



Emergency Use Listing Procedure

Version 9 August 2022

Emergency Use Listing Procedure

Emergency Use Listing Procedure

Table of contents

Abbreviations.....	5
1. Background	6
2. Rationale for the revision of the EUAL.....	6
3. Scope and purpose of the EUL procedure	7
4. Eligibility of candidate products.....	8
5. Phases of the procedure	9
5.1. Pre-emergency phase	9
5.1.1 Establishment of the assessment platform	10
5.1.1.1 Agreements with NRAs of record for information sharing.....	10
5.1.1.2 Framework for interaction with NRAs and Ethics Committees of potentially affected countries	10
5.1.1.3. Establishment of a roster of experts to support the different phases of the procedure	10
5.1.1.4. Consensus on essential requirements on quality, safety, efficacy/immunogenicity/ performance and lot release (when applicable) for specific products	11
5.1.1.5. Pre-submission activities/ meetings	12
5.1.1.6 Submission of applications	12
5.1.1.7 Assignment of Assessment pathway	13
5.1.1.8 Assessment of initial information received	13
5.1.1.9 Submission of updates	14
5.2 Emergency phase activities.....	14
5.2.1 Expert Groups	14
5.2.2 WHO decision on emergency use listing.....	14
5.2.3 Publication of review outcomes and communications.....	14
5.3 Activities after a product has been listed, deployed and used.....	16
5.3.1 Post listing monitoring	16
5.3.2. Post-listing changes.....	16
6. Resolution of Disputes	16
7. Privileges and Immunities of WHO	17
Figure 1: Flowchart of the EUL process	19
Annex 1: Terms of Reference for Experts and Advisory Groups.....	20
Terms of Reference for the Product Evaluation Group (PEG)	21

Emergency Use Listing Procedure

Terms of Reference for the Technical Advisory Group for Emergency Use Listing (TAG-EUL).....	26
Memorandum of Agreement - Terms and Conditions for Temporary Advisers.....	30
Annex 2: Pre-submission meetings.....	31
Annex 3: Application letter model	34
Annex 4: Letter of Agreement	35
Annex 5: Essential data requirements for EUL for vaccines, medicines and in vitro diagnostics.....	40
Annex 6: Criteria for selection of assessment pathways	48
Annex 7: Template of Assessment reports	51
Product Evaluation Group - Vaccines (PEG-V)	52
Product Evaluation Group - Medicines (PEG-M).....	55
Product Evaluation Group - IVDs (PEG-D).....	58
Advisory Group for EUL (TAG-EUL)	61
Annex 8 Notes and disclaimers - EUL List of candidate products.....	64
Authors.....	66
Acknowledgments.....	66

Emergency Use Listing Procedure

Abbreviations

CTD	Common technical document
DOI	Declaration of Interest
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
EUAL	Emergency Use Assessment and Listing
EUL	Emergency Use Listing
EVD	Ebola Virus Disease
GCP	Good clinical practice
GLP	Good laboratory practice
GMOs	Genetically Modified Organisms
GMP	Good manufacturing practices
QMS	Quality Management Systems
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IVDs	In vitro diagnostics
LOQ	List of Questions
NRA	National regulatory authority
PEG	Product Evaluation Group
PHE	Public Health Emergency
PHEIC	Public Health Emergency of International Concern
PQT	Prequalification Team
PSUR	Periodic safety updated report
R&D	Research and Development
RPQ	Regulation and Prequalification Department
SRA	Stringent Regulatory Authority
TAG-EUL	Technical Advisory Group for Emergency Use Listing
TORs	Terms of Reference
TRS	Technical report series
WLA	WHO Listed Authority
WHO	World Health Organization

Emergency Use Listing Procedure

1. Background

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 unlicensed vaccines, therapeutics and in vitro diagnostics (IVDs) for use primarily during public health emergencies of international concern (PHEIC) but also in other public health emergencies if appropriate.

Two submissions for Ebola vaccines were received but none was listed. No therapeutic products that were in development were submitted during the 2014-2016 Ebola outbreak. Twenty-five applications for IVDs were received for Ebola assays of which seven were listed. Also, three out of thirty-three applications received for Zika assays were listed.

Based on the above experience, vaccine developers and national regulators identified the need to revise and simplify the procedure, in order to improve clarity on procedural aspects, and to avoid overlap or gaps in their respective functions.

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.

2. Rationale for the revision of the EUAL

The WHO Informal Consultation on options to improve regulatory preparedness to address public health emergencies (Geneva, May 2017)¹ concluded that some aspects of the WHO EUAL procedure needed to be reconsidered and revised. The consensus was : a) the process should be reframed as the Emergency Use Listing (EUL) procedure ; b) the revised procedure should be used primarily during a Public Health Emergency of International Concern (PHEIC) ², although the Director-General may authorize the 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.

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

² The term Public Health Emergency of International Concern is defined in the IHR (2005) as “an extraordinary event which is determined, as provided in these Regulations:

- i. to constitute a public health risk to other States through the international spread of disease; and
- ii. to potentially require a coordinated international response”. This definition implies a situation that: is serious, unusual or unexpected; carries implications for public health beyond the affected State’s national border; and may require immediate international action.

Emergency Use Listing Procedure

For the purpose of this document, a PHEIC or other public health emergency for which the use of this procedure is authorized are referred to as a “PHE” ; c) WHO should ensure that the use of an unlicensed product under the EUL framework is based on a pre-determined rationale and pre-determined criteria; d) the role of National Regulatory Authorities (NRAs) and the degree of reliance upon their assessments should be clear, and NRAs of potentially affected countries should be involved in the EUL procedure during public health emergencies, and; e) the EUL should also include plans for pre-emergency activities to allow a rapid listing decision once the emergency is declared.

Accordingly, this Emergency Use Listing (EUL) procedure, replaces the Emergency Use Assessment and Listing (EUAL) procedure.

3. Scope and purpose of the EUL procedure

The goal of the procedure is to define the steps that WHO will follow to establish eligibility of unlicensed products for assessment under this procedure, the essential information required, and the process to be used in conducting the assessment to determine whether an unlicensed product can be listed on a time limited basis, while further data is being gathered and evaluated.

The Prequalification Team has been assigned the role as EUL Secretariat, as this team possesses the required expertise in product evaluation and interacts with procurement organizations and NRAs (i.e. NRAs responsible for the regulatory oversight of products and NRAs from potential user countries). However it is very important to note that the EUL is not equivalent or an alternative to WHO prequalification, and should not be thought of as such. The EUL is a special procedure for unlicensed vaccines, medicines and in vitro diagnostics in the event of a PHE 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, diagnosis/detection or prevention options. It is intended to provide a time-limited listing (see section 5.2.3) for unlicensed products in an emergency context when limited data are available and the products are not yet ready for application for prequalification³. As part of the EUL, it is expected that the manufacturer will complete the development of the product and submit for licensure and WHO prequalification.

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

The EUL is not intended to interfere with ongoing clinical trials. This means that the clinical development should proceed as planned after the initial submission and subsequent updates.

³ While EUL applies to unlicensed products, prequalification only considers products that have been licensed by the responsible NRA. See <https://www.who.int/topics/prequalification/en/>
EUL-v 9 August 2022

Emergency Use Listing Procedure

It should be noted that it is the sole prerogative of WHO Member States to use the EUL as the basis to authorize the use of an unlicensed vaccine/medicine/IVD at the national level.

This document is intended to guide 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.

4. Eligibility of candidate products

The three product streams (vaccines, therapeutics and IVDs) each have specific requirements for products to be eligible for evaluation under the EUL procedure.

In order to qualify for assessment under this procedure, the following criteria must be met:

- The disease for which the product is intended is serious or immediately life threatening, has the potential of causing an outbreak, epidemic or pandemic and it is reasonable to consider the product for an EUL assessment, e.g., there are no licensed products for the indication or for a critical subpopulation (e.g., children);
- Existing products have not been successful in eradicating the disease or preventing outbreaks (in the case of vaccines and medicines);
- 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, and;
- The applicant undertakes to complete the development of the product (validation and verification of the product in the case of IVDs) and apply for WHO prequalification once the product is licensed. For that purpose, the remaining clinical trials and other testing needed to complete the development of the product must already be underway at the time of the application for an EUL⁴.

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.

⁴ A future prequalification application should incorporate all information submitted for the EUL plus any other information needed to complete a prequalification application

5. Phases of the procedure

There are 3 phases of the EUL procedure:

- Pre-emergency phase;
- Emergency phase, and;
- Post-listing phase.

5.1. Pre-emergency phase

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) Blueprint⁵ 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- on the activities that can be done in advance, thus minimizing the time required for a final decision about possible listing of a product once the public health emergency is declared.

If pre-emergency activities have not been conducted, either at the time when a PHE occurs or whilst a PHE is in progress, they would be implemented during the emergency phase. In this situation, timelines for the process will be impacted.

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

- Establishment of an assessment platform.

This includes activities that are intended to establish a platform for collaboration between WHO, external experts, NRAs responsible for the oversight of the product and NRAs from potential user countries. Activities include establishment of a roster of experts to be called upon to set up the necessary advisory Groups at the different stages of the procedure, consultations, strategic planning and oversight of systems/procedures to support the implementation of the EUL.

- 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 data and updates), with reports thereon. These aspects are part of the eligibility and assessment process and use the resources and output of the assessment platform.

⁵ <https://www.who.int/blueprint/about/en/>

Emergency Use Listing Procedure

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

5.1.1 Establishment of the assessment platform

5.1.1.1 Agreements with NRAs of record for information sharing

For vaccines, an agreement is required for information sharing between WHO and the NRA that is responsible for the regulatory oversight of the unlicensed product (NRA of record). This is consistent with the principles for use of the streamlined procedure for prequalification of vaccines. These agreements will allow WHO to rely on the NRA's assessment of quality, pre-clinical and clinical information and facilities. The NRA of record may also have issued an authorization for emergency use of the unlicensed product.

For medicines, reliance by WHO on the assessment by Stringent Regulatory Authorities/WHO Listed Authorities (SRAs/WLAs)⁶ does not require an agreement for information sharing. Reports of the inspections conducted by the SRA/WLA that issued the authorization under extraordinary circumstances such as a public health emergency will also be considered to waive the requirement for an inspection by WHO. Reliance upon the SRA/WLA 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 possible EUL listing may have an impact on the time required to complete the evaluation. (See "Selection of assessment pathways" below.)

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

As priority diseases are identified and products are considered eligible for assessment, WHO will discuss with NRAs and Ethics Committees of potentially impacted countries, to define their level of participation during the pre-emergency, emergency and post listing phases for each specific product.

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

A roster of experts will be established through a selection process by WHO's Regulation and Prequalification Department (RPQ) (former Regulation of Medicines and other Health Technologies Department).

Experts may be selected among suitably qualified members of existing ad hoc or standing advisory Groups, relevant WHO expert panels, including representatives from NRAs of

⁶ WHO Listed Authority (level 4).

Emergency Use Listing Procedure

manufacturing countries, NRAs responsible for the regulatory oversight of products, 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 phases, so that the required Groups (see 5.1.1.4) can be rapidly established when required for assessment and recommendations relevant to specific products.

The selected experts will be assessed for conflicts of interest and be required to enter into a confidentiality undertaking.

There are two types of Groups that will be established on an ad hoc basis from the roster of experts:

a) Product Evaluation Group (PEG)

This Product Evaluation Group (PEG) will be called during the pre-emergency phase of the procedure to: i) determine what sets of guidelines, requirements and scientific consensus guidelines -when available- will be used to assess a product; ii) evaluate applications of products that have met the EUL eligibility criteria and have passed the initial screening; iii) perform a risk-based assessment of the scientific data for a product, including quality, safety/efficacy/performance, and programmatic aspects; iv) prepare a report with the PEG's recommendations for submission to WHO. WHO may submit this report to the Advisory Committee for Emergency Listing (TAG-EUL) (See below) for consideration when a PHE is declared.

Should a submission be received once the PHE had been declared, the PEG will be convened in the emergency phase. Timelines for review and report will in this case be impacted but shortened as much as possible.

b) Technical Advisory Group for Emergency Use Listing (TAG-EUL):

This group will be established once a PHE has been declared (see emergency phase below).

Each PEG and each TAG-EUL will be coordinated by the Leader of the relevant Prequalification Team Group (Vaccines, Medicines, IVDs). (See Terms of Reference of PEG in Annex 1) .

5.1.1.4. 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 be no official WHO standards or national regulatory guidelines that are fully applicable to a specific unlicensed product. The prioritization process for the development of product-specific WHO guidelines takes into account not only the priority list of diseases as per the R&D Blueprint but also several other competing global public health needs.

However, some WHO, international and national guidelines that are of a more general nature (i.e. cell substrates for vaccine production, 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. Guidelines from WHO or NRAs, relevant international

Emergency Use Listing Procedure

guidelines, as well as literature to support scientific consensus on aspects related to the specific type of product, will be considered and discussed by the Product Evaluation Group in order to decide which ones will be used to assess a specific product. The report will indicate the list of guidelines and other scientific literature that has been used by the PEG as the basis for the assessment.

5.1.1.5. 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 the 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.

5.1.1.6 Submission of applications

Applications:

The manufacturer must submit an application letter using the template set forth in Annex 3 hereto, duly completed, signed and dated by each applicant/manufacturer with the product, to WHO's Director of RPQ, with a copy to the relevant PQT Team Lead and the NRA responsible for the regulatory oversight of the unlicensed product. The application letter should include details of country and sites of manufacture, the presentations proposed for the product and information on whether or not the NRA has issued an authorization for emergency use or equivalent.

WHO will acknowledge receipt of the application letter by e-mail, with a copy to the relevant NRA. The acceptance of an application will also be confirmed by email, with a copy to the NRA. WHO will only respond with an official letter in those cases where the product cannot be accepted, including but not limited to because: the product does not meet the eligibility criteria. WHO will endeavour to advise the applicant and the NRA of a rejection of the application within 2 weeks of receipt of the official request.

Once the product has been accepted for review under the EUL procedure, the applicant will be required to submit a duly signed Letter of Agreement (as per the template in Annex 4) and the dossier in the appropriate format for each product stream. (See Annex 5).

Emergency Use Listing Procedure

5.1.1.7 Assignment of Assessment pathway

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

The criteria for use of abridged review and full review for each type of product according to reliance on the NRA that has previously assessed the product (and, for vaccines, the manufacturer's previous WHO prequalification record), are detailed in Annex 6.

5.1.1.8 Assessment of initial information received

Once the product has been considered eligible for assessment under the EUL procedure, the PQT Team Lead of the relevant product stream will designate a focal person for the EUL assessment of a specific product.

The focal person will perform the screening of the submission to ensure that sufficient information is available to initiate the assessment by the PEG based on the essential data requirements (See Annex 5). If the screening indicates that the assessment cannot start due to lack of information, this will be communicated to the applicant. A complete dossier may be submitted any time afterwards.

In addition to the EUL dossier review process, a WHO 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 outcome of the desk review or if the PEG so recommends.

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

A consolidated report of the PEG 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 report of the PEG and all subsequent versions with updates (see below) will be submitted to WHO. WHO may submit this report to the Committee responsible for a final recommendation on possible listing (TAG-EUL) if/when a PHE is declared before additional data becomes available. The report will provide the TAG-EUL with a documented outcome of the evaluation of the quality, safety, efficacy/immunogenicity/performance of the product by the PEG based on currently available data. The report will also indicate when the next set of data is expected (for example, full report of phase II trials). (See Annex 7 for Assessment report templates.)

Emergency Use Listing Procedure

5.1.1.9 Submission of updates

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

The applicant should – as much as possible- provide tentative timelines for the 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 5).

5.2 Emergency phase activities

5.2.1 Expert Groups

The TAG-EUL for the evaluation of a specific product or group of products for a specific disease will be established by WHO upon declaration of a PHE. In some cases, WHO may establish the TAG-EUL while the PHE declaration procedure is still pending. Members of the TAG-EUL will be selected by WHO from the established roster of experts. The focal point designated by the Team Lead of the relevant PQ product stream may provide the TAG-EUL members with the report prepared by the relevant PEG and any other information considered critical for the deliberations and decisions. (See Terms of Reference of the TAG-EUL in Annex 1)

5.2.2 WHO decision on emergency use listing

This procedure includes provisions to concentrate most of the activities related to the submission and assessment of available data during the pre-emergency phase. Therefore, optimally the TAG-EUL will have all the necessary information to deliberate and issue a recommendation to WHO on whether or not a product should be listed, and if so, under what conditions for use, in a short period of time. The TAG-EUL may request further information from the applicant before making a recommendation. The recommendation of the TAG-EUL will be used by WHO to decide whether or not the product can be granted an EUL.

5.2.3 Publication of review outcomes and communications

Upon making a decision whether or not to grant a recommendation (acceptance or non-acceptance) for emergency use listing of the evaluated product, WHO will (without prejudice to any confidential information of the applicant/manufacturer) publish information about the product in a public report available on a dedicated portal of the WHO website. This may include negative assessment outcomes.

As WHO is responsible for the EUL assessment process, the ownership of the reports arising from or relating to the EUL assessment process lies with WHO. Thus, WHO shall be entitled to use and

Emergency Use Listing Procedure

publish such reports, subject always, however, to the protection of any commercially sensitive confidential information of the manufacturer. Confidential information in this context means:

- confidential intellectual property, know-how, and trade secrets (including, e.g. formulas, processes or information contained or embodied in a product, unpublished aspects of trademarks, patents, etc.); and
- commercial confidences (e.g. structures and development plans of a company).

Subject to the protection of commercially sensitive confidential information, WHO will publish on the WHO website and make publicly available the following information in connection with the prequalification assessment process:

- the names of products and of manufacturers that have applied for EUL, the product code(s) submitted for EUL and the EUL status of each application;
- a WHO EUL public report summarizing the findings of the EUL assessment; and
- any negative outcomes of the EUL assessment.

In addition, WHO reserves the right to share full reports with the relevant authorities of any interested Member State of the Organization and interested United Nations agencies.

Furthermore, at any time during the EUL assessment process, WHO will have the right to use, publish, issue, share with national regulatory authorities (NRAs) and other relevant authorities of WHO Member States and/or with United Nations agencies and other relevant intergovernmental organizations, and/or make publicly available any outcomes, reports, notices and/or results—whether in draft or final form, and whether positive or negative—arising from or relating to the EUL assessment process and/or any listed product and/or any confidential information (as defined above) to which WHO may gain access in the course of the EUL assessment process. WHO's aforementioned rights will be exercised in accordance with the provisions of this EUL procedure regarding the protection of any commercially sensitive information of the applicant/manufacturer.

The validity of an emergency use listing in the context of a PHE will generally be for 12 months.

All decisions to list a product in the EUL will be reassessed at 12 months intervals (or sooner, if further data become available that could alter the original decision). 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 termination of the PHE.

Emergency Use Listing Procedure

5.3 Activities after a product has been listed, deployed and used

5.3.1 Post listing monitoring

After a product has been listed, WHO will take into consideration reports on safety surveillance, efficacy/effectiveness/performance monitoring, quality complaints and other relevant data that may impact the validity of the listing status.

The sources of such information will inter alia be based on existing surveillance mechanisms in affected countries (as discussed with relevant NRAs during the pre-emergency phase) and on post-listing surveillance commitments of the manufacturer, set as conditions for the listing.

WHO reserves the right to issue an information notice for procurement agencies and relevant programs, if at any time, WHO deems that the EUL holder is not responding to a post-listing quality/safety issue in a timely and/or scientifically sound manner. If quality/safety issues are identified post listing, WHO may seek advice from the TAG-EUL. If a quality/safety issue cannot be resolved to WHO's satisfaction, WHO reserves the right to restrict or revoke the emergency use listing of the product.

5.3.2. Post-listing changes

Once a product has been listed under the EUL procedure, the development of the product must -whenever possible- continue to completion for marketing authorization and be submitted to WHO for prequalification, once licensure has been obtained.

The applicant must promptly inform WHO of all changes regarding formulation, manufacturing process, testing methods, specifications, facilities and any other aspects that might (a) result in a change of the safety and/or efficacy and/or performance of the product or (b) change the basis for the listing recommendation. Such changes to the product must follow the procedure for submission of updates described in 5.1.1.9.

Changes to products listed based on an abridged procedure must be accepted for emergency use by the original NRA responsible for the oversight of the product, and WHO must be notified of the accepted changes.

6. Resolution of Disputes

Any and all claims or disputes arising from or in connection with this EUL procedure, including, but not limited to, any rejection of an application, any assessment hereunder and/or any decision whether or not to grant an EUL recommendation for an evaluated product (hereinafter, collectively, "Disputes") must be submitted in writing to WHO's Director of RPQ, with a copy to the relevant PQT Team Lead.

WHO's Director of RPQ, or one of his/her authorized representatives, will acknowledge in writing receipt of the relevant Dispute and will conduct an investigation into the Dispute within
EUL-v 9 August 2022

Emergency Use Listing Procedure

30 days of receipt. Following the investigation, WHO's Director of RPQ, or one of his/her authorized representatives, will provide a written response to the applicant/manufacture that submitted the Dispute. If the applicant/manufacture is dissatisfied with the written response, then it must object in writing to WHO within 30 days of the date of WHO's aforementioned written response. In the event that the applicant/manufacture does not object to WHO in writing within such 30 day period, then the content of WHO's written response (including, without limitation, any findings or decisions contained therein) will be final and can no longer be challenged by the applicant/manufacture in any way. However, if the applicant/manufacture does object to WHO in writing within such 30 day period, then the Dispute will be referred to WHO's Director-General for his or her decision which will be final and binding on the parties.

7. Privileges and Immunities of WHO

By virtue of WHO's status as a Specialized Agency of the United Nations, WHO, its officials and experts performing missions for WHO (including, e.g. assessors and inspectors) enjoy privileges and immunities under national and international laws and conventions, including without limitation: (i) the Convention on the Privileges and Immunities of the Specialized Agencies, adopted by the General Assembly of the United Nations on 21 November 1947 (the "1947 Convention"), and (ii) the United States' International Organizations Immunities Act of 1945 and Executive Order 9698 relating thereto (collectively, the "IOIA"). Nothing contained in or in connection with this EUL procedure and/or any assessment process hereunder will constitute or be deemed as a waiver of any of the privileges or immunities which WHO, its officials and/or experts performing missions for WHO enjoy pursuant to the 1947 Convention, the IOIA or otherwise under any national or international law, convention or agreement, and/or as submitting WHO, its officials and/or experts aforesaid to any national court jurisdiction.

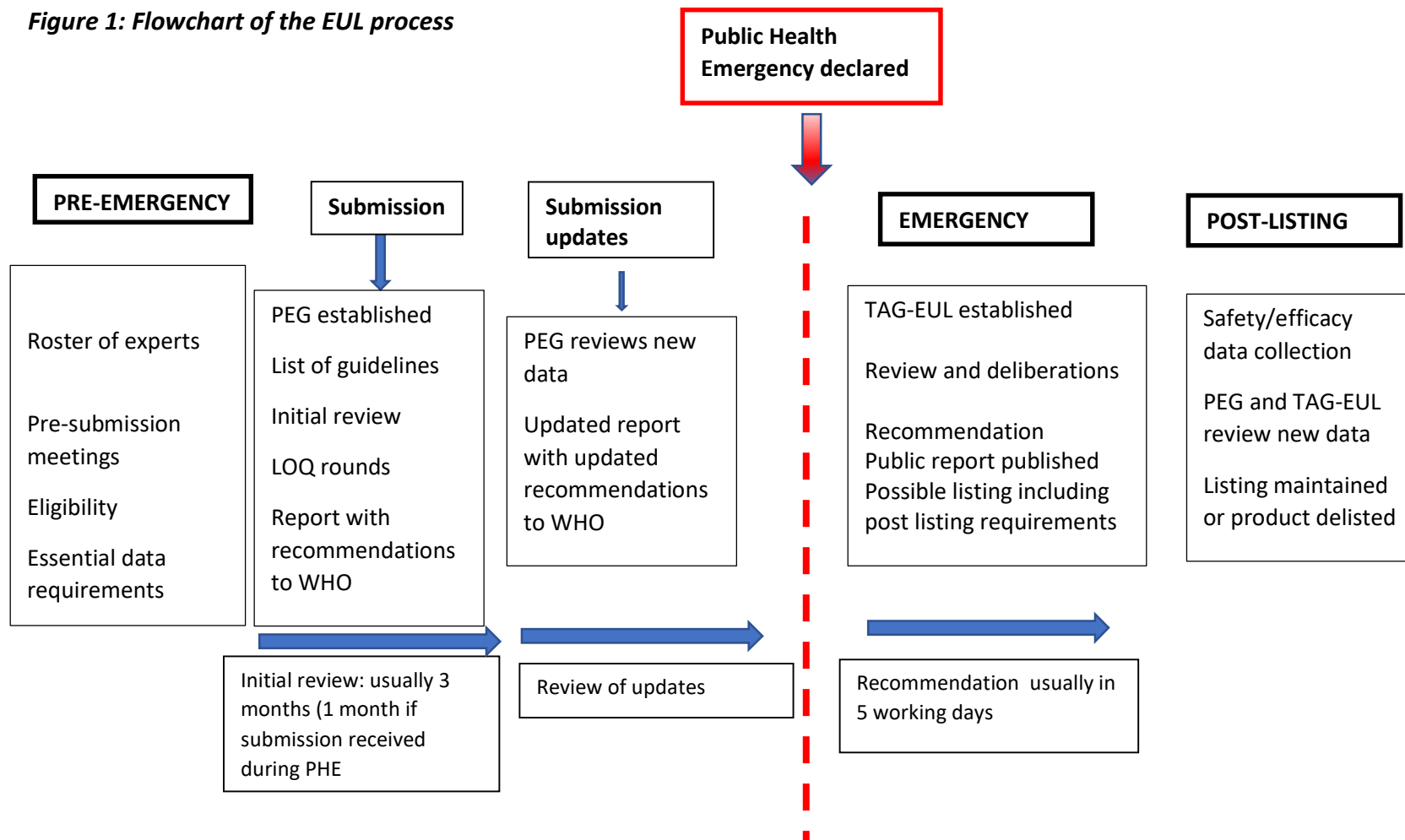
Emergency Use Listing Procedure

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

Activity	Pre-emergency	Emergency	Post-listing
Agreements between WHO and relevant NRAs	✓		
Establishment of roster of experts by WHO	✓		
Assessment by WHO of eligibility of specific products	✓	✓	
Development of consensus by the PEG on requirements	✓	✓	
Pre-submission meetings between WHO and applicant	✓	✓	
Assignment of assessment pathway by WHO	✓	✓	
Establishment of Experts Groups (PEG and TAG-EUL) by WHO	✓	✓	
Assessment of submission by PEG	✓	✓	
Assessment of PEG report by TAG-EUL		✓	
Submission of updates by manufacturer	✓	✓	✓
Decision on listing by WHO		✓	
Post listing monitoring			✓
Decision by WHO on whether to extend listing		✓	✓
Possible post-listing changes by WHO			✓

Emergency Use Listing Procedure

Figure 1: Flowchart of the EUL process



**Annex 1: Terms of Reference for Experts and Advisory Groups
(PEG and TAG-EUL)**

Terms of Reference for the Product Evaluation Group (PEG)

Background

In the context of the World Health Organization (WHO) procedure for emergency use listing (EUL) of medical products, the WHO PQ Secretariat will require advice from an independent evaluation group known as the Product Evaluation Group (PEG).

There will be three PEGs, one for each product stream under the EUL (vaccines, medicines and IVDs) :

- **PEG-V:** for evaluation of vaccines, which will be selected, convened and coordinated by the WHO Vaccine PQ Team Lead
- **PEG-M:** for evaluation of medicines, which will be selected, convened and coordinated by the WHO Medicines PQ Team Lead
- **PEG-D:** for evaluation of Diagnostics, which will be selected, convened and coordinated by the WHO In Vitro Diagnostics PQ Team Lead.

The experts will be selected from a pre-established roster, according to the requirements for evaluation under the EUL procedure.

The PEG will have the functions described below.

Members must respect the impartiality and independence required of WHO. In performing their work, they may not seek or accept instructions from any Government or from any authority external to the Organization. They must be free of real, potential or apparent conflict of interest. To this end, proposed members will be required to complete a declaration of interest form and their appointment, or continuation of their appointment, will be subject to the evaluation of completed forms by the WHO Secretariat, determining that their participation would not give rise to a real, potential or apparent conflict of interest.

Information and documentation to which members may gain access in performing PEG related activities will be considered as confidential and proprietary to WHO and/or parties collaborating with WHO, including in particular, but not limited to, the applicants. PEG members shall not purport to speak on behalf of, or represent, the PEG or WHO to any third party, and treat the deliberations of the PEG as strictly confidential. All proposed members will be required to commit to an appropriate confidentiality undertaking and agree to provisions on ownership. To this end, each member will be required to enter into a Memorandum of Agreement with WHO.

Experts selected for the PEG from the pre-established roster will be required to commit to make every effort to be available on a short notice to perform their PEG related responsibilities.

Emergency Use Listing Procedure

Functions

The functions of the PEG are:

- a) To assess what published guidelines, requirements/recommendations and international guidance documents are available from WHO and regulatory agencies that are relevant for the evaluation of a product.
- b) To conduct a search for relevant publications with evidence of scientific consensus with regards to safety, immunogenicity or clinical efficacy of a product.
- c) To agree on a set of guidelines, requirements/recommendations and other parameters that will be used to evaluate a product or group of products
- d) To screen submissions for completeness of the information required
- e) To review the quality, clinical and performance information of the unlicensed medical product (See Annex 5 for information required, after the product has been determined to be eligible for EUL assessment)
- f) To make a recommendation to WHO on the risk/benefit balance (positive/negative) of the product, should a PHE occur which justifies the need for the product before additional data is provided as the development of the product advances. This recommendation should be based on a review of the available data and the Applicant's response to the PEG List Of Questions (LOQs).

The report and recommendation by the PEG will be based on the following:

- a) Complete application submitted by the applicant to the WHO PQ Team
- b) Responses from the applicant to the LOQs prepared after the initial review (if applicable)
- c) Additional information or updates submitted by the applicant at any point, and
- d) Other information related to the product that the committee deems important for the review

The report of the PEG should follow the template in Annex 7 and will be submitted by the Chair to WHO (PQ Team Lead for the product stream).

The Chair may assign reviewers from among the PEG members for specific reviews.

If after initial review of the submission, the PEG decides to address additional questions to the applicant, the Chair will prepare a consolidated LOQ that will be sent to all members for consensus. This LOQ will be submitted to the WHO PQ Team focal person who will forward it to the applicant. There will be no direct communications between the PEG (or any of its members) and the applicant.

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

Emergency Use Listing Procedure

Membership

PEG members shall serve in their personal capacities, as temporary advisers to WHO, and will be selected to represent the broad range of disciplines relevant to the product under review. As such, they need to enter into the standard Memorandum of Agreement for Temporary Advisers with WHO.

1) PEG-V

The PEG-V consists of a maximum of 10 members from the established roster of experts and should include the following areas of expertise:

- production and quality control;
- quality systems, quality risk management and GMP;
- non-clinical and clinical assessment
- pharmacovigilance
- infectious disease specialists

Note: One of two experts may be selected for each area of expertise

2) PEG-M

The PEG-V consists of a maximum of 10 members from the established roster of experts and should include the following areas of expertise:

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

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

3) PEG-D

The PEG-D consists of a maximum of 10 members from the established roster of experts and should include the following areas of expertise:

- Quality management system
- Validation and verification studies and labelling of IVDs
- Infectious disease specialists
- Laboratory scientist with expertise in diagnosis of the disease

Emergency Use Listing Procedure

Term

All PEG members will commit to serve on an ad hoc basis until the evaluation of the product in question has been completed, including post listing data. WHO may terminate a member's membership at any time prior to his/her term.

Chair

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

The Chair is responsible for:

- chairing the meeting(s) of the PEG;
- managing communications with the WHO PQ Secretariat (including submitting adopted reports to the PQ focal person)
- managing the process of review, consolidation of any LOQs and preparation and approval of agendas and reports;
- ensuring compliance with time frames.

Operation

Schedule of the PEG activities

The WHO PQ Secretariat will act as secretariat to the PEG and will facilitate the documentation and minutes for the PEG meetings. As such, the WHO PQ Secretariat will distribute a submission to the members of the PEG, convene virtual or face-to-face meetings for deliberations and assist the Chair in the preparation of proposed agendas and reports.

The WHO PQ Secretariat will not participate in the deliberations and taking of decisions by the PEG.

Once the PQ focal point has provided the Chair and other members of the PEG with the submission, the experts will normally have 3 months to review the information received and prepare a report. If additional information is required, each expert will prepare questions to be added to the LOQ and submit these to the Chair. In case the submission is received after a PHE has been declared, the timeline will be reduced to 1 month, provided the submission is complete. The Chair may coordinate a discussion among PEG 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 to the Chair if the answers are satisfactory or if there are inadequacies. There may be more than one round of LOQs, until no further information is required or forthcoming from the applicant. Based on the information available, the Chair will prepare a consolidated report (template in Annex 7) and will circulate to all PEG members for adoption. The PEG will adopt its reports and develop its recommendations by consensus. Any dissenting views will be noted in the report.

Emergency Use Listing Procedure

The timeline to submit the consolidated report of the PEG to WHO will depend on the number of questions, the time the applicant takes to respond, and the volume of information sent in the responses, among other factors.

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

Management of communications

The PQ focal person will manage all communications between the PQ Secretariat and the PEG, and with the applicant, respectively.

For each review the focal person will:

- a) provide the Chair and other members of the PEG with the submission received and electronic copies of all relevant WHO recommendations and guidelines as well as relevant guidance documents from regulatory bodies, relevant scientific meeting reports and scientific publications;
- b) communicate to the applicant that the submission will be reviewed by the PEG according to the EUL procedure. The timeline for completion will depend on the need for clarifications and additional information requested by the PEG;
- c) facilitate the arrangements for teleconferences, face to face meetings and any other means of communication among members of the PEG;
- d) monitor progress with the PEG Chair;
- e) submit LOQs to the Applicant, and forward responses submitted by the applicant to the PEG;
- f) assist the PEG Chair in the preparation of draft agendas and reports, receive the final report with recommendations from the PEG Chair, and formally close the review. Should no additional data become available before a public health emergency occurs that justifies the use of the product, WHO may submit the final report to the TAG-EUL. If additional data are submitted (i.e. updates on clinical trial results, completion of validation of processes and tests, etc.), the PEG will be requested to update its final report and submit the updated final report to WHO, through the Chair. The report shall be prepared using a standardized format (Annex 7) that will include an executive summary, the assessment of the information reviewed, List of Questions and responses and the final recommendation.

All PEG recommendations are advisory to WHO, who retains full control over any subsequent decisions and actions, including whether or not to publish the findings and recommendations of the PEG in a WHO EUL public report and whether or not to submit the report of the PEG to the TAG-EUL.

Terms of Reference for the Technical Advisory Group for Emergency Use Listing (TAG-EUL)

Background

In the context of the World Health Organization (WHO) procedure for emergency use listing of medical products, the WHO PQ Secretariat will require advice from an independent advisory group known as the Technical Advisory Group for Emergency Use Listing (TAG-EUL).

There will be three TAG-EULs, one for each product stream under the EUL (vaccines, medicines and IVDs):

- TAG-EUL-V: for listing of vaccines, and will be selected, convened and coordinated by the Vaccine PQ Team Lead
- TAG-EUL-M: for listing of medicines and will be selected, convened and coordinated by the Medicines PQ Team Lead
- TAG-EUL-D: for listing of Diagnostics and will be selected, convened and coordinated by the In Vitro Diagnostics PQ Team Lead.

The experts will be selected from a pre-established roster, according to the requirements for evaluation under the EUL procedure.

Members must respect the impartiality and independence required of WHO. In performing their work, they may not seek or accept instructions from any Government or from any authority external to the Organization. They must be free of real, potential or apparent conflict of interest. To this end, proposed members will be required to complete a declaration of interest form and their appointment, or continuation of their appointment, will be subject to the evaluation of completed forms by the WHO Secretariat, determining that their participation would not give rise to a real, potential or apparent conflict of interest.

Information and documentation to which members may gain access in performing TAG-EUL related activities will be considered as confidential and proprietary to WHO and/or parties collaborating with WHO, including in particular, but not limited to, the applicants. TAG-EUL members shall not purport to speak on behalf of, or represent, the TAG-EUL or WHO to any third party, and treat the deliberations of the TAG-EUL as strictly confidential. All proposed members will be required to commit to an appropriate confidentiality undertaking and agree to provisions on ownership. To this end, each member will be required to enter into a Memorandum of Agreement with WHO.

Functions

The function of the TAG-EUL is to provide a recommendation on whether or not an unlicensed medical product should be listed for emergency use under the EUL procedure once a PHE occurs, and if so, under what conditions.

In formulating its recommendation, the TAG-EUL will use any information deemed critical by WHO for consideration by the TAG-EUL. This may include the report on quality, safety and

Emergency Use Listing Procedure

efficacy or performance, prepared by the Product Evaluation Group (PEG), including the initial evaluation and any updates based on additional information submitted by the applicant

The TAG-EUL will furthermore consider any emergency program needs when applicable, as well as any additional information which the TAG-EUL may request from the PQ Team or the applicant through the PQ focal person.

The report prepared by the TAG-EUL should follow the template in Annex 7 and will be submitted by the Chair to WHO/PQ team Lead for the product stream.

Membership

1) TAG-EUL-V

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

- one member with expertise in the epidemiology of the disease that should be prevented with the vaccine in question;
- one member with regulatory expertise relating to vaccine evaluation and risk management plans;
- one or more members from the NRA of the affected countries
- one member from the PEG-V with expertise in quality assessment
- one member from the PEG-V with expertise in clinical assessment
- one or more 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 .

2) TAG-EUL-M

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

- one member with expertise in the epidemiology of the disease or condition of interest.
- one member with regulatory expertise relating to the product and potential risk management plans
- one or more members from the NRA of the affected countries
- one member from the PEG-M with expertise in quality assessment
- one member from the PEG-M with expertise in clinical assessment
- one or more 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.

Emergency Use Listing Procedure

3) TAG-EUL-D

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

- one member with expertise in quality management systems for IVDs
- one member with expertise in validation and verification studies and labelling

Term

All TAG-EUL members will commit to serve on an ad hoc basis until the process of developing the required recommendation has been completed.

Chair

A Chair will be selected by the WHO PQ Secretariat from among the TAG-EUL members.

The Chair is responsible for:

- chairing the meeting (s) of the TAG-EUL
- managing communications with the WHO PQ Secretariat (including submitting adopted reports to the PQ focal person);
- managing the process of review and preparation and approval of agendas, records and reports;
- assuring compliance with time frames;

Operation

Schedule of the TAG-EUL activities

The WHO PQ Secretariat will convene the members of the TAG-EUL on short notice in a virtual or face to face meeting and provide them with the information deemed critical by WHO for consideration by the TAG-EUL. This may include the consolidated report prepared by the PEG for the specific product and any other data considered relevant for the discussions.

The TAG-EUL should in principle submit its recommendation to WHO within five (five) working days after the virtual or face to face meeting. If additional information is requested, a recommendation should in principle be issued within three days of receipt of this information.

The Chair will prepare a consolidated report (template in Annex 7) and will circulate to all TAG-EUL members for adoption. The TAG-EUL will adopt its reports and develop its recommendations by consensus. Any dissenting views will be noted in the report.

Emergency Use Listing Procedure

Management of communications between the WHO PQ Secretariat and the TAG-EUL

A focal person, designated by the WHO PQ Secretariat, will manage all communications between the PQ Secretariat and the TAG-EUL and the PQ Secretariat and the applicant respectively.

For each review the WHO PQ focal person will:

- provide the TAG-EUL Chair with the information deemed critical by WHO for consideration by the TAG-EUL. This may include the consolidated report prepared by the PEG for the specific product and any other data considered relevant for the discussions;
- communicate to the applicant that the submission will be reviewed by the TAG-EUL according to the EUL procedure and the expected timeline for completion;
- facilitate the arrangements for teleconferences, face-to-face meetings and any means of communication among members of the TAG-EUL;
- monitor progress, with the TAG-EUL Chair, of each review;
- manage communications with the applicant as required;
- assist the TAG-EUL Chair in the preparation of draft agendas and reports and receive the final report with the recommendations from the TAG-EUL Chair and formally close the review. The report shall be prepared using a standardized format (Annex 7) that will include the recommendation (positive or negative) and a summary justification.

All TAG-EUL recommendations are advisory to WHO, who retains full control over any subsequent decisions and actions. WHO also retains full control over the publication of the reports of the TAG-EUL, including whether or not to publish to share them with Members States and UN procurement agencies.

Emergency Use Listing Procedure

Memorandum of Agreement - Terms and Conditions for Temporary Advisers

I, the undersigned, in accepting to act as a Temporary Adviser to the World Health Organization (WHO), agree to the following:

1. RELATIONSHIP BETWEEN THE PARTIES

The execution of the work as Temporary Adviser does not create any employer/employee relationship as between WHO, on the one hand, and me and/or persons claiming under me, on the other hand. Thus, WHO shall not be liable to me or any other person whatsoever for any damage, loss, accident, injury, illness and/or death sustained by me in connection with, or as a result of, my assignment as Temporary Adviser to WHO, including travel.

2. TRAVEL COSTS, PER DIEM AND INCIDENTALS

I understand that my travel, per diem and incidentals will be paid by WHO, in accordance with WHO rules described in Annex 1 attached hereto.

3. CONFLICT OF INTERESTS

I agree to truthfully complete the Declaration of Interests for WHO Experts and disclose any circumstances that may give rise to a real, potential or apparent conflict of interest in relation to my work as Temporary Adviser. I will ensure that the disclosed information is correct and will truthfully declare that no other situation of real, potential or apparent conflict of interest is known to me. I undertake to promptly inform WHO of any change in these circumstances, including if an issue arises during the course of my work as Temporary Adviser. I understand and agree that this Memorandum of Agreement may be cancelled by WHO if WHO determines that the information disclosed by me in the Declaration of Interests requires modification or cancellation of the invitation extended to me to serve as Temporary Adviser to WHO.

4. INSURANCE

I agree that the insurance arrangements set forth below are being made by WHO without any prejudice whatsoever to section 1 above. Thus, I agree that WHO shall not be liable for any damage, loss, accidents, injury, illness and/or death sustained by me in connection with, or as a result of, my assignment as Temporary Adviser to WHO, including travel.

While travelling, my baggage and personal effects will be insured by WHO up to an amount of US\$ 5000 (five thousand United States dollars). This insurance covers all hand baggage carried by me with the exception of documents, travel tickets, currency/cash/travellers cheques, stamps, stamped paper, identity papers, household goods and *objets d'art* (art works). Personal computers and accessories are also not included in WHO's personal baggage insurance cover unless it is noted on the travel authorization that a personal computer is required during the journey. Laptops must be hand-carried on board airplanes and not checked as registered baggage. Fees to replace stolen travel tickets, credit cards and official documents may be claimed under the insurance policy.

Annex 2: Pre-submission meetings

Introduction

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 WHO/PQT team that is responsible for the determination of eligibility of their product, and the initial assessment of their submission.

A pre-submission meeting allows WHO/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 as much as possible the need for further clarifications after the meeting.

To request a pre-submission meeting, the applicant must send the completed Pre-submission Meeting Request Form (see below) to the Prequalification Team Coordinator with copy to the relevant Team Lead. The Team 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 (up to a maximum of 10 participants per applicant) not later than 15 days before the meeting. The information package should be sent not later than 10 business days before the proposed meeting date.

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

The manufacturer will record meeting minutes, including summary of information presented, the questions raised and the responses, as well as follow up actions if applicable. These will be sent to WHO within 15 days for final review and comments.

Emergency Use Listing Procedure

**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 Team Lead as appropriate.

Vaccines: whooul@who.int

Medicines: prequalassessment@who.int

IVDs: diagnostics@who.int

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 relevant 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), or IVD type/analyte detected, etc. and the expected date for submission to WHO for EUL

Specific objectives/outcomes expected from the meeting

Preliminary proposed agenda including estimated time needed for each agenda item (up to a maximum of 3 hours for the entire meeting) and designated speaker(s)

Emergency Use Listing Procedure

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 (up to a maximum of 10 proposed participants).

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: Application letter model

[Name of the Director of PQT]

World Health Organization

Team Lead **[product stream]** assessment Prequalification Team

Regulation of Medicines and other Health Products

CH-1211 GENEVA 27

SWITZERLAND

Date

Product: [name of the product]

Subject: Letter of application for Emergency Use Listing (EUL) of [name of product]

Contact person: [name of applicant's contact person]

Title

Tel:

Email:

Dear [name of Team Lead]

Following our pre-submission meeting on [date of pre-submission meeting], we hereby confirm that [name of the company] intends to submit the dossier for EUL assessment on [intended date of submission].

{name of product} is a [type of product, presentation].

The target in indication for [name of product] is [description of intended use].

The product has been granted [authorization of emergency use] by [name of National Regulatory Authority, Country].

[Signature, name, title and date]

CC: Name of the relevant PQT Team Lead

Annex 4: Letter of Agreement

WHO Emergency Use Listing Procedure - Letter of Agreement

Product name: **[insert full product name]**

Application number: **[insert application number]**

Dear **[insert salutation and last name]**,

This letter is with reference to the application dated **[insert day / month / year]** submitted by **[insert full legal name of applicant]** (hereinafter “**you**” or the “**applicant**”) to the World Health Organization (WHO) for the assessment of the **[insert full name of product]** product under the WHO Emergency Use Listing (EUL) Procedure (such application is hereinafter referred to as your “**application**”).

Your application been given the following WHO reference number: **[insert application number]**. Please use this reference number in all future communications pertaining to this application. Receipt of this letter does not reflect a decision on EUL listing of the **[insert full name of product]** product. This letter should not be used to inform procurement, as it does not constitute an endorsement or WHO EUL listing of the final product.

Please be advised that the signature and completion (duly and in full) of this letter of agreement by the applicant is a prerequisite for WHO proceeding with the EUL assessment of your application concerning the **[insert full name of product]** product. The EUL assessment of your application *will not proceed* until this letter of agreement has been duly and fully signed, completed and dated by the applicant, and returned to WHO, as indicated in this letter.

With respect to your application under the EUL Procedure, by signing this letter of agreement, the following points are hereby accepted and agreed to by the applicant:

1. The applicant confirms that it has read, agrees with, and will adhere to and comply with all of the provisions, terms and conditions of the EUL Procedure and of this letter of agreement.
2. The applicant represents, warrants and shall ensure that all of the applicant’s suppliers, service providers, manufacturers and other contractors for the product (hereinafter collectively referred to as “**Contractors**”) have been legally bound by, and have agreed to adhere to and comply with, all of the provisions, terms and conditions of the EUL Procedure and of this letter of agreement.
3. The applicant confirms that it is the manufacturer of, and that it has intellectual property ownership of or has obtained all necessary rights to, the product submitted for assessment under the EUL Procedure (the “**product**”). If the applicant has concluded any agreements or otherwise established any arrangements with any third party (including, without limitation, with any Contractors) regarding the production and/or distribution of the product, then the applicant: (a) must clearly

Emergency Use Listing Procedure

state the same in the information package presented to WHO in the pre-submission meeting, and (b) shall ensure that all such third parties comply with the obligations under paragraph 2 above. In addition, the applicant is responsible for obtaining all consents, cooperation, assistance and information from any such third party (including, without limitation, any Contractor) as are necessary or reasonably requested by WHO in connection with the EUL process.

4. *For in vitro diagnostics only:*

4a) The applicant understands and agrees, and shall ensure that each Contractor understands and agrees, that WHO reserves the right to require the product to undergo a performance evaluation conducted by an independent laboratory commissioned by WHO and/or to require the product to undergo blinded testing of a performance panel as requested by WHO. Any such performance evaluation testing shall be conducted using the protocol and technical criteria established by WHO. For the avoidance of doubt, WHO may exercise its aforementioned rights at any time during the EUL assessment process and/or after the product has been granted EUL recommendation.

4b) The applicant understands and agrees, and shall ensure that each Contractor understands and agrees, that in the event WHO exercises any of its rights described under paragraph 4a) above, then the applicant shall provide, and shall ensure that each Contractor provides, sufficient quantities (as determined by WHO) from different lots of the product, as required by WHO, for the relevant performance evaluation and/or blind panel testing, as applicable, of the product; and such quantities of the product shall be provided at no charge to WHO and/or any relevant evaluating laboratories collaborating with it. The applicant further understands and agrees, and shall ensure that each Contractor understands and agrees, that the product submitted for the performance evaluations and/or blind panel testing, as applicable: (i) shall be identical to the product described in this letter; (ii) shall have a minimum shelf-life of six months at the time of delivery to the laboratory; and (iii) shall be sent **Free Domicile** in accordance with detailed shipping instructions which shall be given to the applicant in due time. If necessary, the applicant shall also make available, and shall ensure that each Contractor also makes available, any special equipment needed to perform the performance evaluation of the product at no charge to the WHO and/or any relevant evaluating laboratories collaborating with it (customs declaration and payment of customs duties, transport, etc., shall be taken care of by the applicant).

5. The applicant understands and agrees, and shall ensure that each Contractor understands and agrees, that WHO will have absolute, exclusive, unfettered control over the manner in which the EUL assessment is carried out, including the publication of the results of the EUL assessment, regardless of the outcome.

6. The applicant also understands and agrees, and shall ensure that each Contractor understands and agrees, that WHO reserves the right to use, publish, issue, share

Emergency Use Listing Procedure

with national regulatory authorities (NRAs) and other relevant authorities of WHO Member States and/or with United Nations agencies and other relevant intergovernmental organizations, and/or make publicly available any outcomes, reports, notices and/or results—whether in draft or final form, and whether positive or negative—arising from or relating to the EUL assessment process and/or any listed product and/or any confidential information (as defined in the EUL Procedure) to which WHO may gain access in the course of the EUL process. WHO’s aforementioned rights shall be exercised in accordance with the provisions of the EUL Procedure, including but not limited to its provisions regarding the protection of any commercially sensitive information of the applicant and/or any of the manufacturers.

7. The applicant acknowledges and agrees, and shall ensure that each Contractor acknowledges and agrees, that WHO shall have the right to share with the applicant any reports, documents and/or correspondence regarding any inspections conducted by or on behalf of WHO in connection with the EUL assessment of the product. In this respect, it shall be the applicant’s sole responsibility to promptly ensure that appropriate confidentiality obligations/arrangements are agreed to and put in place among the applicant and its Contractors to enable WHO to fully exercise its aforementioned right.
8. For the sake of good order, the applicant acknowledges and agrees, and shall ensure that each Contractor acknowledges and agrees, that it is not in WHO’s mandate to issue any approvals, certificates or licenses for medical products. As that responsibility lies with the regulatory authority of each country, it is thus the sole prerogative of national authorities to decide whether or not to allow the emergency use of an unlicensed product in their country. Furthermore, the applicant acknowledges and agrees, and shall ensure that each Contractor acknowledges and agrees, that WHO does not, as a matter of policy, endorse any specific commercial product over others. The purpose of the WHO EUL of medical products is to provide guidance to interested UN agencies and WHO Member States in determining the acceptability of using a specific product in the context of a public health emergency. In this regard, the applicant acknowledges and agrees, and shall ensure that each Contractor acknowledges and agrees, that the results of the EUL assessment, the participation in the WHO EUL process, the inclusion of any product in the EUL list and/or the WHO name and emblem, shall not be used by or on behalf of the applicant or any Contractors for any commercial and/or promotional purposes.
9. The applicant understands and agrees, and shall ensure that each Contractor understands and agrees, that by virtue of WHO’s status as a Specialized Agency of the United Nations, WHO, its officials and experts performing missions for WHO (including, e.g., inspectors) enjoy privileges and immunities under national and international laws and conventions, including without limitation: (i) the Convention on the Privileges and Immunities of the Specialized Agencies, adopted by the General Assembly of the United Nations on 21 November 1947 (the “**1947 Convention**”), and (ii) the United States’ International Organizations Immunities Act of 1945 and Executive Order 9698 relating thereto (collectively, the “**IOIA**”). Nothing contained in or in connection with this EUL procedure and/or any assessment process hereunder

Emergency Use Listing Procedure

will constitute or be deemed as a waiver of any of the privileges or immunities which WHO, its officials and/or experts performing missions for WHO enjoy pursuant to the 1947 Convention, the IOIA or otherwise under any national or international law, convention or agreement, and/or as submitting WHO, its officials and/or experts aforesaid to any national court jurisdiction.

10. Any and all claims or disputes arising from or in connection with this EUL procedure, including, but not limited to, any rejection of an application, any assessment hereunder and/or any decision whether or not to grant an EUL recommendation for an evaluated product (hereinafter, collectively, **“Disputes”**) must be submitted in writing to WHO’s Director of RPQ, with a copy to the relevant PQT Team Lead. WHO’s Director of RPQ, or one of his/her authorized representatives, will acknowledge in writing receipt of the relevant Dispute and will conduct an investigation into the Dispute within 30 days of receipt. Following the investigation, WHO’s Director of RPQ, or one of his/her authorized representatives, will provide a written response to the applicant/manufacture that submitted the Dispute. If the applicant/manufacture is dissatisfied with the written response, then it must object in writing to WHO within 30 days of the date of WHO’s aforementioned written response. In the event that the applicant/manufacture does not object to WHO in writing within such 30 day period, then the content of WHO’s written response (including, without limitation, any findings or decisions contained therein) will be final and can no longer be challenged by the applicant/manufacture in any way. However, if the applicant/manufacture does object to WHO in writing within such 30 day period, then the Dispute will be referred to WHO’s Director-General for his or her decision which will be final and binding on the parties.
11. The applicant should please: (i) arrange for this letter of agreement to be duly and fully signed, completed and dated by a duly authorized representative of the applicant, and (ii) **by no later than [insert date of letter plus 30 calendar days]**, return the original of this letter of agreement once fully signed (i.e., once duly and fully signed, completed and dated by a duly authorized representative of the applicant) to WHO’s attention by pre-paid registered mail or pre-paid international courier. An electronic copy of this letter of agreement once fully signed should also be sent to WHO by e-mail to **[insert email for relevant WHO/PQ product team]**.

Thank you in advance for your collaboration.

Yours sincerely,

[Name of WHO Signatory]

[Title of WHO Signatory]

Prequalification Unit

Regulation and Prequalification Department

Emergency Use Listing Procedure

By signing in the spaces provided below, each of the applicant and the manufacturers agrees to the terms of this Letter of Agreement, dated **[insert day / month / year]**, with WHO reference number: **[insert reference number of application]**

Agreed to and accepted by and on behalf of the applicant: **[insert full legal name of the applicant]**

Commercial name of product: **[insert full name of the product]**

Signature of duly authorized representative of the applicant:

Name of duly authorized representative of the applicant:

Title of duly authorized representative of the applicant:

Date:

Annex 5: Essential data requirements for EUL for vaccines, medicines and in vitro diagnostics

Since the expectation is that the manufacturing/quality control and clinical development of the product submitted for EUL will continue to product licensure and ultimately be 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/

For IVDs, the dossier content requirements may differ depending on the analyte being detected and clarification of specific data requirements will require discussion between the applicant and WHO in advance of submission.

Vaccines

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 the application.

A. Manufacturing and quality control Data:

1. Full characterization of cell banks according to WHO Technical Report Series (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.
3. Process validation (based on quality risk assessment for the development stage) and demonstration of consistency of production at the production scale used for the lots to be distributed. If deemed appropriate by WHO 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 characterization 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. Validation of potency tests and other critical assays. If novel test methods have been developed, full description of the test development and qualification must be presented.

4. Justified specifications for starting material, intermediates, and final products.

Emergency Use Listing Procedure

5. Stability data for the vaccine produced at the scale produced for the lots to be supplied. If available, accelerated stability data must be included. For vaccines being assessed for emergency use, WHO and the Advisory Committee for the Emergency Use Listing (TAG-EUL-V – see below), when convened, will consider programmatic suitability and may consider candidate vaccines with characteristics that would not be accepted for prequalification.
 - a) Vaccines requiring storage at less than -20°C are generally not accepted for prequalification. However, under this emergency procedure, such vaccines can be considered. Upon receipt of such an application, WHO staff responsible for emergency response vaccine deployment will be informed by the WHO EUL Secretariat, and will be requested to evaluate and consider whether recipient countries will require assistance with regards to infrastructure for vaccine storage and distribution at required temperatures.
 - b) Routinely, if a vaccine presented for prequalification requires storage below +2°C during its shelf-life period, it should have a minimum period of storage between +2°C and +8°C of 6 months. Under this emergency procedure, vaccines with a shelf life at +2 to +8°C of less than 6 months may be considered. The application should include stability data at +2 to +8°C to determine the minimum acceptable storage period at +2 to +8°C. Upon receipt of such an application, WHO staff responsible for emergency response vaccine deployment will be informed by the WHO EUL Secretariat, and will be requested to evaluate and consider whether recipient countries will require assistance with regards to infrastructure for vaccine storage and distribution at required temperatures. 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 procedure 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 inspection team showing compliance with GMP requirements – if available, 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. These changes should be submitted as updates as indicated in section 5.1.1.9.

B. Non-clinical and Clinical Data:

Non-clinical data demonstrating acceptable safety, immunogenicity, and efficacy – if available- 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.

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

Emergency Use Listing Procedure

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 confirmation that immunogenicity is a 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 if applicable.

Note: products developed under the animal rule will also be considered for review.

C. Plan for monitoring and reporting of adverse events

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 should discuss with WHO in pre-submission meetings, the plans to ensure the collection and analysis of information on the safety and effectiveness of the product during the period when the EUL listing would be 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.

D. Labelling:

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

Note: When the product is listed, the labelling should clearly indicate that that product is for emergency use only.

E. Environmental Risk Assessment (ERA)

If the product contains a Genetically Modified Organism, the applicant must submit a completed Environmental Risk Assessment report.

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 the application.

Emergency Use Listing Procedure

A. 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 SRA/WLA or from a WHO prequalification inspection showing compliance with GMP requirements for other, but similar products. Based on the acceptability of the SRA/WLA report, WHO may or may not need to perform its own assessment of GMP compliance.

B. Non-clinical and Clinical Data:

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

C. Labelling

1. Summary of product characteristics (information for health care provider)

Emergency Use Listing Procedure

2. Patient information leaflet
3. Primary and secondary labelling
4. Any other instructional materials provided to the user.
5. A plan to help ensure 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 labelling should clearly indicate that that product is for emergency use only.

In Vitro Diagnostics

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 the application.

A. QMS Review

A review of the manufacturer's quality management system (QMS) documentation and specific manufacturing documents is the first step in the process. At the conclusion of this step, WHO may either decide to proceed or to 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 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;
- If the product was approved for Research Use Only (RUO), details on the experience with the product;
- Details on the manufacturing capacity (existing inventory, minimum time to provide finished product, maximum batch/lot size).
- Procedure/s relevant to control of non-conforming goods, including but not limited to procedures for corrective and preventative actions, recalls, field safety notices etc.

Emergency Use Listing Procedure

B. 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 EUL assessment. Based on the submitted documentation, a risk-based judgment will be made on whether there is a favourable 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.

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*:

1. Product Information

- a) Regulatory versions of this product⁷
- b) Product description including variants (configurations) and accessories
- c) Essential principles checklist
- d) Risk analysis and control summary

2. Design and Manufacturing Information

- a) Product design
 - Design overview
 - Formulation and composition
 - Biological safety
 - Documentation of design changes

- b) Manufacturing processes

⁷ The submitted version is defined by all of the documentation related to development, manufacture and intended use, labelling and post-market surveillance of the product and all the documented evidence supporting the safety and performance claims associated with that submission. If any aspect of this documentation differs in any way between the submissions to different regulatory authorities or assessment bodies (United States Food and Drug Administration, Health Canada, a Notified Body for CE marking, etc.) it is considered to be a different regulatory version.

Emergency Use Listing Procedure

- Overview of manufacture
 - Sites of manufacture
- c) Key suppliers

3) Product Performance Specification, and Associated Validation and Verification Studies

- a) Analytical performance
- a.1. Stability of specimens
 - a.2. Validation of specimens
 - a.3. Metrological traceability of calibrators and control material values
 - a.4. Accuracy of measurement
 - a.4.1. Trueness
 - a.4.2. Precision (repeatability & reproducibility)
 - a.5. Analytical sensitivity (LOD & LOQ)
 - a.6. Analytical specificity
 - a.7. High dose hook effect
 - a.8. Measuring range of the assay
 - a.9. Validation of assay cut-off
 - a.10. Validation of assay procedure
 - a.11. Usability/human factors
 - a.12. Stability of the IVD
 - a.12.1 Claimed shelf-life⁸
 - a.12.2 In-use stability (open pack or open vial stability)
 - a.12.3 Shipping stability
- b) Clinical evidence
- b.1. Clinical/diagnostic sensitivity
 - b.2. Clinical/diagnostic specificity

⁸ Accelerated studies or extrapolated data from real time data are acceptable for initial shelf life claim but need to be followed up with real time stability studies.

Emergency Use Listing Procedure

C. Plan for monitoring and reporting of adverse events/incidents/non-conforming goods and processes

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

Annex 6: Criteria for selection of assessment pathways

a) Vaccines

For vaccines, the initial EUL assessment will use similar principles as those used for prequalification and take into account agreements with NRAs to share reports, past inspections of the manufacturer's facilities, the assessment of the manufacturer's quality systems and any record of performance of the manufacturer and its product (s).

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 vaccines
Vaccine approved for emergency use by a stringent NRA/WLA for the target disease and agreement in place between WHO and the NRA for the exchange of information	A	C
Vaccine not approved for emergency use by a stringent NRA/WLA for the target disease or no agreement in place with the NRA	B	C

Table 2: Vaccines assessment approach for each category

Category	Assessment approach
A	<i>Abridged assessment, consisting of initial assessment of:</i> - Report(s) from the responsible SRA/WLA (Summary basis for the emergency use approval or equivalent) - Programmatic aspects *
B**	<i>Abridged assessment, consisting of initial assessment of:</i> - Application (see content above) - Programmatic aspects
C	<i>WHO will conduct a full initial review of:</i> - Application (see content above) - Inspection report (conducted by WHO) - Programmatic aspects

* Programmatic aspects include: indication, dosage, conservative, storage temperature, autodisable syringe, etc.

** Company has prequalified products, therefore, they have been inspected by WHO

Emergency Use Listing Procedure

a) Medicines

Table 3: Medicines assessment approach

	Assessment approach	Inspection
Product authorized for emergency use by an SRA/WLA for the target disease	Abridged assessment based on the SRA/WLA report	Desk review of available SRA/WLA inspection reports, and/or if required, inspection by WHO.
Product not approved for emergency use by an SRA/WLA for the target disease	Full assessment by WHO of the submitted dossier information. The review will also consider available assessment reports written by NRAs. ⁹	Inspection by WHO and/or desk review of available WHO, SRA/WLA, or PIC/s member inspectorate reports ¹⁰

b) In vitro diagnostics

Table 4: IVDs assessment approach

	Assessment approach	Inspection
Product assessed through another emergency mechanism of an acceptable standard?	Abridged initial assessment of reports	Desk review of the QMS
Product not assessed through another emergency mechanism of an acceptable standard?	Full initial assessment by WHO of the submitted documentary evidence	Desk review of the QMS and/or inspection if required

⁹ Reports from some non-SRA/WLAs might be useful

¹⁰ Inspections reports covering other but similar products.

Emergency Use Listing Procedure

Abridged IVD EUL assessment

For IVDs, some submissions 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 two steps of the review.

However, WHO EUL is designed to provide a minimum level of assurance of the quality, safety, and performance of unlicensed products for the primary purpose of use in the setting of a current PHE. This focus means that WHO may still undertake some extra assessment activities if deemed necessary or request the dossier that was assessed previously through other emergency mechanisms.

Annex 7: Template of Assessment reports



Assessment Report
Product Evaluation Group - Vaccines (PEG-V)
Emergency Use Listing
Product
Manufacturer

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

1. Executive summary

1.1 The product

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

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 unlicensed product for emergency use, or exceptional circumstances, etc.

1.3. Recommendation

Based on the review of the available data and the Applicant's response to the PEG LOQs on quality, safety and efficacy, this Committee considers that should a PHE occur justifying the need for the product before additional data on (quality), (safety) (efficacy) is provided as the development of the product advances, the risk-benefit balance of this product is

Positive

Negative

The major objections are related to the following deficiencies (indicate all that apply if the outcome is negative):

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

2. Guidelines used for the assessment

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

3. Scientific review of the submission

3.1. Quality assessment

- 3.1.1. Summary of reviewed information
- 3.1.2. Rounds of questions and answers from the applicant
- 3.1.3. Conclusion

Emergency Use Listing Procedure

3.2. *Non-Clinical assessment*

- 3.2.1. Summary of reviewed information
- 3.2.2. Rounds of questions and answers from the applicant
- 3.2.3. Conclusion

3.3. *Clinical assessment*

- 3.3.1. Summary of reviewed information
- 3.3.2. Rounds of questions and answers from the applicant
- 3.3.3. Conclusion

3.4. *GMP/GLP/GCP compliance*

- 3.4.1. Summary of reviewed information
- 3.4.2. Rounds of questions and answers from the applicant
- 3.4.3. Conclusion

3.5. *Proposed labelling*

Summary of reviewed information
Rounds of questions and answers from the applicant
Conclusion

3.6. *Benefit-risk assessment*

3.7. *Proposed post listing measures*

4. Final remarks



Assessment Report

Product Evaluation Group - Medicines (PEG-M)

Emergency Use Listing

Product

Manufacturer

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

Emergency Use Listing Procedure

1. Executive summary

1.1. The product

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

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 unlicensed product for emergency use, or exceptional circumstances, etc.

1.3. Recommendation

Based on the review of the available data and the Applicant's response to the PEG LOQs on quality, safety and efficacy, this Committee considers that should a PHE occur justifying the need for the product before additional data on (quality), (safety) (efficacy) is provided as the development of the product advances, the risk-benefit balance of this product is

Positive

Negative.

The major objections are related to the following deficiencies (indicate all that apply if the outcome is negative):

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

2. Guidelines used for the assessment

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

3. Scientific review of the submission

3.1 Quality assessment

- 3.1.1. Summary of reviewed information
- 3.1.2. Rounds of questions and answers from the applicant
- 3.1.3. Conclusion

Emergency Use Listing Procedure

3. 2. *Non-Clinical assessment*

- 3.2.1. Summary of reviewed information
- 3.2.2. Rounds of questions and answers from the applicant
- 3.2.3. Conclusion

3.3. *Clinical assessment*

- 3.3.1. Summary of reviewed information
- 3.3.2. Rounds of questions and answers from the applicant
- 3.3.3. Conclusion

3.4. *GMP/GLP/GCP compliance*

- 3.4.1. Summary of reviewed information
- 3.4.2. Rounds of questions and answers from the applicant
- 3.4.3. Conclusion

3.5. *Proposed labelling*

- 3.5.1. Summary of reviewed information
- 3.5.2. Rounds of questions and answers from the applicant
- 3.5.3. Conclusion

3.6. *Benefit-risk assessment*

3.7. *Proposed post listing measures*

4. Final remarks



Assessment Report

Product Evaluation Group - IVDs (PEG-D)

Emergency Use Listing

Product

Manufacturer

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

1. Executive summary

1.1. The product

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

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 unlicensed product for emergency use, or exceptional circumstances, etc.

1.3. Recommendation

Based on the review of the available data and the Applicant's response to the PEG LOQs on quality, safety and performance, this Committee considers that should a PHE occur justifying the need for the product before additional data on (quality), (safety) (performance) is provided as the development of the product advances, the risk-benefit balance of this product is

Positive

Negative.

The major objections are related to the following deficiencies (indicate all that apply if the outcome is negative):

- a) Labelling
 - Labels
 - Instructions for use
- b) Product Performance Specifications, and Associated Validation and Verification Studies
 - Non-clinical evidence (analytical performance)
 - Clinical evidence
- c) Quality management systems (QMS) requirements

2. Guidelines used for the assessment

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

3. Scientific review of the submission

3.1. Labelling

3.2. Product information

3.3. Product Performance Specifications, and Associated Validation and Verification Studies

- Specimen type
- Analytical performance characteristics/non-clinical evidence
- Clinical evidence (clinical or diagnostic sensitivity and specificity)
- Intended testing population

3.4. Quality management system (QMS) requirements

3.5. Benefit-risk assessment

3.6. Proposed post listing measures

4. Final remarks



Assessment Report
Advisory Group for EUL (TAG-EUL)
Emergency Use Listing
Product
Manufacturer

WHO/PQT Focal Person	
TAG-EUL Chair	
TAG-EUL members	
Date of this report	

Emergency Use Listing Procedure

1. The product

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

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 unlicensed product for emergency use, or exceptional circumstances, etc.

3. Information assessed by the PEG

4. Recommendation

Based on information and documentation submitted to the TAG-EUL (which includes [the report prepared by the PEG], [additional information from the applicant] and), and based on the deliberations among the members of this Committee, the Committee considers that since a PHE has been declared justifying the need for the product for emergency use, the risk-benefit balance of this product is:

Positive

Negative

Rationale for the decision:

Therefore, the recommendation from this Group to WHO is to:

List

Not list

Emergency Use Listing Procedure

Assessment Report Templates

List of acronyms

GCP	Good Clinical Practices
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
LOQ	List of Questions
NRA	National Regulatory Authority
PEG	Product Evaluation Group
QMS	Quality Management Systems

Annex 8 Notes and disclaimers - EUL List of candidate products

General notes

- The medical products included in this list are unlicensed products, i.e. they have not been granted a marketing authorization by a national regulatory authority. This list is exclusively intended to assist interested UN procurement agencies and Member States in determining the acceptability of using a specific unlicensed product in the context of a public health emergency (PHE). The products included in this list have been evaluated based on a minimum set of available quality, safety, and efficacy data or performance and an agreed plan for their further development. It is the sole prerogative of national authorities to decide whether or not to allow the emergency use of an unlicensed products in their country. This list is updated regularly. Unlicensed products may be added to the list as and when (following the voluntary participation by relevant manufacturers) the available data on such products are evaluated and, if necessary, relevant sites are inspected by WHO, and are - at the time of evaluation - found to meet the requirements outlined in the EUL Procedure for a recommendation for the use of such products in the context of a PHE. WHO cannot in respect of any listed product represent that these requirements will continue to be met. WHO may suspend or remove products from the list based on information that may subsequently become available to it.
- The list is not an exhaustive list of products that may be used in a PHE. It reflects those unlicensed products which have been submitted to WHO for evaluation by interested parties.
- The fact that certain unlicensed products and suppliers are not included in the list does not mean that if evaluated, they would not be found to meet the above-mentioned requirements
- Inclusion in the list does not imply any approval or endorsement by WHO of the products and manufacturing sites in question (which is the sole prerogative of national authorities).
- This list may not be used by manufacturers and suppliers for commercial or promotional purposes.

Listing of products in the EUL list based on emergency approval by stringent regulatory authorities/WHO listed authorities

WHO may recognize the emergency evaluation and approval of products by regulatory authorities that apply stringent standards for quality, similar to those recommended by WHO, such as, but not limited to, the US Food and Drug Administration (USFDA), the European Medicines Agency (EMA) and Health Canada (HCnda).

Suggestions relating to procurement

- Any interested UN procurement agency and Member States intending to use the EUL list of unlicensed vaccines for procurement and/or use should ensure that only products from the manufacturing sites mentioned in this list are supplied to it.

Disclaimer to the WHO EUL List Vaccines

1. Inclusion in this list does not constitute an endorsement of the products listed. WHO explicitly disclaims any warranty of the fitness of any listed unlicensed product for a particular purpose, including in regard to its safety and/or efficacy and/or performance.
2. WHO does not furthermore warrant or represent that:
 - a. the list is complete or error free; and/or that
 - b. the listed unlicensed products which have been found to meet the requirements outlined in the EUL Procedure for use in the context of a PHE will continue to do so; and/or that the unlicensed products listed have obtained emergency use approval for their specified use or any other use in any country of the world, or that their emergency use is otherwise in accordance with the national laws and regulations of any country, including without limitation, any patent laws.
3. In addition, WHO wishes to alert organizations and Members States relying on the EUL list that the improper storage, handling and transportation of medical products may affect their quality, safety, efficacy and performance.
4. WHO disclaims any and all liability and responsibility for any injury, death, loss, damage or other prejudice of any kind whatsoever that may arise as a result of or in connection with the procurement, distribution and use of any unlicensed product included in the list.
5. WHO disclaims any and all liability and responsibility for any loss, damage, liability or other prejudice of any kind whatsoever that may arise as a result of or in connection with any assessment and recommendation under the EUL procedure.

Emergency Use Listing Procedure

Authors

The first proposed draft of the revised procedure was prepared by Liliana Chocarro-Consultant - WHO and presented to the EUL drafting group coordinated by Carmen Rodriguez – WHO; Regina Lehnert, Consultant – WHO; Raymond Corrin, Consultant – WHO; Ryoko Miyazaki-Krause – WHO; Elisabeth Pluut – WHO; Irena Prat – WHO; Mathias Stahl - WHO; Ute Ströher – WHO; Wondi Worku – WHO.

The final draft was circulated among other WHO units and posted on the WHO biologicals web site for public consultation. Comments were compiled and discussed among the drafting group and the final version prepared by Liliana Chocarro on the basis of comments received from all contributors and from the drafting group.

Acknowledgments

Acknowledgements are due to the following organizations and experts for their comments on the draft Emergency Use Listing Procedure: Bill and Melinda Gates Foundation; Coalition for Epidemic Preparedness Innovations; International Federation of Pharmaceutical Manufacturers & Associations; PATH; Office of the Assistant Secretary for Preparedness and Response within the United States Department of Health and Human Services; Global Health Security Initiative Medical Countermeasures Task Force including the Italian Ministry of Health – Italian Medicines Agency, the Public Health Agency of Canada and HHS; United States Food and Drug Administration; WHO - MSF Access Campaign; WHO Polio department; WHO Legal Office and David Wood independent contractor.