NATIONAL AGENCY FOR FOOD AND DRUGS ADMINISTRATION AND CONTROL (NAFDAC)

Drug Registration & Regulatory Affairs (D R & R) Directorate

Guidance on Emergency Use Authorization for Medical Products

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Abbreviations

ACEUA	Advisory Committee for Emergency Use Authorization
CTD	Common technical document
DOI	Declaration of Interest
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
EUA	Emergency Use Authorization
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 Harmonization of Technical Requirements forPharmaceuticals for Human Use
IVDs	In vitro diagnostics
LOQ	List of Questions
NRA	National Regulatory Authority
RT	Review Team
PHE	Public Health Emergency
PHEIC	Public Health Emergency of International Concern
PSUR	Periodic safety updated report
R&D	Research and Development
SRA	Stringent Regulatory Authority
TORs	Terms of Reference
TRC	Technical Review Committee
TRS	Technical Report series
WLA	WHO Listed Authority
WHO	World Health Organization

Acknowledgments
This guidance document is technically and structurally inspired by the World Health Organization (WHO) Emergency Use Listing Procedure and US-FDA's Emergency Use Authorization of Medical Products and Related Authorities Guidance for Industry and Other Stakeholders.

1. Introduction

This guidance outlines NAFDAC's requirements and procedures applicable to the authorization of unlicensed vaccines, therapeutics, and in vitro diagnostics (IVDs) (Medical Products) for use primarily during declared public health emergencies but also in other public health emergencies if appropriate. Such emergencies shall include a heightened risk of affliction or attack on the life, health, safety and security of the general public or any incident with a significant potential to affect national security

The guidance document specifically provides the general principles for evaluating Medical Products and establishing basic emergency procedures for regulating Medical Products. A strong emphasis is placed on the decision-making processes that have been put in place to minimize duplication and make much-needed medical products available for use without unnecessary delay during pandemic emergencies. Other relevant NAFDAC product-specific guidelines should also be consulted as appropriate.

2. Scope and purpose of the EUA procedure

The goal of the procedure is to define the steps that NAFDAC 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 authorized on a time-limited basis, while further data is being gathered and evaluated.

It is very important to note that the EUA is not equivalent to Registration and issuance of Certificate of Registration (Marketing authorization) and should not be thought of as such. The EUA is a special procedure for unlicensed vaccines, therapeutics, and in-vitro diagnostics in the event of a PHE when the community 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 authorization for unlicensed products in an emergency context when limited data are available and the products are not yet ready for application for registration. As part of the EUL, it is expected that the manufacturer will complete the development of the product and submit for licensure.

NAFDAC has developed the EUA process to expedite the availability of unlicensed medical products needed in public health emergencies, based on an essential set of available quality, safety, and efficacy/immunogenicity/ performance data.

The EUA 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.
This document is intended to guide manufacturers willing to submit applications, to obtain authorization for their product (s) for use during public health emergencies. Participation in the procedure is voluntary.

3. 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 EUA procedure.

To qualify for assessment under this procedure, the following criteria must be met:

3.1. 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 EUA assessment, e.g., there are no licensed products for the indication or for a critical subpopulation (e.g., children).

3.2. Existing products have not been successful in eradicating the disease or preventing outbreaks (in the case of vaccines and medicines).

3.3. The product is manufactured in compliance with current Good Manufacturing Practices (GMP) in the case of medicines and vaccines and under a functional Quality ManagementSystem (QMS) in the case of IVDs.

3.4. The applicant undertakes to complete the development of the product (validation and verification of the product in the case of IVDs) and apply for licensure (A future registration application should incorporate all information submitted for the EUA plus any other information needed to complete a registration application). For that purpose, the remaining clinical trials and other testing required to complete the development of the product must already be underway at the time of the application for an EUA.

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

4. Phases of the procedure

There are 3 phases of the EUA procedure:

- Pre-emergency phase
- Emergency phase
- Post-listing phase

4.1. Pre-emergency phase

Past experiences with emergency situations have shown that a preparedness plan is key to a rapid response when an emergency is declared.

As products in development are added to the pipeline for each priority disease, several activities 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 authorization of a product once the public health emergency is declared.

If pre-emergency activities have not been conducted, when a PHE occurs or while in progress, they would be implemented during the emergency phase. In this situation, timelines for the process may 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 NAFDAC, external experts, and NRAs responsible for the oversight of the product. Activities include establishment of a roster of experts to be called upon to set up necessary advisory committees at the different stages of the procedure, consultations, strategicplanning, and oversight of systems/procedures to support the implementation of the EUA.

- 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 aspectsare part of the eligibility and assessment process and use the resources and output of the assessment platform.

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

4.1.1. Establishment of the assessment platform

4.1.1.1. Agreements with NRAs of record for information sharing

In situations where reliance platforms are not in place, an agreement may be required for information sharing between NAFDAC and the NRA that is responsible for the regulatory oversight of the unlicensed product (NRA of record). These agreements will allow NAFDAC 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.

Where reliance platforms such as WHO, Regional bodies, SRA CRP have been

established, reliance by NAFDAC on the assessment by SRAs/WHO Listed Authorities (WLAs) does not require an agreement for information sharing. Reports of the inspections conducted by the WHO, SRA/WLA, or other regional bodies 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 NAFDAC. Reliance upon SRA/WLA originally responsible for the regulatory oversight of a product, will determine whether the assessment pathway under the EUA procedure will be based on an abridged or a full review process. An abridged pathway to possible EUA may have an impact on the time required to complete the evaluation.

4.1.1.2. Framework for interaction with NRAs, WHO, and Regional bodies

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

4.1.1.3. Establishment of a team of experts to support the different phases of the procedure

A team of experts will be established by NAFDAC drawn from a suitably qualified pool of experts that are currently members of standing advisory committees, and external expert panels, including representatives from 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.

Two types of committees will be established on an ad hoc basis from the roster of experts:

4.1.1.3.1. Technical Review Committee (TRC)

This Committee should be drawn from the existing Dossier Review Team, Vaccine Committee or IVD dossier review team depending on the type of medical product.

They 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 EUA 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 TRC's recommendations for submission to Advisory Committee on Emergency Use Authorization (ACEUA).

NAFDAC may submit this report to the ACEUA (See below) for consideration when a PHE is declared.

If a submission is received once the PHE has been declared, the TRC will be convened in the emergency phase. Timelines for review and reporting will be impacted but shortened as much as possible.

4.1.1.3.2. Advisory Committee on Emergency Use Authorization (ACEUA):

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

Each TRC and each ACEUA will be coordinated by the Leader of the relevant TeamGroup (Vaccines, Medicines, IVDs).

4.1.1.4. 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 EUA procedure starts, there will be no NAFDAC guideline, official WHO standards other national regulatory guidelines that are fully applicable to a specific unlicensed product.

However, some NAFDAC, WHO, international and national guidelines that are more general (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 NAFDAC guidelines. Guidelines from WHO, relevant international 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 Committee 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 was used by the TRC as the basis for the assessment.

4.1.1.5. Pre-submission activities/ meetings

If considered necessary or desirable by the applicant and NAFDAC, a discussion may be held between the applicant and NAFDAC 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 NAFDAC in advance by the applicant. Such meetings are important fordiscussing the availability of essential data required for specific products, expected timelines forsubmission and updates, monitoring of safety and effectiveness after deployment, and other relevant information. Additional meetings may be held during the assessment process, as required.

4.1.1.6. Submission of applications

The manufacturer, responsible government or non-governmental Agency or local Agent must submit an application letter to The Director General of NAFDAC. The application letter should include details of the 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. Or Listed by WHO.

NAFDAC 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. NAFDAC 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 EUA procedure, the applicant will be required to submit the dossier in the appropriate format for each product stream.

4.1.1.7. Assignment of Assessment pathway

Where products submitted for EUA have undergone a previous assessment and/or obtained an extraordinary authorization by WHO or an SRA/WLA, it is not the intent of NAFDAC to undertake duplicative work, if a review by NAFDAC of the NRAs emergency mechanism deems it to be of a satisfactory standard.

The criteria for the 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 2.

4.1.1.8. Assessment of initial information received

Once the product has been considered eligible for assessment under the EUA procedure, the TRC Lead of the relevant product stream will designate a focal person for the EUA assessmentof 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 TRC based on the essential data requirements (See Annex 1). 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 at any time afterward.

In addition to the EUA dossier review process, NAFDAC 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 TRC so recommends.

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

A consolidated report of the TRC will indicate whether the information received is considered sufficient for a recommendation, or if additional information is needed before 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 TRC and all subsequent versions with updates (see below) will be submitted to DG NAFDAC. DG NAFDAC may submit this report to the Committee responsible for a final recommendation on possible Authorization (ACEUA), if/when a PHE is declared before additional data becomes available. The report will provide the ACEUA with a documented outcome of the evaluation of the quality, safety, efficacy/immunogenicity/performance of the product by the TRC based on currently available data. The report will also indicate when the next set of data is expected (for example, a full report of phase II trials).

4.1.1.9. 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 NAFDAC, 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.

4.2. Emergency phase activities

4.2.1. Ad hoc Committees

The ad-hoc Advisory Committee for Emergency Use Authorization (ACEUA) for the evaluation of a specific product or group of products for a specific disease will be established by DG NAFDAC upon declaration of a PHE. In some cases, DG NAFDAC may establish the ACEUA while the PHE declaration procedure is still pending. The focal point designated by the TRC Lead of the relevant product stream may provide the

ACEUA members with the report prepared by the relevant TRC and any other information considered critical for the deliberations and decisions.

4.2.2. NAFDAC decision on emergency use authorization

This procedure includes provisions to concentrate most of the activities related to the submission and assessment of available data during the pre-emergency phase. Consequently, in an ideal scenario, the ACEUA would possess all the required data to consider and propose advisement to the DG of NAFDAC regarding the authorization of a product. This would include any stipulations for its usage, with the aim of reaching a decision swiftly.

The ACEUA may request further information from the applicant before making a recommendation. The recommendation of the ACEUA will be used by NAFDAC to decide whether or not the product can be granted an EUA.

4.2.3. Publication of review outcomes and communications

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

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

NAFDAC will publish on the NAFDAC 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 EUA, the product code(s) submitted for EUA and the EUA status of each application;
- A NAFDAC EUA public report summarizing the findings of the EUA assessment;
- Any negative outcomes of the EUA assessment.

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

All decisions to list a product in the EUA 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 EUA list earlier, if new data become available that change the benefit-risk balance of the product or immediately upontermination of the PHE.

4.3. Activities after a product has been listed, deployed, and used

4.3.1. Post listing monitoring.

After a product has been authorized, NAFDAC 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.

NAFDAC reserves the right to issue an information notice to the general public, if at any time, NAFDAC deems that the EUA holder is not responding to a post-listing quality/safety issue in a timely and/or scientifically sound manner. If a quality/safety issue cannot be resolved to NAFDAC's satisfaction, NAFAC reserves the right to restrict or revoke the emergency uselisting of the product.

4.3.2. Post-listing changes

Once a product has been listed under the EUA procedure, the development of the product must whenever possible- continue to completion for marketing authorization.

The applicant must promptly inform of all changes regarding formulation, manufacturing process, testing methods, specifications, facilities, and any other aspects that might (a) result in achange of the safety and/or efficacy and/or performance of the product or (b) change the basis for the Authorization recommendation. Such changes to the product must follow the procedure for submission of updates described in 4.1.1.9.

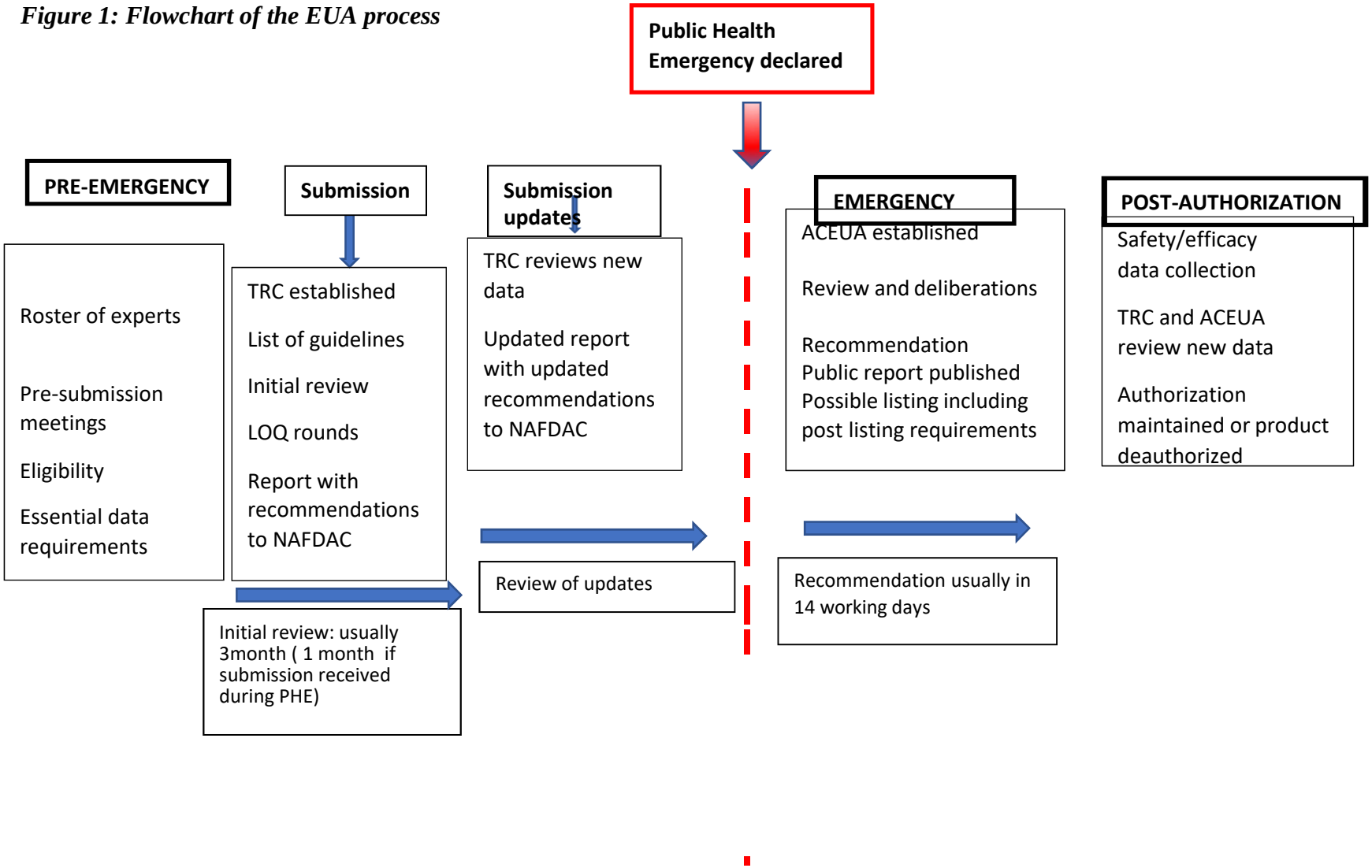
Changes to products listed based on an abridged procedure must be accepted for emergency use by the original NRA responsible for the oversight of the product or WHO Prequalification team, and NAFDAC must be notified of the accepted changes.

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

Activity	Pre-emergency	Emergency	Post-listing
Agreements between NAFDAC and relevant NRAs	✓		
Establishment of roster of experts by NAFDAC	✓		
Assessment by NAFDAC of eligibility of specific products	✓	✓	
Development of consensus by the TRC on requirements	✓	✓	
Pre-submission meetings between NAFDAC and applicant	✓	✓	
Assignment of assessment pathway by NAFDAC	✓	✓	
Establishment of ad hoc committees (TRC and ACEUA) by NAFDAC	✓	✓	
Assessment of submission by TRC	✓	✓	
Assessment of TRC report by ACEUA		✓	
Submission of updates by manufacturer	✓	✓	✓
Decision on EUA by NAFDAC		✓	
Decision by NAFDAC on whether to extend listing		✓	✓
Possible post-listing changes by NAFDAC			✓
Post listing monitoring			✓

Emergency Use Listing Procedure

Figure 1: Flowchart of the EUA process



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

Since the expectation is that the manufacturing/quality control and clinical development of the product submitted for EUA will continue to product licensure and ultimately be submitted for licensure, the submission for EUA of medicines and vaccines should follow the ICH CTD format. In the CTD dossier, sections for which no information is availableat 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, applicants should follow the dossier structure requirements laid down .

For IVDs, the dossier content requirements may differ depending on the analyte being detected and clarification of specific data requirements will require discussion between theapplicant 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.
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, NAFDAC and the Advisory Committee for the Emergency Use Authorization, when convened, will consider programmatic suitability and may consider candidate vaccines with characteristics that would not be accepted for registration.

a) Vaccines requiring storage at less than -20°C are generally not accepted for registration. However, under this emergency procedure, such vaccines can be considered. Upon receipt of such an application, NAFDAC staff responsible for emergency response vaccine deployment will be informed by the NAFDAC EUA Secretariat and will be requested to evaluate and consider whether recipient Agencies possess requisite 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 shelflife 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, NPHCDA and other Agencies responsible for emergency response vaccine deployment will be informed by the NAFDAC EUA Secretariat and will be requested to evaluate and consider whether they possess requisite infrastructure for vaccine storage and distribution at required temperatures. Routinely, multi-dose vaccines for registration 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 processis not finalized and that numerous changes will have to be applied after the first Authorization.These changes should be submitted as updates as indicated in section 4.1.1.9.

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 publichealth emergency.

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, NAFDAC 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 authorization can proceed, provided there are trials underway that will ultimately confirm 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 authorized under the EUA 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 NAFDAC 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 EUA 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 characteristics (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 authorized, 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 NAFDAC. Applicants are highly encouraged to contact NAFDAC as early as possible to discuss the specifics of the application.

A. ***Manufacturing and Quality Data:***

1. Information on the active ingredient(s) and finished product, including characterization (including known and potential impurities), composition, preparation, and controls (specifications, analytical methods and their validation).
2. A list of intended changes for scale-up, if any, along with a discussion on the 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 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 ownassessment 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 modeling performed).
2. Data on efficacy and safety in *in-vitro* tests and in animal model(s) under well-controlled and documented conditions. The preferred model depends on the disease and may vary according to the medicine's mechanism of action. The applicant must justify the choice of animal model.
    a) Evidence of efficacy should include improved survival and/or reduced morbidity of animals in the preferred model under relevant conditions. Surrogate markers, validated or reasonably expected to predict efficacy, would be supportive.
    b) All available evidence of the medicine's activity *in vitro* and in other animals, together with pharmacokinetics and efficacy in humans, also against other diseases should be submitted
3. A rationale should be provided for the proposed dosing in humans, with reference to drug exposures shown to be safe and effective in suitable models. Ideally, human pharmacokinetic data should be available, demonstrating similar levels of the drug following administration at the proposed dose, compared to blood levels found to be safe and efficacious in the relevant animal model.

4. If human pharmacokinetic trials or studies in other indications at the exposure level proposed for treatment of the PHE disease have been conducted, an 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)
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 labeling 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 NAFDAC. Applicants are highly encouraged to contact NAFDAC as early as possible to discuss the 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. After this step, NAFDAC may either decide to proceed or request further documentation or 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.

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 EUA assessment. Based on the submitted documentation, a risk- based judgment will be made on whether thereis 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 proceeds 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:

1. ***Product Information***
   a) Regulatory versions of this product[1]
   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

   - Overview of manufacture
   - Sites of manufacture

[1]The submitted version is defined by all of the documentation related to development, manufacture and intended use, labeling 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 DrugAdministration, Health Canada, a Notified Body for CE marking, etc.) it is considered to be a different regulatory version.

c) Key suppliers

3. ***Product Performance Specification, and Associated Validation and Verification Studies***

a) Analytical performance
Stability of specimens
Validation of specimens
Metrological traceability of calibrators and control material values
Accuracy of measurement
Trueness
Precision (repeatability & reproducibility)
Analytical sensitivity (LOD & LOQ)
Analytical specificity
High dose hook effect
Measuring the range of the assay
Validation of assay cut-off
Validation of assay procedure
Usability/human factors
Stability of the IVD

Claimed shelf-life (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)
In-use stability (open pack or open vial stability)
Shipping stability

b) Clinical evidence
Clinical/diagnostic sensitivity .
Clinical/diagnostic specificity

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

Minimizing the potential harm of an IVD authorized for emergency use is achieved by active post-market surveillance. It will be critical for the manufacturer to detail which post-emergency-use-authorization safety monitoring activities are planned if the EUA is granted.

Annex 2: Criteria for selection of assessment pathways

a) Vaccines

For vaccines, the initial EUA assessment will use similar principles as those used for registration and take into account agreements with NRAs to share reports, past inspections of the manufacturer's facilities, the assessment of the manufacturer's qualitysystems 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

	Manufacturers with PQd vaccines	**Manufacturers without PQd vaccines**
Vaccine approved for emergency use by WHO or a stringent NRA/WLA for the target disease and agreement in place between NAFDAC and the NRA for the exchange of information	A	C
Vaccine not approved for emergency use by WHO or a stringent NRA/WLA for the target disease or no agreement in placewith the NRA	B	C

Table 2: Vaccines assessment approach for each category

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

* Programmatic aspects include: indication, dosage, conservative, storage temperature, auto disablesyringe, etc.

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

a) Medicines

Table 3: Medicines assessment approach

	Assessment approach	**Inspection**
Product authorized for emergency use by WHO or 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 NAFDAC of the submitted dossier information. The review will also consider available assessment reports written by NRAs.	Inspection by NAFDAC and/or desk review of available WHO, SRA/WLA, or PIC/s member inspectorate reports[2]

b) In vitro diagnostics

Table 4: IVDs assessment approach

	Assessment approach	**Inspection**
Product assessed through another emergency mechanism of an acceptablestandard?	Abridged initial assessment ofreports	Desk review of the QMS
Product not assessed through another emergency mechanism of an acceptablestandard?	Full initial assessment by NAFDAC of the submitted documentary evidence	Desk review of the QMS and/or inspection if required

[2] Inspections reports covering other but similar products.

Abridged IVD EUA assessment

For IVDs, some submissions for NAFDAC EUA 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 NAFDAC 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 EUA assessment in these circumstances can be applied to any of the two steps of the review.

However, NAFDAC EUA 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 NAFDAC may still undertake some extra assessment activities if deemed necessary or request the dossier that was assessed previously through other emergency mechanisms.

Annex 3: Pre-submission meetings

Introduction

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

A pre-submission meeting allows the responsible NAFDAC team to have an overview of the product and a) ensurethat the applicant has substantial information for a submission, b) provide general guidanceon 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-EUA 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 a copy to the relevant Group Lead. The Group Lead will reply to the applicant with a proposed date for the meeting as appropriate and the deadline to submit the information package. The applicant must send the list of proposed participants (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 Group Lead may invite members of the roster of experts to join the PQ team for the pre-submission meeting.

The Meeting

Meetings are organized by the NAFDAC Group Lead and will be held at NAFDAC premises or by audio/video conference. The time allocated will not exceed 3 hours, depending on the agenda prepared by NAFDAC team 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 a summary of information presented, the questions raised and the responses, as well as follow-up actions if applicable. These will be sent to NAFDAC within 15 days for final review and comment.

Pre-submission meeting request form

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

Vaccines:

Medicines:

IVDs:

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 NAFDAC Assessment Group Lead, NAFDAC office complex, Isolo, Lagos Nigeria.

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 NAFDAC for EUA.

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).

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 NAFDAC internal use Only

Internal Reference	
Scheduled date and time of meeting	
Location	