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UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

GUIDELINES FOR EMERGENCY USE AUTHORIZATION OF MEDICINAL PRODUCTS

(Made under Section 51 (1) (a) and 57 (1) of the Tanzania Medicines and Medical Devices Act, Cap 219)

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Abbreviations and Acronyms

AMA	-	African Medicines Agency
AVAREF	-	African Vaccines Regulatory Forum
BfArM	-	Federal Institute for Drugs and Medicinal Devices of Germany
COVID-19	-	Corona Virus Disease 2019
EAC-MRH	-	East Africa Community Medicines Regulatory Harmonization Programme
EMA	-	European Medicines Agency
EUA	-	Emergency Use Authorization
EUL	-	Emergency Use Listing
GCP	-	Good Clinical Practices
Ghana FDA	-	Ghana Food and Drugs Authority
GHPP	-	Global Health Protection Programme
GLP	-	Good Laboratory Practices
GMP	-	Good Manufacturing Practices
GRevP	-	Good Review Practices
ICH	-	International Council for Harmonization
ISO	-	International Organization for Standardization
IVDs	-	In-Vitro Diagnostics
MAH	-	Marketing Authorization Holder
MER-EWG	-	Medicines Evaluation and Registration Expert Working Group
MoH	-	Ministry of Health
NMRAs	-	National Medicines Regulatory Authorities
PPB	-	Pharmacy and Poisons Board, Kenya
PHE	-	Public Health Emergency
PHEIC		Public Emergency of International Concern
PHENC	-	Public Health Emergency of National Concern
SADC	-	Southern African Development Community
SOP	-	Standard Operating Procedure
SRA	-	Stringent Regulatory Authorities
TMDA	-	Tanzania Medicines and Medical Devices Authority
TRS	-	Technical Report Series
USFDA	-	United States Food and Drugs Administration
WHO	-	World Health Organization

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Dr. Yonah H. Mwalwisi
Acting Director of Medicines Control

Glossary of Terms

The definitions given below apply to the terms used in this document. They may have different meanings in other contexts

“Act” means the Tanzania Medicines and Medical Devices Act, Cap 219;

“Authority” means the Tanzania Medicines and Medical Devices, or the acronym “TMDA” established by section 4 of the Act;

“Applicant” means person or company who submits an application for emergency use authorization of a medicinal product, an update to an existing or a variation to an existing authorization;

“Application” means the information provided by the applicant to the Authority for evidence-based evaluation and emergency use authorization decision;

“Assessor” means any qualified personnel who participate in the technical aspects of medicinal product evaluation process;

“Evaluation” means highly complex, multidisciplinary assessment of medicinal products applications to determine whether they meet scientific and evidentiary standards for safety, efficacy and quality. It forms the scientific foundation for the emergency use regulatory decisions;

“Marketing authorization” means approval to market a medicinal product in Tanzania. It is a legal document issued by the Authority that permits the marketing or free distribution of a medicinal product in Tanzania after evaluation of safety, efficacy and quality. In terms of quality, it establishes inter alia the detailed composition and formulation of the product and the quality requirements for the product and its ingredients;

“Standard operating procedure (SOP)” means an authorized written procedure giving instructions for performing operations (both general and specific);

“Public Health Emergency of National Concern (PHENC)” means an extra ordinary event which is determined to constitute a public health risk through wide spread of disease and to potentially requires a coordinated national response;

“Public Health Emergency of International Concern (PHEIC)” means an extra ordinary event which is determined to constitute a public health risk through wide spread of disease and to potentially requires a coordinated international response;

“Emergency use” means approval for use when public health emergency has been declared i.e. the use of a medicine (therapeutic), vaccine, or in vitro diagnostic or medicinal device) on patients

in a life-threatening situation or condition, including chemical, radiologic or nuclear attack, in which no standard treatment or diagnostic is available, and in which there is no sufficient time to obtain product registration. Emergency use authorization procedure may also be applied in extreme situations such as during war.

“Biological product” means items derived from living organisms (ranging from normal or genetically modified microorganisms to fluids, tissues and cells derived from various animal and human sources) or containing living organisms that are used for therapeutic or diagnostic purposes.

“Sameness of product” means that two products have identical essential characteristics (i.e., the product being submitted to the relying authority and the product approved by the reference regulatory authority should be essentially the same).

Foreword

The Guideline for Emergency Use Authorization (EUA) provides for minimum regulatory requirements and describes the TMDA's procedure for authorizing the emergency use of medicinal products in Tanzania during Public Health Emergency of National Concern (PHENC) or International Concern (PHEIC). The recommendations under these guidelines will improve the Authority's preparedness to deal with public health emergencies including chemical, biological, radiological and emerging infectious threats, such as, COVID-19. The EUA is a risk-based procedure for assessment and authorization of unregistered medicinal products for use primarily during public health emergencies. The purpose of the guideline is to prescribe the procedure for expedited review and rapid decision making once a public health emergency of national concern is declared.

The guideline has been developed to provide guidance to industry (manufacturers), applicants, local technical representatives and other stakeholders on the documentation requirements and procedure for Emergency Use Authorization of medicinal products. The EUA procedure has been developed to expedite the availability of unregistered medicinal products needed in public health emergency situations, to assist the Authority 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 or immunogenicity data.

The guideline defines the steps that TMDA would use to establish the eligibility of the unregistered products (including unapproved indication of a registered product) for assessment under this procedure, mandatory information required and the process to be used in conducting the assessment to determine whether the unregistered product or indication would be approved on time limited basis, while further data is being collected and evaluated. The document illustrates three phases of the EUA process: (1) pre-emergency phase, (2) emergency phase and (3) post EUA phase. These key areas are significant for the EUA process of approval of medical products with focus on enhancing emergency preparedness. The implementation of, and compliance with these guidelines play a key role for combating on outbreak of public health emergency.

It should be noted that, the EUA is not an alternative to the marketing authorization of the medicinal products. It is intended to be used only during declared emergencies where the Authority would tolerate less certainty about the quality, safety and effectiveness of products given the mortality and/or morbidity of the disease and the lack of treatment, diagnostic or prevention options at that particular moment in time. It is therefore not intended to interfere with ongoing trials and thus the trials would be expected to proceed as planned after initial submission and subsequent updates.

Adam M. Fimbo
DIRECTOR GENERAL

1. Introduction

The public health emergencies (PHEs) have been brought into the focus of attention due to continuous threats of infectious disease outbreaks and other emergencies. As a result, public health systems around the world have been increasingly under pressure. Depending on the cause, PHEs can involve emerging and re-emerging infectious disease outbreaks, natural disasters, social unrest and conflict, food contamination, or industrial accident including chemical or radioactive nuclear spills, among other hazard risks.

Recently COVID-19 has presented one of the greatest challenges to the public health and healthcare, the pandemic has also caused social and economic disruption and placed enormous strains on health not only Tanzania but also around the globe. The COVID-19 pandemic, lead international organisations watched carefully the global trend of rapidly evolving pathogens contributing to the emergency and spread of new infectious diseases with the potential to cause PHEs of international concern. Further, current developments showed clearly that emergencies can occur any time and have the ability to hit the international communities regardless of borders. Consequently, it is of great interest to develop robust strategies to overcome the public health disaster and have in place a thoroughly prepared system for responding to such catastrophes. This requires evidence-based planning in order to ensure a timely and effective response.

TMDA has taken a precautionary approach in line with preparedness and response guidance for a pandemic, working collaboratively with health sectors and other stakeholders to implement strategies to minimize disease transmission by making medical products for prevention, diagnosis, treatment, and rehabilitation promptly available in the market during the emergence situation.

It is against this background TMDA has taken the effort to develop a guideline which prescribe data requirement and rapid review of the quality, safety and efficacy of medical products during the emergence situation. In general principle, before a product is considered for approval, sufficient scientific including clinical evidence must be collected to show that it is safe, efficacious and of suitable quality. The scientific evidence includes quality data, safety and efficacy results from human clinical trials or non-clinical studies. Notwithstanding these general principles, less sufficient information on quality, safety and efficacy/immunogenicity/performance may be accepted in times of public health emergencies where benefits of the product outweigh risks associated or in the event where there is no other available treatment alternative. In this context, the Authority may grant expedited approval.

Following approval, the trial studies should continue as planned after initial submission and submit data to the Authority. Further, the Authority has additional mechanisms to monitor the quality, safety and efficacy including Post-Market Surveillance and Pharmacovigilance (Safety monitoring) throughout the period of emergency.

Furthermore, where necessary inspections of manufacturers, packagers/labelers, testing laboratories, importers, distributors and wholesalers of the product may be conducted to ensure

that they comply with Good Manufacturing Practices (GMP) and Good Storage and Distribution Practices (GSDP). Alternatively, available and reliable evidence of compliance and non-compliance with good practice requirements can be leveraged as part of the risk-based inspection planning process as prescribed in TMDA's desk review procedure.

2. Legal Framework for EUA

TMDA is mandated under the Tanzania Medicines and Medical Devices Act, Cap 219 to regulate quality, safety and efficacy of medicines, medical devices, diagnostics, biocidals and tobacco Products. Pursuant to Section 51 (1) (a) and Section 57 (1) of the Act, during the declared public health emergency the Authority may approve the use of unregistered medicinal products considering the availability of that medical product is of public interest and fulfill the conditions set thereof. Further, Section 124 of the Act gives the Minister responsible for health following advice from the Authority, mandate to exclude any product regulated under the Act from operation of any or all provisions of the Act. According to Section 15 (3) of the Tanzania Medicines and Medical Devices (Registration of Premises, Importation and Exportation of Pharmaceutical Products and Raw Materials) Regulations, 2015, the Authority may, upon request by any person or institution and on public interest, approve the importation of unregistered medicinal products.

The aforementioned provisions in the Act and Regulations, gives the Authority mandate to allow access of unregistered medicines in emergency situations. Therefore, legitimacy drawn from these provisions; the Authority has crafted this guideline to define requirements and procedures to be used for granting emergency use authorization during public health emergencies.

3. Objective of the Guideline

The primary objective of this guideline is to expedite the availability of medicines needed in public emergency situation. The specific objectives were to: -

a) Establish eligibility of unregistered products for assessment under this procedure;
b) Prescribe the essential information required during submission; and
c) Define the processes to be used in conducting the review to determine whether an unregistered product or unapproved indication of a registered product can be authorized on a time limited basis, while further data is being gathered and evaluated.

4. Scope

This document is meant to guide manufacturers, applicants, other relevant stakeholders and TMDA staff on the review and approval process of unregistered human medicinal products or unapproved indications of a registered human medicinal products used during public health emergency. This guideline also intends to provide general considerations and guidance on content for regulatory submission of applications for Emergency Use Authorization of medicinal products in Tanzania.

Although this document is developed to provide guidance on medicinal products used in humans, the principles may be applied to other types of medical products such as medical devices, in vitro diagnostics and veterinary medicinal products.

5. Requirements for Emergency Use Authorization

5.1 Declaration of a Public Health Emergency

The Minister responsible for Health shall declare a public health emergency pursuant to the Public Health Act, 2009 or an emergency declared as per the scenarios presented under section 6.1 of this guideline when a situation which poses an immediate risk to health, life, property or the environment arises. To meet the criteria for a public health emergency, the incident may include but not limited to: -

(a) Immediately threaten life, health, property or the environment;

(b) Have already caused loss of life, health detriments, property damage or environmental damage; or

(c) Have a high probability of escalating to cause immediate danger to life, health, property and the environment.

5.2 Eligibility criteria of EUA candidate products

In order to qualify for assessment under the EUA procedure the following criteria must be met: -

(a) The disease for which the product is intended is serious, immediately life threatening or has the potential of causing an outbreak, an epidemic or pandemic and there are no registered products for the indication or for a critical subpopulation.;

(b) Existing products have not been successful in eradicating the disease or preventing outbreaks. Potential EUA product may also be an antidote that may be effective to mitigate disease or condition caused by use of an already registered product;

(c) The potential benefits of the product must outweigh potential risks. Products are eligible for Emergency Use Authorization (EUA.), if TMDA determines that the known and potential benefits of the product, when used to diagnose, prevent, or treat the identified disease or condition, outweigh the known and potential risks of the product. In determining whether the known and potential benefits of the product outweigh the known and potential risks, the Authority intends to assess the quality and quantity of the evidence, given the current state of scientific knowledge, of risks and benefits;

(d) The product is demonstrated to be manufactured in compliance with Good Manufacturing Practices (medicines and vaccines); and

(e) The applicant undertakes to complete the development of the medicinal products (Clinical Trials, Chemistry, Manufacturing and Control data) before subsequently applied for marketing authorization of the product.

Applications for EUA submission includes candidates from the pharmaceuticals, biologicals including vaccines. Examples may consist: -

(a) Use of unapproved indication for a registered product;
(b) New Investigational product under EUA (refer also to TMDA's Clinical Trials Guidelines); and
(c) Unregistered products.

It should be noted that, the three product categories above would each have specific requirements for eligibility for evaluation under the EUA procedure. The Authority may consider reviewing a candidate product for EUA that does not meet all the requirements; this must be justified (e.g., in case it is the only option available at the time of the public emergency).

5.3 Eligibility Criteria for Issuance of the EUA

The following criteria should be met for an EUA to be issued to a product: -

(a) the agent/pathogen/item specified in the declaration of emergency can cause a serious or life-threatening disease or condition;
(b) based on the totality of scientific evidence available, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing a disease or condition caused by an agent;
(c) the known and potential benefits outweigh the known and potential risks of the product when used to diagnose, prevent, or treat the serious or life-threatening disease or condition that is the subject of the declaration; and
(d) There is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating such serious or life-threatening disease or condition. TMDA may issue a EUA if it determines that there is no adequate, approved, and available alternative to the candidate product and considers any potential alternative product.

5.4 Call for an application for consideration of EUA

In the event of a public health emergency, the Director General shall publish a call for submission of applications for approval of required medicine (by name, dosage form and strength) and prescribe minimum data package to be accepted at the time of the submission. For more detailed information on the minimum data requirements for the Quality data, Non-clinical and Clinical Data to be submitted please refer section 7 of this document.

6. Phases of the EUA Procedure

The EUA procedure constitutes three phases: -

(a) Pre-Emergency Phase;
(b) Emergency Phase; and
(c) Post-authorization Phase.

6.1 Pre-Emergency Phase

Pre-emergency Phase will include activities that can be done in advance (pre planned activities to tackle emergencies) thus reducing the time required to make final decisions for EUA of a product. Pre-emergency phase will be in place, for instance, where an infectious disease has been declared a public health emergency in neighboring countries or when the WHO has declared a disease of the Public Health Emergency of International Concern (PHEIC). In case such activities are not implemented in the pre-emergency phase, they should be implemented in the subsequent phase.

In general, the acceptance of EUA application under the Pre-Emergency Phase by TMDA will include the following scenarios: -

(a) The time when an immediate threat to the public's health is anticipated and the PHE is officially declared by the WHO;
(b) A time between emergencies when the current PHE ends but has the potential of causing another outbreak in the future. No official PHE declaration by WHO; and
(c) The time when an immediate threat to the public's health is anticipated and the PHE is officially declared by neighbouring authorities or authorities that NMRA aligns with.

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

6.1.1 Pre-Emergency Activities

Pre-emergency Phase activities will include but not limited to selection of key experts within TMDA or from the Medicines Evaluation and Registration Expert Working Group (MER EWG) of the East African Medicines Regulatory Harmonization Programme (EAC-MRH), SADC Medicines Regulatory Harmonization Assessments Group and team or experts from other recognized organizations to support implementation of EUA in line with the existing procedures for gathering experts from a respective regional block. Further, determination of eligibility of products will be done through pre-submission meetings, selection of products for assessment in line with the laid out eligibility criteria, assignment of evaluation pathway and review of submitted data.

6.1.2 Data requirements for EUA procedure under Pre-Emergency Phase

In general, an applicant submitting data as part of Pre-emergency phase (pre-EUA) activities should include a well-organized summary of the available scientific evidence of the product's quality, safety and effectiveness, risks (including adverse events profile) and benefits, and any available approved alternatives to the product.

Consensus will be built on essential requirements on quality, safety, efficacy/immunogenicity and lot release (when applicable, particularly vaccines) for specific products. This is critical as it is very likely that in emergency circumstances in which case there may be no existing standards that are fully applicable to a specific unregistered product. However, the existing general guidelines (TMDA, WHO and ICH guidelines) may be used for the assessment of products that are under development and for which there are no published product specific guidelines taking into consideration the available data.

The TMDA, WHO, ICH guidelines or scientific literature from peer reviewed journals or anecdotal literature may be used to support a scientific opinion/consensus on aspects related to the specific product. This will be considered and discussed by the Product Evaluation Team and where necessary in pre-submission meetings. Under section 7 of this guideline (Application Process) the general data requirements is prescribed which is expected to be uniform in all submissions for EUA and an Overview of required data for EUA submission, EUA decision making and for the EUA post-authorization is appended as Annex I.

6.1.3 Review of Initial Information (Full Assessment)

Product yet to be authorized for use by any regulatory agency or for products although approved by SRA but the assessment reports are not available to TMDA will undergo initial evaluation by the Authority and regulatory decision made. In addition to the EUA dossier review process, the Authority may conduct a desk review of available inspection reports. If appropriate, the GMP & GCP inspectors where it is deemed necessary to do so may conduct on-site inspection of manufacturing and clinical sites respectively.

An assessment report generated through the evaluation of the product dossier by the Authority, East African Community Medicines Regulatory Harmonization (EAC MRH) Expert Working Group on Medicines Evaluation and Registration, SADC - MRH Assessments Group, AVAREF, WHO or any other recognized reliance or harmonization initiative by TMDA at that particular time in combination with the GMP and GCP inspections reports and form a basis for making decision.

The evaluation report will include documented outcome of the evaluation of quality, safety, efficacy/immunogenicity of the product and outcome of the inspections by the assessors and inspectors respectively. The report shall also indicate when the next set of data e.g., Clinical Trials Report for subsequent Phase or additional product data including stability data is expected. The applicant will be expected to provide tentative timelines for the submission of additional data based on the expected dates of completion or planned interim analyses of studies currently

ongoing or being initiated. The submission of additional data should be clearly numbered as per the respective product specific guidelines.

In instances where external expertise apart from the regulatory reliance and harmonization initiative is needed, the Authority may use its technical committees or form ad-hoc committees that shall also include the internal regulatory experts for accelerated review of data.

6.1.4 Abridged Evaluation Pathway

Any product that has been approved for use under extraordinary circumstances, such as public health emergency, by a national medicines regulatory authority (NMRA), particularly by a stringent regulatory authority (SRA), like the ICH member countries, EMA, USFDA and EAC Member States, AMA or AVAREF and the assessment reports are made available to TMDA will undergo abridged evaluation and regulatory decision through reliance mechanisms. The applicant will be required to submit quality and abridged clinical data together with evidence of authorization in SRA.

6.2 Emergency Phase

Once a determination of actual or potential emergency has been declared in Tanzania, the Authority in consultation with the Minister, where appropriate may rely on the Emergency Use Listing Procedure of the WHO during Emergency Phase, to identify products that may be eligible for an EUA in light of the circumstances of the emergency and to facilitate timely submission of the EUA request or listing of products to be allowed for emergency use in the country.

6.2.1 EUA Based on Unilateral Reliance

In an event that, TMDA has not fully participated in joint review or no access to the assessment report or product dossier, the Authority may use unilateral reliance on the regulatory decision of the trusted competent National Medicines Regulatory Authorities or Organization such as WHO Prequalification, EMA, USFDA, Swiss medic, Health Canada, AMA, MHRA, Australia TGA and PMDA.

The following unilateral reliance may be employed by the Authority: -

(a) Verification Review: The Authority shall establish the sameness of the medical product applied for EUA to ensure that it is the same as that assessed by the reference regulatory authority. Therefore, the role of the manufacturer is essential to confirm the sameness of a product and to provide the same documentation to the Authority, except for additional country-specific information submitted for review, such as product stability data according to the stability zone and the local product label;

(b) Abridged assessment: The Authority shall undertake an abbreviated review focusing on benefit risk assessment of data on quality, safety and efficacy taking into account information in the assessment reports of the reference regulatory authority; and

(c) Recognition review: The Authority shall confirm the applicability of the assessment outcomes of another authority or organization for regulatory decision making in the national context, for example, in terms of legal and regulatory settings, benefit–risk assessment, co-morbidities, unmet medical needs, risk management plans and any quality-related specificities such as climatic zones for product stability. In case of differences, such as in target population, epidemiology and other features of the disease, medicines used concomitantly and other factors that can substantially affect the benefit–risk profile of a medicine, as well as quality parameters, especially in relation to the stability under different climatic conditions, appropriate evidence should be provided by the manufacturer.

6.3 Approval of Medicinal Products for EUA

When the Authority is satisfied with the positive recommendations, may call for Technical Committee to peer review the reports and provide further opinions before a final decision is reached. The date of approval by the Director General shall be the date of issuance of EUA for a particular product and shall be valid for the whole period until when the public emergency has been declared to have ceased by the Minister responsible for health. The Authority once it approves the product, shall publish it on the website and issue a public notice on the same.

6.4 Post-Authorization Phase

The Authority shall strive to collect and analyze reports on safety surveillance, efficacy, quality complaints and other relevant data that may impact the validity of the Emergency Use Authorization.

The existing Pharmacovigilance surveillance mechanisms shall be applied in effecting collection and dissemination of safety information, efficacy, quality complaints and other relevant data.

The Marketing Authorization Holder is expected to provide the following post approval commitments in addition to meeting other Pharmacovigilance obligations as stipulated in the Authority's Pharmacovigilance Guidelines: -

(a) An outline of the post marketing pharmacovigilance plan for the product;
(b) Periodic benefit-risk evaluation report in accordance with ICH Guideline E2C(R2) Clinical Safety Data Management: Periodic benefit risk evaluation report; and
(c) Applicant should provide information on any on-going phase II/III/IV studies or on any active monitoring of the safety profile that is taking place.

Once a product has been authorized under the EUA procedure, the development of the product must, if possible, continue to completion for attainment of marketing authorization.

The applicant should inform TMDA in case of any post authorization changes that may include but not limited to changes in formulation, manufacturing process, testing methods, specifications, facilities and any other aspect that might result in a change of the safety and/or efficacy of the

product or change the basis for authorization. The post Authorization changes shall follow the specific Variations Guidelines. In case of unilateral reliance changes to the authorized products must be first accepted for emergency use by the SRA or WHO.

It should also be noted that, advertisements and/or promotions shall adhere to the legal and regulatory requirements.

7. EUA Application Process

In general, the dossier submitted for any application for a EUA should contain, the following minimum information: -

(a) A description of the product and its intended use (the serious or life-threatening disease, how the product is anticipated to be used and /or the populations for which the product is to be used;

(b) Description of TMDA's registration status i.e., whether the product is NOT registered or if registered the requested EUA is for an unapproved or off-label use. Whether the product or intended use is under an Investigational application (with TMDA, any other NMRA from EAC or SADC or SRA country), whether the product is authorized in any SRA country or WHO Emergency Use listed;

(c) The justification for the need of the product i.e., if there are any alternatives or not;

(d) Available safety and effectiveness information;

(e) A discussion of risks and benefits;

(f) Information on chemistry (as applicable), manufacturing and controls, including a list of all manufacturing sites and the cGMP status of the manufacturing site (s);

(g) Information on the quantity of the FPP in stock and the surge capabilities of the manufacturing site(s);

(h) Product information equivalent to the product information requirements as per established product specific guidelines;

(i) Information on product stability, storage and handling conditions;

(j) With regard to safety information-

   i. In general: It will depend on whether the product is already registered for other indications or a new investigational product; it will depend on the stage of development. Clinical trials may be mandatory although this can be provided on Phase by Phase approach as the data accumulates from clinical trials. In other

circumstances, a clinical experience from case studies may be used. Sponsors are encouraged to apply for clinical trials authorization from the Authority;

ii. For unapproved uses of already registered products. If the new indication uses a similar dose (or dose range as established through previous clinical trials), duration, route of administration or mechanism of action and the intended patient population is similar to the approved product, a right of reference to the registered product is applicable; and

iii. Unapproved products. The available data may vary considerably. It is recommended that a EUA application should include preclinical testing data i.e., in vitro testing and animal toxicology data. The applicant is also encouraged to submit human safety information from clinical trials and individual patient experience, if available. If only animal data (including data on non-human primates) is available an extrapolation to humans should be provided. Any safety information on humans on related compounds should be provided.

(k) It is known that comprehensive efficacy data are unlikely to be available for every EUA candidate product. The efficacy data shall be assessed by the Authority on a case by case basis;

The following minimum information should be provided: -

i. Product(s) mechanisms of action to diagnose treat or prevent a disease or condition identified in the EUA;
ii. For medicines, preclinical testing data on the effectiveness in treating the identified agent;
iii. Data on activity or effectiveness in appropriate animal models that would enhance understanding of the drug's potential effects in humans (Animal efficacy studies);
iv. Evidence from human experience, particularly published case reports, uncontrolled trials or clinical trials;
v. Data to support the proposed dosage (Pharmacokinetics and Pharmacodynamics data) for Medicines and Immunogenicity or achievement of protective levels of immunity using other parameters (for vaccines); and
vi. Evidence to show that nonclinical studies were conducted in compliance with Good Laboratory Practice (GLP) for Non-clinical laboratory studies and whether the clinical studies were conducted in compliance with Good Clinical Practices. If the nonclinical laboratories studies were not conducted under GLP, evidence of quality systems put in place to ensure the quality and integrity of data from animal studies should be provided.

(l) Ongoing studies e.g., Long-term stability studies should be provided promptly whenever available

(m) A discussion on Risk-benefit analysis should include the following: -

i. Measures taken to mitigate risks;
ii. Uncertainties and data gaps;
iii. Contraindications; and
iv. Information concerning threats posed by the Chemical, Biological, including infectious agents and anticipated responses; and

(n) The applicant should provide a Pharmacovigilance Plan and Risk Management Plan.

The Authority, after eligibility assessment is completed shall issue a rejection letter for applications that do not meet eligibility criteria for EUA. Once an application is accepted for EUA procedure, the Authority will assign the product to a particular assessment pathway.

8. EUA Application Submission Format

The applicant shall submit an application through online system with a cover letter addressed to the Director General of TMDA. The cover letter should include details of the country of origin, sites of manufacture, proposed presentations for the product and information on whether or not an authorization for emergency use or equivalent has been issued by the national competent authority from the country of origin.

The application should be accompanied with a dossier in the appropriate format for each product category (Please refer to the product specific guidelines).

9. EUA Regulatory Process

Upon submission of application, screening of the application will be conducted for acceptance of application. Successful applications will proceed for evaluation under the EUA. If no screening queries are raised the application will be recommended for emergency use authorization.

After the initial submission of the EUA procedure, application with all the mandatory information for initial assessment, applicants are requested to promptly submit any additional information on the development of the product to TMDA. Any unsatisfactory application may be rejected upon screening or unsatisfactory response. An applicant may request for withdrawal of the application after screening, before evaluation, during query response and after unsatisfactory query response. Applicants of rejected applications may appeal to the Authority as per the existing appeal process.

The emergency use authorization shall be subject to but not limited to the following conditions: -

(a) The emergency use authorization will automatically terminate upon declaration of end of public health emergency;

(b) The applicant shall adhere to all commitments including additional data updates, continued clinical studies, safety reports, risk management plans and adherence to advertisements

and/or promotions, regulatory requirements and safety and vigilance guidelines on medicinal products; and

(c) After declaration of the end of the public health emergency and based on the outcome of the continued studies, the applicant will be expected to submit a complete dossier for the evaluation for marketing authorization.

10. Regulatory Timelines

Screening, assessment and approval timelines shall be determined on a case by case basis and may be as short as deemed possible. However, the following general timelines are applicable

S/N	Stage/process	Time line in working days
1.	Receiving and screening	2
2.	Evaluation under national procedure	15
3.	Evaluation under reliance procedures	10
4.	Evaluation of Query responses	10
5.	Review by Technical committee	3
6.	Approval process	5
7.	Total Regulatory Time	45

NOTE: The clock starts when the Authority receives a completed document. Applicant's time are excluded in the above timelines.

11. Revision and Revocation

The Authority may revise or revoke an EUA if the circumstances justifying its issuance no longer exist, the criteria for its issuance are no longer met, or other circumstances make a revision or revocation appropriate to protect the public health. Such circumstance may include: -

(a) Additional information provided by applicant on the progress made with respect to approval does not support the continuation of an EUA of the respective product;

(b) Significant adverse inspection findings (e.g., when an inspection of the manufacturing site and processes has raised significant questions regarding the purity, potency, or safety of the EUA product that materially affect the risk/benefit assessment upon which the EUA was based);

(c) Reports of adverse events (number or severity) linked to, or suspected of being caused by the EUA product;

(d) Product quality failure;

(e) Product ineffectiveness (such as newly emerging data that may contribute to revision of TMDA's initial conclusion that the product "may be effective" a request from the applicant to revoke the EUA; and/ or

(f) Change in the risk/benefit assessment based on evolving understanding of the disease or condition a change in the approval status of the product may make an EUA unnecessary.

12. Termination of EUA and Continued Use

The duration of EUA shall be up to when the emergency declaration is terminated as determined by the Minister, Ministry of Health. The applicants of products under EUA shall be encouraged to transition them to the marketing authorization status i.e., registration.

(a) Termination: Upon termination of the declaration, unapproved product or labeling and product information for an unapproved indication shall be discontinued. A manufacturer may choose to have unapproved product returned after termination for registration. Notwithstanding any such termination, an authorization shall continue to be effective to provide for continued use in any patient who began treatment before termination (to the extent found necessary by the patient's attending physician); and

(b) Continued Use: Any use of a EUA product beyond the term of a declaration will be regarded as investigational product under clinical trials guidelines, except for use by patients who began treatment when the declaration was in effect.

13. Publishing Products Approved Under EUA

TMDA shall publish on the Authority's website and make publicly available the following information of products authorized through EUA procedure: -

(a) The name of the products, the applicants and the manufacturers that have applied for EUA;
(b) A TMDA EUA public assessment report summarizing the findings of the assessment; and
(c) Include any negative outcomes of the EUA assessment.

TMDA reserves the right to share full assessment reports with other NMRAs for consultation purposes including the EAC and SADC member states.

14. Annex 1: Data for EUA submission, EUA decision making and EUA post-authorization

S/N	Data/information requirement	EUA Submission	EUA Decision	EUA Post-authorization
1.	A description of the product and its intended use	x		
2.	A description of the product's international registration/Marketing Authorization (MA) status with TMDA	x		
3.	The need for the product including of any approved alternative product(s) and their availability and adequacy for the proposed use, and the unmet medicinal need(s) the EUA address	x		
4.	Available safety and efficacy information for the product	x		x
5.	A discussion of risks and benefits	x	x	x
6.	Information on chemistry, manufacturing, controls and stability	x	x	x
7.	A list of each site where the product, if authorised, would be (or was) manufactured and the Good Manufacturing Practices (GMP) status of the manufacturer as per the country of origin	x		
8.	Information about the quantity of finished product on hand and the	x		

S/N	Data/information requirement	EUA Submission	EUA Decision	EUA Post-authorization
	surge capabilities of the manufacturing site(s)			
9.	Information comparable to an approved package insert or instruction use	x	x	
10.	Proposed labelling of primary and secondary package	x	x	x
11.	Product variations			x

15. Bibliography

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