Guideline

On the Issuance of Emergency Use Authorization (EUA)

Non-formal translation

Food and Drug Department

2021

Contents

Preface

COVID-19 outbreak continues to spread widely in many countries around the world and this has led to Public Health Emergency declared in many countries. Currently, besides the preventive measures to avoid the exposure to and mitigate the spread of COVID-19, drugs and vaccines for COVID-19 have been developed for the prevention and treatment of COVID-19 diseases. As the research, development and clinical trial of COVID-19 vaccines have been conducted in an accelerated time table and thus its quality, efficacy and safety may not be fully accepted for granting marketing authorization. However due to the still worsening outbreak of this COVID-19 and to prevent the transmission in the country, immediate access to the COVID-19 is critical and a prerequisite to have access to those vaccines which are not registered yet, Emergency Use Authorization (EUA) regulation is needed. Therefore, the MoH developed and endorsed the EUA regulation No 0833/MoH on 18 February 2021 which give the authority to Food and Drug Department (FDD) for granting EUA for drugs and medicines. This EUA is a prerequisite for regulatory preparation to assure immediate access to drugs and vaccines for COVID-19, and to assure its potential benefits outweigh its potential risks, there is a need to introducing the detailed process for the issuance of Emergency Use Authorization (EUA). In this regard, there is a need to develop the guideline.

Therefore, with the support from WHO FDD has developed this Guideline on Issuance EUA for drugs and Vaccines for COVID-19 which aims to assure the implementation the EUA regulation No 0833/MoH effectively and efficiently. This guideline explains each detailed step in the process from receiving application, conducting review and assessment of documents prior to the issuance of the EUA and monitoring in the post authorization.

This guideline has been developed for the first time as a guide for the issuance of EUA, and it may need to be improved, and therefore your feedback is welcome.

This guideline shall become effective from the date of signing.

Vientiane Capital, Date 28 APR 2021

Director General

Sonthavy CHANGVISOMMID

I. OBJECTIVES

This Guideline aims to guide for ensuring the implementation of regulation for Emergency Use Authorization (EUA) for drugs and vaccines for COVID-19 effectively and efficiently.

II. SCOPE AND APPLICATION

This guideline applies to the pharmaceutical industry and government entities such as the national procurer or health program implementers intending to apply for an EUA for drugs and vaccines for COVID-19, and shall pertain only to unregistered (anywhere in the world) drugs and vaccines for prevention, diagnosis and treatment of COVID-19 or less than 5 years registered in origin country or granted an EUA by the National Regulatory Authority (NRA) of the country of origin or any other mature and established NRA as identified by FDD.

III. DEFINITION OF TERMS

Emergency Use Authorization (EUA) – is an authorization issued for unregistered drugs and vaccines in a public health emergency. The EUA is not a Certificate of Product Registration (CPR) or a marketing authorization. The evaluation process of the product may be facilitated by reliance and recognition principles, but stricter conditions on the use and monitoring following authorization shall be imposed.

Drugs – as used in this issuance, refer to pharmaceutical products that pertain to chemical compounds or biological substances, other than food, intended for use in the treatment, prevention, or diagnosis of disease in humans or animals, including the following:

1. Articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in human,

2. Articles (other than food) intended to affect the structure or any function of the body of humans, and

3. Articles intended for use as a component of any articles specified in the foregoing clauses but do not include devices or their components, parts or accessories.

Recognition – shall refer to the acceptance of the regulatory decision of another trusted institution. It shall be based on evidence of conformity that the regulatory requirements of the reference regulatory authority are sufficient to meet the regulatory requirements of the FDD.

Reliance – shall refer to the act whereby the NRA in one jurisdiction may take into account and give significant weight to assessments performed by another NRA or trusted institution, or to any other authoritative information in reaching its own decision.

National Regulatory Authorities: is an organization which responsible for the control of quality, efficacy and safety of drug and medical products.

IV. GENERAL GUIDELINES

The EUA shall only be issued and remain valid under all of the following conditions provided herein.

1. The applicant shall submit requirements to support the application for EUA.

2. The Food and Drug Department (FDD) and an Expert Panel shall review the application and provide recommendations on the COVID-19 drug or vaccine being applied for EUA.

3. FDD shall act on the application by either issuing the EUA or a Letter of Disapproval (LOD).

4. A COVID-19 drug or vaccine with issued EUA shall be subject to post authorization surveillance. Pharmacovigilance obligations and post-authorization commitments shall be imposed on the holder of the EUA. The pharmacovigilance obligations and post-authorization commitments by the holder of the EUA shall also be shared with the national procurer and health program implementers.

A flowchart of the process for the issuance of the EUA for drugs and vaccines is provided in Annex 1 of this Guideline.

V. REQUIREMENT FOR ISSUANCE OF THE EUA

5.1 Conditions for issuance of the EUA

The EUA shall only be issued and remain valid only when all of the following circumstances are present:

1. Based on the totality of evidence available, including data from adequate and well- known controlled trials, it is reasonable to believe that the drug or vaccine may be effective to prevent, diagnose, or treat COVID-19;

2. The known and potential benefits of the drug or vaccine, when used to diagnose, prevent, treat COVID-19, outweigh the known and potential risks of the drug or vaccine, if any; and

3. There is no adequate, approved and available alternative to the product for diagnosing, preventing or treating COVID-19.

The last condition is deemed present when there is no exists registered drug or vaccine in the country for diagnosing, preventing or treating COVID-19.

5.2 Required documents for issuance of the EUA

Documents shall be submitted to FDD and shall include as follows:

1. Cover letter requesting to issue an EUA by the pharmaceutical industry or government entities with the application form;
2. Valid License to Operate as Drug Importer, with copy of the exclusive distributorship agreement with the manufacturer of the drug or vaccine;
3. Good Manufacturing Practice (GMP) Certificate or equivalent document issued by the National Regulatory Authority or other competent regulatory authority. For drugs or vaccines coming from non-PIC/S countries or non-WHO-Prequalified, the application must be supported by a Foreign current Good Manufacturing Practice (FcGMP) (see Annex 2 for list PIC/S Member Countries);
4. List of Countries where the EUA is approved, with proof of approval for emergency use (or equivalent document) from the corresponding approving counterpart NRAs;
5. Reports on actual use from the issuance of EUA of approving counterpart NRA to the application for EUA;
6. Complete assessment report including question and answer documents from the approving counterpart NRAs;
7. Clinical trial data and results with the inclusion of racial distribution showing (Asians/ Pacific);
8. Currently available stability studies and list of ongoing studies;
9. Risk Management Plan;
10. Summary of Product Characteristics;
11. Summary Lot Protocol;
12. Product labeling with minimum information including name of vaccine, type of vaccine, method of administration, dose per vial, storage, batch or lot number, manufacturing and expiration dates; and
13. Proof of Payment (if available).

Should the above stated requirements be unavailable, a sufficient justification should be provided with an undertaking to submit the requirement when available.

The above stated requirements may be updated or supplemented by the FDD through circulars on the matter. Further, the FDD may require additional documents should it deem necessary for proper review of the drug or vaccine applied for EUA.

In all applications for EUA, a sworn assurance of sameness that the product including but not limited to the composition/ formulation, strength, manufacturing of finished product and active pharmaceutical ingredients, specifications, packaging, product information and others, at the time of the submission and after EUA, are the same in all respects as the product given the EUA. Also, the application should be accompanied by an undertaking by the manufacturer to complete the development of the drug and vaccine applied for EUA.

VI. THE ASSESSMENT AND ISSUANCE OF THE EUA

1. FDD shall review the quality of the drug or vaccine applied for an EUA based from the requirements submitted. In addition, FDD shall also consult Expert Panel and Covid-19 Vaccine Committee.

2. The committee shall review the quality of the drug or vaccine applied for an EUA based from the requirements submitted.
3. The Expert Panel shall be composed of at least three (3) experts on drug and vaccine development or related fields such as immunology, infectious disease, pharmacology, public health, toxicology and others.
4. The review of the expert panel shall identify whether (a) based on
    - the totality of evidence available, including data from adequate and well-known controlled trials, it is reasonable to believe that the drug or vaccine may be effective to prevent, diagnose, or treat COVID-19, and the known and potential benefits of the drug or vaccine, when used to diagnose, prevent;
    - treat COVID-19, outweigh the known and potential risks of the drug or vaccine.
    - The identity and recommendations of the Expert Panel shall be strictly confidential.
    - The recommendations of Committee and the Expert Panel are for the consideration of the FDD.
5. The FDD may rely on and/or recognize EUAs of mature and established NRAs as enumerated in Annex 4 of this Guideline. The FDD may also issue circulars at any point to include other regulatory agencies that it deems mature and established.
6. Only the Director General shall approve the application for EUA. The Director General shall issue the EUA after having been satisfied that all of the conditions as provided in this issuance exist.
7. The approval may include one or more special conditions for use. These can include post-authorization safety and effectiveness reporting requirements, limitations, restrictions on advertising and promotion, and other special conditions.
8. The following shall be considered as basis for disapproval of the application:
    - Failure to satisfy all of the conditions for the issuance of the EUA;
    - Failure to demonstrate the safety, effectiveness, and quality profile to prevent, diagnose, and treat COVID-19;
    - Failure to settle unresolved problems regarding quality, safety, and effectiveness;
    - Failure to disclose other relevant quality, safety, and effectiveness issues; and
    - The label of the product (including package insert) is false and misleading.

The decision to disapprove an application is final and irrevocable. An applicant may re-apply in case of a disapproval of its application for EUA provided that the deficiencies initially noted have been complied.

Violation of pharmacovigilance obligations and post authorization commitments; and violation of any provision of the Circular and applicable laws, rules and regulations as identified by FDD.

The EUA shall be valid only within the duration of the declared public health emergency due to COVID-19, or upon issuance of full market authorization/Certificate of Product Registration.

In the event that the declared public health emergency is lifted, or when a COVID-19 drug or vaccine is registered with the FDD, any issued EUA shall have a provisional validity for a period of one (1) year from date of lifting of the declaration or registration of the drug or vaccine for the sole purpose of exhausting remaining products.

The foregoing is without prejudice to the discretion of the Director General to revisit or revoke any issued EUA, as may be appropriate, to protect the general public health and safety.

VII. POST AUTHORIZATION

7.1 Application for import permit

After granting EUA, the EUA holder should submit a completed Request for Importation form (available from FDD) request for importation including supporting documents to MoH Cabinet. The Cabinet will send the document to FDD for review. The supporting documents are

- A Certificate of lot release of the imported lot(s) or equivalent;
- Certificate of Origin;
- Waybill (if any);
- An Invoice for the products;
- The Packing list for the products.

7.2 Monitoring

The holder of the EUA has the ultimate responsibility for monitoring the safety of their products. These responsibilities include inventory control and maintenance of appropriate storage until delivery, among others.

The FDD together with concerned offices shall conduct post-authorization monitoring to track product deployment, additional relevant information, and the status from the manufacturer concerning full-product life-cycle. Post-authorization monitoring shall include adverse events following immunization (AEFI) or adverse drug reactions (ADR).

7.3 Commitments of the Holder of the EUA

1. Complete specific pharmacovigilance obligations (ongoing or new studies, or additional activities) with a view to providing comprehensive data confirming a positive benefit-risk balance. Pharmacovigilance obligations shall adhere to the guidelines and subsequent circulars as issued by the FDD.

2. Complete pending studies and trials. The holder of the EUA shall subsequently proceed to a marketing authorization following FDD guidelines on the condition that it has proven to be safe and effective for the proposed indication.

3. Complete unavailable documents or submit additional necessary documents as may be required by FDD, including provision of further data and response to inquiries; and

4. Secure Lot/Batch Release Certification for all biologicals from the NRA of origin country prior importation to Lao PDR.

7.4 Pharmacovigilance

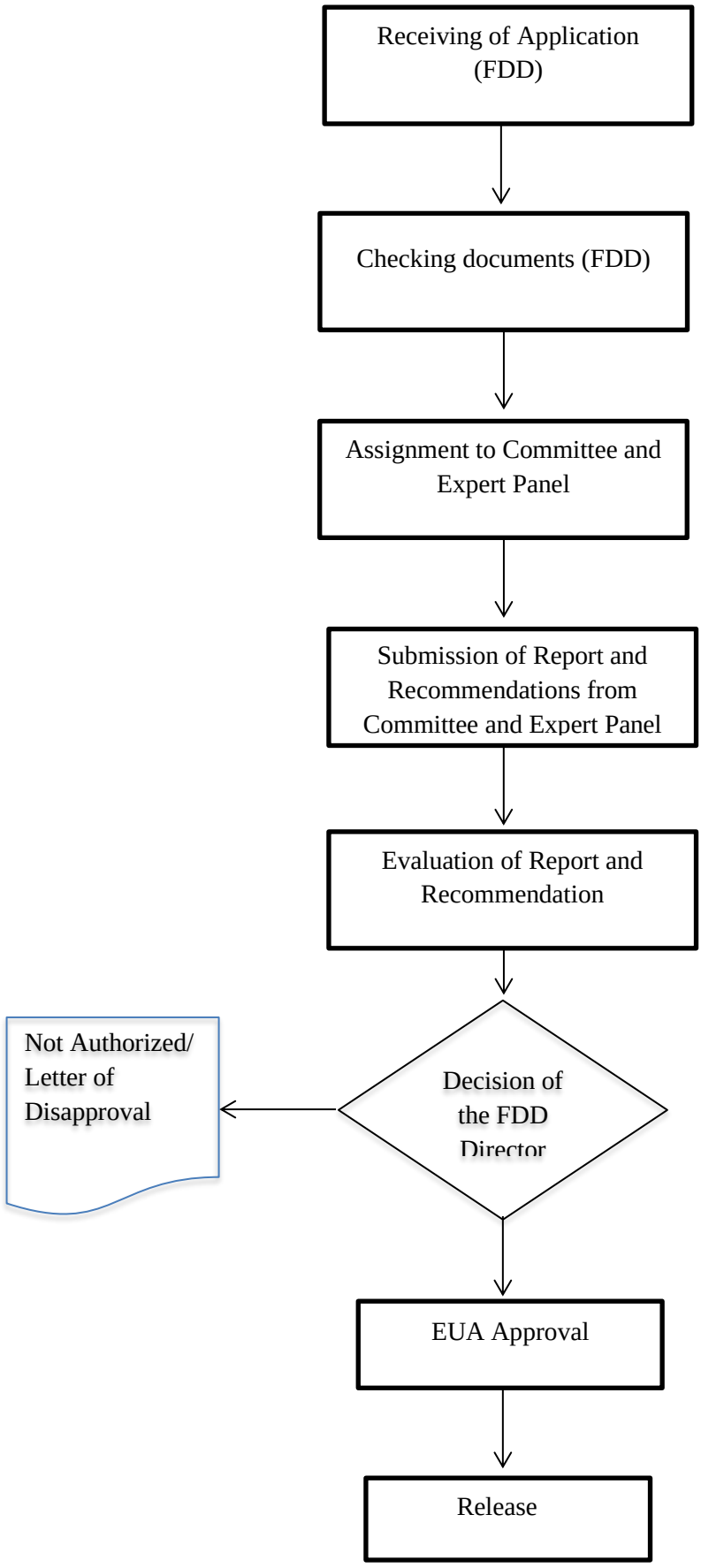
The holder of the EUA shall have a comprehensive pharmacovigilance system for their product following the system or protocol for a registered drug and biological product.

The holder of the EUA shall ensure compliance with the Risk Management Plan (RMP) including additional pharmacovigilance activities. A summary of RMP shall be provided containing information on product safety profile and explain the measures to characterize the risk including ongoing, new studies or additional activities. The summary of RMP shall be published in the FDD website.

7.5 Post Authorization Changes

Any deviation from or changes to the manufacture and changes in label of the product must be notified with the FDD.

Annex 1: EUA issuance flow chart



Annex 2: Pharmaceutical Inspection Co-operation Scheme (PIC/S) Member Countries

Argentina	National Institute of Drugs (INAME)
Australia	Therapeutic Goods Administration (TGA)
Austrian	Austrian Agency for Health and Food Safety (AGES)
Belgium	Federal Agency for Medicines and Health Products
Brazil	National Health Surveillance Agency (ANVISA)
Canada	Health Canada
Chinese Taipei	Taiwan Food and Drug Administration (TFDA)
Croatia	Agency for Medicinal Products and Medical Devices of Croatia
Cyprus	Pharmaceutical Services (CyPHS)
Czech Republic	State Institute for Drug Control
	Institute for State Control of Veterinary Biologicals and Medicine
Denmark	Danish Medicines Agency (DKMA)
Estonia	State Agency of Medicines (SAM)
Finland	Finnish Medicines Agency (FIMEA)
France	French National Agency for Medicines and Health Products Safety
	Agency for Food, Environmental & Occupational Health Safety
Germany	Federal Ministry of Health Central Authority of the Laender for Health Protection regarding Medicinal Products and Medical Devices
Greece	Greek National Organisation for Medicines
Hong Kong SAR, China	Pharmacy and Poison Board of Hong Kong
Hungary	National Institute of Pharmacy and Nutrition (NIPN)
Iceland	Icelandic Medicines Agency (IMA)
Indonesia	National Agency for Drug and Food Control (NADFC)
Iran	Iran Food and Drug Administration (IFDA)
Ireland	Health Products Regulatory Authority (HPRA)

Israel	Institute for Standardization and Control of Pharmaceuticals (ISCP)
Italy	Italian Medicines Agency (AIFA)
	Directorate General for Animal Health and Veterinary Medicinal Products (DGSAF)
Japan	Ministry of Health, Labour and Welfare (MHLW)
	Pharmaceuticals and Medical Devices Agency (PMDA)
Korea	Ministry of Food and Drug Safety (MFDS)
Latvia	State Agency of Medicines
Liechtenstein	Office of Healthcare
Lithuania	State Medicines Control Agency (SMCA)
Malaysia	National Pharmaceutical Regulatory Agency (NPRA)
Malta	Malta Medicines Authority (MMA)
Mexico	Federal Commission for the Protection Against Sanitary Risks (COFEPRIS)
Netherlands	Health and Youth Care Inspectorate (IGJ)
New Zealand	Medicines and Medical Devices Safety Authority (Medsafe)
Norway	Norwegian Medicines Agency (NOMA)
Poland	Chief Pharmaceutical Inspectorate (CPI)
Portugal	National Authority of Medicines and Health Products, IP
Romania	National Agency for Medicines and Medical Devices of Romania (NAMMDR)
Singapore	Health Sciences Authority (HSA)
Slovak Republic	State Institute for Drug Control (SIDC)
Slovenia	Agency for Medicinal Products and Medical Devices
South Africa	South African Health Products Regulatory Authority (SAHPRA)
Spain	Spanish Agency of Medicines and Medical Devices
Sweden	Swedish Medical Products Agency (MPA)
Switzerland	Swiss Agency for Therapeutic Products (Swissmedic)
Thailand	Food and Drug Administration (Thai FDA)
Turkey	Turkish Medicines and Medical Devices Agency (TMMDA)
Ukraine	State Service of Ukraine on Medicines and Drugs Control (SMDC)

United Kingdom	Medicines & Healthcare Products Regulatory Agency (MHRA)
	Veterinary Medicines Directorate (VMD)
U.S.A	U.S. Food and Drug Administration (US FAD)

Annex 3: International Health Organization

World Health Organization

Annex 4: National Regulatory Authorities as reference for recognition

1. **European Medicines Agency (EMA)**
2. **Therapeutic Goods Administration (TGA) - Australia**
3. **Pharmaceuticals and Medical Devices Agency (PMDA)- Japan**
4. **Medicines & Healthcare Products Regulatory Agency (MHRA)- United Kingdom**
5. **Swiss Agency for Therapeutic Products (Swissmedic)- Switzerland**
6. **Health Canada - Canada**
7. **Federal Agency for Medicines and Health Products - Belgium**
8. **French National Agency for Medicines and Health Products Safety - France**
9. **Federal Institute for Vaccines and Biomedicines (PEI) - Germany**
10. **Italian Medicines Agency (AIFA) - Italy**
11. **Medicine Evaluation Board- Netherlands**
12. **Swiss Agency for Therapeutic Products (Swissmedic) - Switzerland**
13. **U.S. Food and Drug Administration (US FAD) - U.S.A**

LAO PEOPLE'S DEMOCRATIC REPUBLIC

Peace Independence Democracy Unity Prosperity

APPLICATION FOR EMERGENCY USE AUTHORIZATION FOR MEDICINES AND VACCINES FOR COVID-19

PART I	**APPLICANT INFORMATION** **(☐ SUPPLIER, ☐ IMPORTER. ☐ PROCUREMENT AGENT, ☐ MANUFACTURER)**
Name	
Address	
Telephone	
Fax	
Contact person	
Beneficiary Disease program	*Attach MOU or other type of contract between beneficiary project in Lao PDR and the MOH*
PART II	**Manufacturer Information**
Name	
Address of specific Manufacturing site(s)	
Country of Origin	
Valid GMP Certificate attached	**Nr:** **Issued by:** **Valid thru:**
WHO Pre-qualified site	☐ *Yes* ☐ *No*
PART III	**Product Information**
Brand name	

Non-proprietary name				
Dosage form				
Active ingredients *Or Active substance/s*	*INN*	*Qty per/* *dosage unit*	*INN*	*Qty per* *dosage unit*
	1.		***4.***	
	2.		***5.***	
	3.		***6.***	
Standard Batch size				
For sterile product	Method of sterilization used: Preservatives used in formulation (multi-dose):			
For multi-source (generic) product	Applicable Pharmacopoeial standard:			
For New Chemical Entity (NCE)	Attach the Summary of Product Characteristics (SPC)			
Stability	*Primary packaging:*			
	Recommended Storage Condition:			
	Claimed Shelf Life: _____ (months)	*Summary (real time) stability studies available* *☐ 25C/60% RH ☐ 30C/75%RH*		
Unit Pack Size (standard secondary packaging)				
Labeling specimen attached (in English for translation to lao)	*Labels (primary pack label and insert text)* *☐ Yes ☐ No*			
WHO EUL (approved)	*☐ Yes ☐ No*			
PART IV	**Regulatory Information**			
EUA issued of origin country	***☐ Yes ☐ No*** **Nr:_____** **Reason:_____**			

Other countries where currently granted EUA AND ACTIVELY USED	***-*** ***(since:_____)*** ***-*** ***(since:_____)*** ***-*** ***(since:_____)***
Countries where application for EUA in process	***-*** ***(since:_____)*** ***-*** ***(since:_____)*** ***-*** ***(since:_____)***

I certify that the above information is complete and accurate. I also certify herewith that critical/major changes of manufacturing, or in product will be communicated by us to the FDD as applicable,

Name:

Signature

At …….. Date……..

Authorized signature Applicant