impact of these changes on the quality and safety/efficacy profile of the product.

(3) Stability data.

(4) Inspection report(s) from an NRA or from a prequalification inspection showing compliance with the GMP requirements needed for the extenuating public health emergency circumstances. Based on the acceptability of the NRA report, WHO may or may not need to perform its own assessment of GMP compliance.

2. Non-clinical and Clinical Data:

(1) All relevant *in vitro* and *in vivo* pharmacodynamic (PD) data, e.g., on microbiologic/virologic activity (including any modeling performed).

(2) Data on efficacy and safety in *in-vitro* tests and in animal model(s) under well-controlled and documented conditions. The preferred model depends on the disease and may vary according to the medicine's mechanism of action. The applicant must justify the choice of animal model.

a. Evidence of efficacy should include improved survival and/or reduced morbidity of animals in the preferred model under relevant conditions. Surrogate markers, validated or reasonably expected to predict efficacy, would be supportive.

b. All available evidence of the medicine's activity *in vitro* and in other animals, together with pharmacokinetics and efficacy in humans, also against other diseases should be submitted

(3) A rationale should be provided for the proposed dosing in humans, with reference to drug exposures shown to be safe and effective in suitable models. Ideally, human pharmacokinetic data should be available, demonstrating similar levels of the drug following administration at the proposed dose, compared to blood levels found to be safe and efficacious in the relevant animal model.

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- (4) If human pharmacokinetic trials or studies in other indications at the exposure level proposed for treatment of the PHE disease have been conducted, assessment of safety using standard parameters (e.g., adverse events, clinical laboratory monitoring, etc.) will be done. This safety evaluation may be supplemented by any other non-clinical and clinical data at different exposure levels.
- (5) If available, clinical data demonstrating safety and efficacy at the proposed dose for PHE field use should be submitted.

3. Labelling:

- Summary of product characteristics (information for health care provider)
- Patient information leaflet
- Primary and secondary labeling
- Any other instructional materials provided to the user.
- A plan to help assure that prospective recipients and health care providers are adequately informed about the uncertainties regarding both the potential benefits and risks.

Note: When the product is listed, the labeling should include a statement regarding risk assessment and clearly indicate that that product is for emergency use only.

In Vitro Diagnostics

1) QMS Review

A review of the manufacturer's QMS documentation and specific manufacturing documents is the first step in the process. At the conclusion of this step, the recommendation will be to proceed, request further documentation, or to terminate the application. The decision to proceed with the assessment process will be made if there is sufficient evidence that the applicant is the legal manufacturer, that there is evidence of an adequate QMS in place, and that the requisite manufacturing capability exists.

- Evidence of implementation of a manufacturing quality management system (e.g., ISO 13485 certificate and most recent regulatory (or certification body) audit report, quality manual, exclusions or non-applications, list of valid quality management documentation, management review report);
- Details of the production workflow including QC points (in process and final release activities);
- Critical supplier list including supplied products (components/raw materials) and services;
- Details on the experience with the product (when was the product developed and when was it first placed on the market, if applicable);
- Details on the manufacturing capacity (existing inventory, minimum time to provide finished product, maximum batch/lot size).

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2) Product dossier review

The second step is the assessment of the documentary evidence of safety and performance. It is acknowledged that many of the required studies to meet full regulatory requirements may not have been performed for IVDs undergoing EUAL assessment. Based on the submitted documentation, a risk based judgment will be made on whether there is a favorable benefit/risk profile. An initial evidence base that includes studies using banked specimens from previous studies, relevant studies in the literature, and studies using contrived specimens to supplement testing of clinical specimens including representative analytes may be acceptable in the absence of complete analytical and/or clinical performance studies, if this evidence base provides a reasonable assurance of safety and performance.

In some jurisdictions, minimizing potential harm of an IVD approved through an emergency authorization mechanism is achieved by active post-market surveillance. However, it cannot be always be assumed that, in the public health emergency settings this EUL process serves, that there are sufficient resources and institutions in place for any consistent effective surveillance. It will be critical for the manufacturer to detail what, if any, post-emergency-use-listing safety monitoring activities are planned if the EUL is granted.

The outcome of this step will determine if the application will proceed to step 3, whether further documentation should be requested, or whether the application should be terminated.

The below sections should be submitted by the applicant, following the requirements laid down in documents *PQDx_018 Instructions for compilation of a product dossier* and *PQDx_049 Product dossier checklist*:

5. Product Information

- 5.1. Regulatory versions of this product
- 5.2. Product description including variants (configurations) and accessories
- 5.3. Essential Principles Checklist
- 5.4. Risk analysis and control

6. Design and Manufacturing Information

- 6.1. Product design
 - 6.1.1. Design overview
 - 6.1.2. Formulation and composition
 - 6.1.3. Biological safety
 - 6.1.4. Documentation of design changes
- 6.2. Manufacturing processes
 - 6.2.1. Overview of
 - 6.2.2. Sites of manufacture
 - 6.2.3. Key suppliers

7. Product Performance Specification, and Associated Validation and Verification Studies³

7.1. Analytical studies

7.1.1. Specimen type

7.1.2. Analytical performance characteristics

7.1.2.1. Accuracy of measurement

7.1.2.1.1. Trueness of measurement

7.1.2.1.2. Precision of measurement

7.1.2.1.2.1. Repeatability

7.1.2.1.2.2. Reproducibility

7.1.2.2. Analytical sensitivity

7.1.2.3. Analytical specificity

7.1.2.4. *Traceability of calibrators and control material values*

7.1.2.5. Measuring range of the assay

7.1.2.6. Validation of assay cut-off

7.1.2.7. Validation of assay procedure – reading time

7.2. Stability (excluding specimen stability)

7.2.1. Claimed shelf life

7.2.2. In-use stability

7.2.3. Shipping stability

7.3. Robustness Studies

7.4. Clinical evidence (clinical or diagnostic sensitivity and specificity)

³ For each study to be submitted, the following must be provided:

- Study description, study identifier, product identifier (e.g., lot numbers), IFU version used, the date of initiation and the date of completion;
- A summary of the study findings including a conclusion that clarifies how the study objectives have been met; and
- The study protocol and full report.

Annex 2: Pre-submission meetings

Pre-submission meetings are an important element in the pre-emergency phase of the EUL procedure. They provide an opportunity for the applicant to meet the PQT that is responsible for the determination of eligibility of their product, and the assessment of their submission.

A pre-submission meeting allows the PQT to have an overview of the product and a) ensure that the applicant has substantial information for a submission, b) provide general guidance on how to proceed with the application and dossier, and c) provide guidance on identified issues that should be dealt with prior to submission. At the same time, it is an opportunity for the applicant to, a) introduce and discuss the intended dossier, b) raise questions and gain valuable feedback and c) address issues prior to submission. The pre-submission meeting aims at enabling an applicant to submit a dossier that may proceed more quickly through the screening and subsequent stages of assessment.

A pre-EUL submission meeting should be planned as early as possible/ The meeting should have a defined agenda and clear objectives to avoid potential hold issues.

To request a pre-submission meeting, the applicant must send the completed Pre-submission Meeting Request Form (see in this Annex) to the Prequalification Team Coordinator. The Group Lead will reply to the applicant with a proposed date for the meeting as appropriate and the deadline to submit the information package . The applicant must send the list of proposed participants not later than 10 days before the meeting.

The PQ Group Lead may invite members of the roster of experts to join the PQ team for the pre-submission meeting.

The Meeting

Meetings are organized by the PQT Group Lead and held at the WHO premises or by audio/video conference. The time allocated will not exceed 3 hours, depending on the agenda prepared by the PQT based on the information package received, the planned presentations and the questions submitted in advance by the applicant.

Minutes will be prepared to record the information presented, the questions raised and the responses, as well as follow up actions if applicable.

PRE-SUBMISSION MEETING REQUEST FORM: EUL ASSESSMENTS

Please complete each section of this application form and submit electronically as a Word document to the PQ Group Lead as appropriate

Vaccines: email address

Medicines: email address

IVDs: email address

If you wish to send information in support of your meeting request. Information attachments in electronic format that are 8MB or less in size can be sent by email. with the completed pre-submission meeting request form, including a proposed agenda for the meeting. Attachments in electronic format that are larger than 8MB should be submitted on CD/DVD, or else be printed and sent by courier or surface mail to the PQ Group Lead, WHO Prequalification Team, World Health Organization, 20 avenue Appia, 1211 Geneva, Switzerland.

Contact Details

Applicant (name of manufacturer)	
Contact person responsible for this application	
Contact person's job title/position	
Contact details (Including full postal address, phone, fax, email)	

Meeting Details

Type of meeting requested

Face-to-face

Teleconference

Brief statement of the intended dossier (INN/strength/dosage form) and the expected date for submission to WHO for EUL

Specific objectives/outcomes expected from the meeting

Emergency Use Listing Procedure

Preliminary proposed agenda including estimated time needed for each agenda item and designated speaker(s)

List of specific questions by technical area

List of all individuals (including titles) who will attend the proposed meeting from the applicant's organization and/or consultants.

Proposed date(s) and time(s) for the meeting

Additional information is attached: Yes No

Additional information will be forwarded separately: Yes No

Completed by:

Date:

For WHO internal use Only

Internal Reference	
Scheduled date and time of meeting	
Location	

Annex 3: Template of Assessment reports



Assessment Report
PRODUCT EVALUATION COMMITTEE-Vaccines (PEC-V)
Emergency Use Listing
Product
Manufacturer

WHO/PQT Focal Person	
PEC Chair	
PEC Reviewers	
Date of this report	

1. Recommendation

Based on the review of the data and the Applicant's response to the PEC LOQs on quality, clinical and other relevant aspects, this Committee considers that should a PHEIC be declared before additional data on (quality), (safety) (efficacy) is provided as the development of the product advances, there is (not) a positive risk benefit balance to recommend the use of this product.

The major objections are related to the following deficiencies:

- a) Quality
- b) safety
- c) efficacy/immunogenicity
- d) GMP, GLP, GCP compliance
- e) Other

2. Executive summary

2.1.1. The product

Description of the product, location of production, stage of clinical development.

2.1.2. Authorizations granted by the NRA responsible for the regulatory oversight of the product

Details of any kind of authorization for use granted for the investigational product for emergency use, or exceptional circumstances, etc.

3. Reference standards used for the assessment

List of guidelines from WHO or regulatory bodies, WHO recommendations, scientific reports and publications and any other relevant documents that the PEC has agreed to use as a set of parameters to assess the information submitted for the product.

4. Scientific review of the submission

4.1 Quality assessment

Summary of reviewed information

Rounds of questions and answers from the applicant

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Emergency Use Listing Procedure

Conclusion

4. 2 Non-Clinical assessment

Summary of reviewed information

Rounds of questions and answers from the applicant

Conclusion

4.3 Clinical assessment

Summary of reviewed information

Rounds of questions and answers from the applicant

Conclusion

4.4 GMP/GLP/GCP compliance

Summary of reviewed information

Rounds of questions and answers from the applicant

Conclusion

4.5 Proposed labelling

Summary of reviewed information

Rounds of questions and answers from the applicant

Conclusion

4. 6. Benefit-risk assessment

5. Final remarks



Assessment Report
PRODUCT EVALUATION COMMITTEE- Medicines (PEC-M)
Emergency Use Listing
Product
Manufacturer

WHO/PQT Focal Person	
PEC Chair	
PEC Reviewers	
Date of this report	

1. Recommendation

Based on the review of the available data and the Applicant's response to the PEC LOQs on quality, safety and efficacy, this Committee considers that should a public health emergency be declared, the risk-benefit balance of this product is

- Positive

- Negative.

Major objections have been identified that

- .

are related to the following deficiencies:

- a) Quality
- b) Safety
- c) Efficacy
- d) GMP, GLP, GCP compliance
- e) Other

2. Executive summary

2.1. The product

Description of the product, location of production, stage of clinical development.

2.2. Authorizations granted by the NRA responsible for the regulatory oversight of the product

Details of any kind of authorization for use granted for the investigational product for emergency use, or exceptional circumstances, etc.

3. Guidelines used for the assessment

List of guidelines from WHO or regulatory bodies, WHO recommendations, scientific reports and publications and any other relevant documents that the PEC has agreed to use as a set of parameters to assess the information submitted for the product.

4. Scientific review of the submission

4.1 Quality assessment

Summary of reviewed information

Rounds of questions and answers from the applicant

Conclusion

4.2 Non-Clinical assessment

Summary of reviewed information

Rounds of questions and answers from the applicant

Conclusion

4.3 Clinical assessment

Summary of reviewed information

Rounds of questions and answers from the applicant

Conclusion

4.4 GMP/GLP/GCP compliance

Summary of reviewed information

Rounds of questions and answers from the applicant

Conclusion

4.5 Proposed labelling

Summary of reviewed information

Rounds of questions and answers from the applicant

Conclusion

4.6. Benefit-risk assessment

4.7 Post listing measures

5. Final remarks

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Assessment Report
PRODUCT EVALUATION COMMITTEE-IVDs (PEC-D)
Emergency Use Listing
Product
Manufacturer

WHO/PQT Focal Person	
PEC Chair	
PEC Reviewers	
Date of this report	

Emergency Use Listing Procedure

1. Recommendation

Based on the review of the data and the Applicant's response to the PEC LOQs on quality, clinical and performance, this Committee considers that should a PHEIC be declared before additional data on (quality), (safety) (efficacy) is provided as the development of the product advances, there is (not) a positive risk benefit balance to recommend the use of this product.

The major objections are related to the following deficiencies:

- Labelling:
- Product information
- Product Performance Specifications, and Associated Validation and Verification Studies
- Specimen type
- Analytical performance characteristics
- Stability (excluding specimen stability)
- Robustness Studies
- Clinical evidence (clinical or diagnostic sensitivity and specificity)
- Quality management systems (QMS) requirements

2. Executive summary

2.1, The product

Description of the product, location of production, stage of clinical development.

Authorizations granted by the NRA responsible for the regulatory oversight of the product

Details of any kind of authorization for use granted for the investigational product for emergency use, or exceptional circumstances, etc.

3. Reference standards used for the assessment

List of guidelines from WHO or regulatory bodies, WHO recommendations, scientific reports and publications and any other relevant documents that the PEC has agreed to use as a set of parameters to assess the information submitted for the product.

4. Scientific review of the submission

- **Labelling**
- **Product information**
- **Product Performance Specifications, and Associated Validation and Verification Studies**

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- Specimen type
 - Analytical performance characteristics
 - Stability (excluding specimen stability)
 - Robustness Studies
 - Clinical evidence (clinical or diagnostic sensitivity and specificity)
- Quality management systems (QMS) requirements

5. Final remarks

Annex 4: Terms of Reference for Ad Hoc Committees

Terms of Reference: Product Evaluation Committee (PEC)

Background

In the context of the World Health Organization (WHO) procedure for emergency use of medical products (EUL), the WHO PQ Secretariat will require support from an independent evaluation group known as the Product Evaluation Committee (PEC)

The PQ Secretariat for each product stream will select experts from a pre-established roster, according to the requirements for evaluation under the EUL procedure

The PEC will have the roles and responsibilities described below.

There will be three branches, one for each product stream:

PEC-V: for evaluation of vaccines, and will be selected, convened and supervised by the Vaccine PQ Team Lead

PEC-M: for evaluation of medicines and will be selected, convened and supervised by the Medicines PQ Team Lead

PEC-D: for evaluation of Diagnostics and will be selected, convened and supervised by the In Vitro Diagnostics PQ Team Lead.

As members of the roster of experts, Members of the PEC have completed the Declaration of Interest and Confidentiality undertaking as per WHO rules and they commit to make every effort to be available on a short notice when a call for the PEC-V is made by WHO.

Roles and responsibilities

The mandate of the PEC is :

- To assess what published guidelines, requirements/recommendations are available from WHO and regulatory agencies that are relevant to the evaluation of a product or group of products.
- To conduct a search for relevant publications with evidence of scientific consensus with regards to safety, immunogenicity or other clinical efficacy of a product
- To agree on a set of guidelines, requirements/recommendations and other parameters that will be used to evaluate a product or group of products
- To screen submissions for completion of information required
- to review the quality, clinical and performance information of the candidate medical product (See Annex 2 for information required, after the product has been determined to be eligible for EUL assessment)

The report and a recommendation by the PEC will be based on the following;

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- Complete application submitted to the PQ Team
- Responses from the applicant to the List of Questions prepared after the initial review (if applicable)
- Additional information or updates submitted by the applicant at any point
- Other information related to the product that the committee deems important for the review

The report prepared by the PEC should follow the template in Annex 4.

The Chair may assign reviewers for specific reviews.

If after initial review of the submission, the PEC decides to address additional questions to the applicant, the Chair will prepare a consolidated List of Questions (LOQ) that will be sent to all members for consensus. This LOQ will be submitted to the PQ Team focal person who will forward to the applicant.

Once the responses are received, they will be reviewed and there may be more rounds of questions until all responses are considered satisfactory or until no more responses can be obtained from the applicant. The PEC will then complete its report, with a recommendation.

Membership

1) PEC-V

The PEC-V consists of members from the established roster of experts and should include:

- quality experts (production and quality control);
- GMP experts ;
- clinical assessment experts
- infectious disease specialists

Members of the roster of experts called to be part of the PEC-V should report if there was any change in affiliation resulting in a conflict of interest.

2) PEC-M

The PEC-M consists of:

a) regulators with the relevant expertise in the assessment of:

- pharmaceutical quality data (production, quality control and GMP)
- toxicological/pre-clinical data
- pharmacokinetic and modelling/simulation data
- clinical efficacy and safety data
- pharmacovigilance measures

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b) Infectious disease specialists (clinician, non-regulator), paediatricians and, depending on the nature of the disease also other clinical specialists.

Members of the roster of experts for PEC-M should report to the PQ Team Lead any real or perceived conflicts of interest.

3) PEC-D

The PEC-D consists of:

Experts with the relevant expertise in the assessment of:

- Quality management system
- Validation and verification studies and labelling

Members of the roster of experts for PEC-M should report to the PQ Team Lead any real or perceived conflicts of interest.

Term

All PEC members will commit to serve on an ad hoc basis until the evaluation of the product in question has been completed.

Chair

A Chair will be selected by the PQ Secretariat from among the PEC members.

The Chair is responsible for:

- managing communications with the PQ Secretariat
- managing the review process and approving all PEC reports and official records;
- assuring compliance with time frames;
- submitting the List of Questions,
- co-ordinate reports and provide a final report to the PQ focal point;

Modus operandi

Schedule of the PEC activities

PQ Secretariat will call members of the PEC committee to convene a planning meeting, distribute submissions, and convene virtual or face-to-face meetings for deliberations and preparation of reports.

Once the PQ focal point has provided the Chair of the PEC and other members with the submission, the experts will have 3 months to review the information received. If additional information is required, each expert will prepare questions to be added to the List of Questions (LOQ) for submission to the Chair. The Chair may coordinate a

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discussion among PEC members as required. The Chair will consolidate the LOQ and will send it to the PQ focal person. Once the responses are received, each expert will report if the answers are satisfactory or if there are inadequacies. There may be more than one round of LOQs, until no further information is forthcoming from the applicant. Based on the information available, the Chair will prepare a consolidated report (template in Annex 3) and will circulate to all PEC members for consensus.

If new data becomes available, the PQ focal person will call the same PEC to review the information and update the report accordingly.

Management of communications between the PQ focal point and the PEC

A focal point, designated by the PQ Group Leads, will manage all communications between the PQ Secretariat and PEC.

Once a submission has been received, the focal point will communicate with the members of the roster of experts to invite them to constitute the PEC to review information, deliberate and prepare an assessment report for one or more products. The focal person will indicate the deadline to respond regarding their availability and the name of the person designated as Chair.

For each review the focal point will:

- provide the PEC Chair with the submission received and electronic copies of all WHO recommendations and guidelines as well as guidance documents from regulatory bodies and reports
- communicate to the applicant that the application will be reviewed by the PEC according to the EUL procedure. The timeline for completion will depend on the need for clarifications and additional information requested by the PEC;
- Facilitate the arrangements for teleconferences or any means of communication among members of the PEC
- monitor progress, with the PEC Chair
- Submit LOQs to the Applicant, and forward responses submitted by the applicant to the PEC Chair.
- collect the final report with recommendations from the PEC Chair, deliver it to the PQ Secretariat, and formally close the review. Should no additional data become available before a PHE(IC) is declared, the final report will be used by the ACEUL. Otherwise, if additional data is submitted (i.e. updates on clinical trial results, completion of validation of processes and tests, etc.), the report will also be updated and filed. The report shall be prepared using a standardized format that will include the assessment of the information reviewed, List of Questions and responses and a final recommendation/opinion.

Terms of Reference: Advisory Committee for Emergency Use Listing (ACEUL)

Background

In the context of the World Health Organization (WHO) procedure for emergency use of medical products, the WHO PQ Secretariat will require support from an independent advisory group known as the Advisory Committee for Emergency Use Listing (ACEUL).

The PQ Secretariat for each product stream will select experts from a pre-established roster, according to the expertise required.

The ACEUL will then have the roles and responsibilities described below. There will be three branches, one for each product stream:

ACEUL-V: for listing of vaccines, and will be selected, convened and supervised by the Vaccine PQ Team Lead

ACEUL-M: for listing of medicines and will be selected, convened and supervised by the Medicines PQ Group Lead

ACEUL-D: for listing of Diagnostics and will be selected, convened and supervised by the In Vitro Diagnostics PQ Team Lead.

As members of the roster of experts, Members of the ACEUL-V have completed the Declaration of Interest and Confidentiality undertaking as per WHO rules and they commit to make every effort to be available on a short notice when a call for the ACEUL-V is made by WHO.

Roles and responsibilities

The mandate of the ACEUL is to provide, on request, an opinion on the acceptability of a medical product for emergency use.

In order to formulate a recommendation, the ACEUL will use the following;

- Report on quality, safety and efficacy, prepared by the Product Evaluation Committee (PEC), including initial evaluation and any updates based on additional information submitted by the applicant
- Programmatic aspects when applicable
- Additional information the ACEUL may request from the PQ Team or the applicant through the PQ Team
- Risk/benefit assessment.

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The recommendation being sought is either:

- acceptance of the product for emergency use;
- non-acceptance of the product for emergency use.

The ACEUL will advise the PQT of its recommendation, and the outcome of the assessment will be made available to interested procurement agencies and member countries. However:

- The ACEUL has no executive, regulatory or decision-making functions
- The ACEUL is an advisory body only, and is not involved in procurement decisions
- The advice provided by the ACEUL is not the same as prequalification
- Products that undergo this procedure may at some point in the future be prequalified if they meet the prequalification requirements.
- The duration of validity of any positive opinion of the ACEUL shall not be longer than 12 months.

Membership

1) ACEUL-V

The ACEUL-V consists of members from the established roster of experts and should include:

- One or Two members with expertise in the epidemiology of the disease that will be prevented with the vaccine in question;
- One or two members should have regulatory expertise relating to vaccine evaluation and risk management plans ;
- One or two members who are from the NRA of the affected countries
- One member will be designated from the WHO specific disease control unit
- One member from the PEC with expertise in quality assessment
- One member from the PEC with expertise in clinical assessment

Members of the roster of experts called to be part of the ACEUL-V should report if there was any change in affiliation resulting in a conflict of interest.

2) ACEUL-M

The ACEUL-M consists of members from the established roster of experts and should include:

- Members with expertise in the epidemiology of the disease or condition of interest.
- Members having regulatory expertise relating to the product and potential risk management plans
- Members from the NRA of the affected countries
- Members from the WHO specific disease control unit
- Members from the PEC with expertise in quality assessment
- Members from the PEC with expertise in clinical assessment
- Members (non-expert) from the affected region who are informed and representative of the local community viewpoint may be included at the discretion of WHO.

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Members of the roster of experts who are part of the ACEUL-M should report to the PQ Secretariat any real or perceived conflicts of interest.

3) ACEUL-D

Experts with the relevant expertise in the assessment of:

- Quality management system
- Validation and verification studies and labelling

Term

All ACEUL members will commit to serve on an ad hoc basis to provide advise on specific products.

Chair

A Chair will be selected by the PQ Secretariat and Director EMP from among the ACEUL members for each consultation, based on the product to be assessed.

The Chair is responsible for:

- managing communications with the PQ Secretariat and Director EMP;
- managing the review process and approving all ACEUL official records;
- assuring compliance with time frames;
- submitting the final recommendations to the Director EMP;
- approving any publications based on these records;

Modus operandi

Schedule of the ACEUL activities

PQ Secretariat will call members of the committee on short notice to convene a planning meeting, distribute reports and convene virtual or face-to-face meetings.

A final recommendation should be issued within five days of receipt of the consolidated reports. If additional information is requested, a recommendation should be issued within three days of receipt of the new data.

Management of communications between the PQ Secretariat and the ACEUL

A focal point, designated by the PQ Secretariat, will manage all communications between the PQ Secretariat and ACEUL and will, in the case of a request for a recommendation or technical advice, monitor and support the review process.

Once the Public Health Emergency is declared, the focal point will communicate with the members of the roster of experts to invite them to constitute the ACEUL to review information, deliberate and issue a recommendation for one or more products. The focal person will indicate the deadline to respond regarding their availability, and the person designated as Chair.

Emergency Use Listing Procedure

For each review the focal point will:

- provide the ACEUL Chair with the consolidated report prepared by the PEC for the specific product and any other data considered relevant for the discussions.
- communicate to the manufacturer that the application will be reviewed by the ACEUL according to the EUL procedure and the expected timeline for completion;
- Facilitate the arrangements for teleconferences or any means of communication among members of the ACEUL
- monitor progress, with the ACEUL Chair, of each review
- facilitate confidential communications with the manufacturer, or other units within WHO as required;
- collect the final report with recommendations from the ACEUL Chair, deliver it to the PQ Secretariat, and formally close the review. The report shall be prepared using a standardized format that will include the recommendation (acceptance or rejection) and a summary justification.

Annex 5: Criteria for selection of assessment pathways

a) Vaccines

For vaccines, the principles used for the streamlined procedure for prequalification will be also considered for the EUL, as well as the experience of the manufacturer with regards to prequalification since their facilities have been audited in the past, their Quality Management Systems have been assessed and there is a record of performance of the producer and their product(s) to support the reliance on their experience. For vaccines, the following criteria will be followed to determine the assessment approach

Table 1: Assignment of assessment category for vaccines

	Manufacturer with PQd vaccines	Manufacturer without PQd products
Agreement with NRA/ reports available	A	C
No agreement with NRA	B	C

Table 2: Assessment approach and timelines for each category

Category	Assessment approach	Timelines
A	WHO will conduct an accelerated review: -Report(s) from the responsible NRA (Summary basis for the emergency use approval or equivalent) - Programmatic aspects	
B	WHO will conduct an accelerated review: - Application (see content above) - Programmatic aspects	
C	WHO will conduct a review: - Application (see content above) - Inspection report from PQ - Programmatic aspects	

Emergency Use Listing Procedure

b) Medicines

	Assessment procedure	Inspection procedure
Product approved for use by an SRA for the target disease	Abridged assessment based on the SRA report	Desk review of available SRA inspection reports, or if required, inspection by WHO.
Product not approved for use by an SRA	Full assessment by WHO of the submitted dossier information. The review will also consider available assessment reports written by NRAs.	Inspection by WHO or desk review of available WHO, SRA, or PIC/s member inspectorate reports

c) In vitro diagnostics

	Assessment procedure	Inspection procedure
Product approved through another emergency mechanism	Abridged assessment of documentary evidence	Desk review of the QMS
Product not approved through another emergency mechanism	Full assessment by WHO of the submitted documentary evidence	Desk review of the QMS

Abridged EUL Assessment

Some submissions submitted for WHO EUL may have undergone a previous assessment through other emergency mechanisms, for example, the US FDA Emergency Use Authorization (EUA) process. Where this is the case, it is not the intent of WHO to undertake duplicative work, if the review of the other emergency mechanism is deemed to be of a satisfactory standard. The ability to waive aspects of the EUL assessment in these circumstances can be applied to any of the three steps. However, WHO EUL is designed to provide a level of assurance of the quality, safety, and performance of these assays for the primary purpose of use in the setting of a current public health emergency. This focus means that WHO may still undertake some extra assessment activities if deemed necessary.

Annex 6: Declaration of Interest for WHO experts

Placeholder

Annex 7: Confidentiality undertaking for WHO experts

Placeholder