Guideline on Emergency Use Authorization (EUA) of Vaccines And Medical Products in Bangladesh

Directorate General of Drug Administration
Health Services Division
Ministry of Health and Family Welfare
Government of the People's Republic of Bangladesh

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MESSAGE FROM THE DIRECTOR GENERAL

Directorate General of Drug Administration (DGDA) is responsible to ensure quality, safety and efficacy of medicines, vaccines, medical devices etc. It has major functions like marketing authorization & registration, regulatory inspection, pharmacovigilance (PV), market surveillance & control, clinical trial oversight, licensing of premises, lab access, and lot release of vaccines. For vaccines/ medical products safety, post marketing surveillance and pharmacovigilance (AEFI monitoring) is needed to be organized.

The Directorate General of Drug Administration (DGDA) is solely responsible for providing Emergency Use Authorization (EUA)/ No Objection Certificate (NOC) for vaccines and medical products and overall quality and safety monitoring of vaccines through post-marketing surveillance (PMS). Because vaccines are crucial to ending the pandemic, DGDA has a keen interest to develop comprehensive procedures on PMS and EUA for vaccines and medical products.

DGDA has developed one standard operating procedure (SOP: NRA-MA-011) on the issuance of EUA for imported vaccines and medical products in Bangladesh; however, the SOP is intended for internal use only. For common regulatory understanding and promoting effectiveness and compliance of regulatory system for EUA, DGDA needs a comprehensive guideline for EUA in Bangladesh.

DGDA has developed "the guideline for emergency use authorization (EUA) of vaccines and medical products" in Bangladesh in consultation with expert committee.

I expect that this guideline will help DGDA, importer, manufacturer, marketing authorization holder's (MAH), and all other relevant stakeholders for emergency use authorization of vaccines and medical products, that will promote standard regulation and better access to quality assured vaccines.

I appreciate all members of the public health emergency committee, USAID funded PQM+ program for technical support to develop the guideline for EUA of vaccines and medical products in Bangladesh.

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Acronyms

AEFI	adverse events following immunization
BMRC	Bangladesh Medical Research Council
CMA	conditional marketing authorization
CMC	chemistry, manufacturing, and controls
CTD	common technical document
DG	director general
DGDA	Directorate General of Drug Administration
EMA	European Medicine Agency
EUA	emergency use authorization
EUL	Emergency Use Listing
GCP	good clinical practice
GMP	good manufacturing practice
icddr,b	International Centre for Diarrhoeal Disease Research, Bangladesh
MCB	Master Cell Bank

MOHFW	Ministry of Health and Family Welfare
NCL	National Control Laboratory
NOC	No Objection Certificate
NRA	National Regulatory Authority
PIL	product information leaflet
PHEC	Public Health Emergency Committee
PQ	Prequalification
PQM+	Promoting the Quality of Medicines Plus
PV	Pharmacovigilance
RMP	Risk Management Plan
RU	Receiving Unit
SmPC	summary of product characteristics
SRA	Stringent Regulatory Authority
SU	Sending Unit
USAID	U.S. Agency for International Development
USP	U.S. Pharmacopeial Convention
WHO	World Health Organization

Definition of Terms

Emergency use authorization: EUA is a special procedure for regulation of medical products (including medicines, vaccines, biologicals, medical devices, and in-vitro diagnostics) in case of any public health emergency when optimized assurance of the safety and efficacy of products are accepted—considering the risk-benefit assessment—given the epidemiological situation of the disease and the absence of or shortfalls in treatment and/or prevention options[8].

Regulatory flexibility: Reducing time for regulatory approval by defining emergency pathways and modifying procedures, such as reviewing the submissions and other relevant evidence on a rolling basis[8].

Regulatory reliance: Applying principles of reliance and recognition to decisions and evidence made available by WHO Emergency Use Listing (EUL) Prequalification (PQ) procedures and by Stringent Regulatory Authorities (SRAs) to allow efficient use of resources[8].

Regulatory cooperation: Establishing links and cooperation agreements to support the regulatory process by joint review and sharing the tasks with neighbouring National Regulatory Authorities

(NRAs) and/or supporting NRAs[8].

Regulatory recognition: A routine acceptance of the regulatory decision of another regulator or trusted institutions. Recognition indicates that the evidence of conformity with the regulatory requirements of country A is sufficient to meet the regulatory requirements of country B[8].

Regulatory agility: Adopting proactive search, review, and use of published evidence on vaccines and medical products with the aim of supporting regulatory decisions, in particular, decisions based on reliance and recognition[8].

Executive Summary

This guidance document addresses the process and the criteria to evaluate vaccines and medical products submitted to Directorate General of Drug Administration (DGDA) for emergency use authorization (EUA). This guideline is intended to direct manufacturers, importers (local agents/distributors/ other importing entities), and/or other interested parties for submission of applications to the DGDA for EUA of vaccines and medical products. The guideline is formulated to establish eligibility criteria, essential information requirements, and procedures for evaluating vaccines and medical products in Bangladesh. As an endeavor, the Government of Bangladesh has published several gazette notifications for strengthening the regulatory framework and formed several expert groups to facilitate regulatory operations of DGDA for EUA of medical products and/or commodities. DGDA defined the EUA pathways based on the source of the vaccines and medical products, and the pathways are:

1. Reliance and recognition pathway
2. Critical review pathway

DGDA classified the sources of vaccines into three categories to formulate the specific steps and evaluation mechanism. These are:

- Imported finished vaccine
- Local manufacturing of Vaccine from imported bulk
- Indigenous Vaccine development and local production

Imported vaccines will be registered following Reliance mechanism / pathway for issuing EUA as per DGDA reliance Guidelines.

The eligibility criteria set in this guideline were aligned and harmonized with global best practices and DGDA's regulatory contexts. DGDA explicitly defined the set of essential data requirements as well as the submission and review procedure. The screening and evaluation procedure for applications is formulated based on the four sources of vaccines with a well-defined evaluation method. The criteria for evaluating vaccines and medical products are demonstrated in this guideline to facilitate the evaluation procedure irrespective of the sources of vaccines. The special case considerations are also defined when DGDA is required to impose conditions during issuing EUA, determining validity, and withdrawal, cancellation, revoke, and/or suspension of EUA. Post-authorization activities, such as lot release, risk management plan (RMP) implementation, market surveillance, and safety surveillance are also addressed. Coordinating, monitoring, and evaluating vaccines and medical products are emphasized for evidence generation, regulatory decision making, and actions for public health protection.

1. Introduction

The DGDA is committed to safeguarding the citizens of Bangladesh from unsafe and infective medical products used in health care, including those intended for use in the treatment of emerging infectious diseases (such as COVID-19). DGDA poses sole responsibility for establishing the requirements, procedures, and times when the vaccine manufacturers and importers request authorization for the introduction and use of their products in Bangladesh. DGDA is also responsible for ensuring that the vaccines and manufacturing facilities meet established standards, including manufacturing, quality control, and distribution, for their clinical study as well as ensuring better access. DGDA needs to develop a time limited EUA guideline to expedite the availability of vaccines that are needed in public health emergency situations, based on an essential set of available quality, safety, and efficacy/immunogenicity/performance data. It is vital to clarify, however, that an EUA is not the same as, or an alternative for, a full marketing authorization. The EUA decision should be reviewed periodically and converted to regular marketing authorization when feasible. Given the disease's prevalence, severity and the scarcity of treatment, diagnosis and detection, and prevention alternatives, the EUA delivers a special procedure for conditionally licensing vaccines like Covid-19. The procedure's purpose is to provide unlicensed vaccines with a time-limited and conditional approval in an emergency where minimal data are available, and the vaccines are not yet ready for a full marketing authorization application.

It needs common understanding for relevant stakeholders and DGDA for import, development, manufacturing, marketing, promotion and overall regulation. This guideline is intended to minimize those gaps for standard regulatory practice regarding vaccines and medical products in Bangladesh.

Currently, Bangladeshi manufacturers are manufacturing some vaccines. They are manufacturing fill finish vaccines and vaccines from master cells.

2. Country Regulatory Framework

Regulatory preparedness is key to a rapid response during a pandemic like COVID-19 and minimizes the time available to reach a final decision on the potential inclusion of products and the consequent importation and national deployment procedures. Delays in regulatory readiness will affect access to medical products. The legal framework for DGDA's regulatory functions is based on The Drug Act 1940, Bengal Drug Rule 1946, Drug (Control) Ordinance 1982, and Drug Policy 2016.

The Drug Rule 1945; Part-IV, Rule-36 under The Drug Act 1940 rolled out the legislative basis of issuing a No Objection Certificate (NOC). The Drug Control Ordinance 1982 rolled out the constitution of a drug control committee with specific functions of regular registration of medical products along the obligation of registration of manufactured/imported/distributed/sold medicines to the licensing authority based on the recommendation of the drug control committee.

The National Drug Policy 2016 placed a strong emphasis on pharmaceutical governance and regulatory systems. As per clause 4.2 of National Drug Policy 2016, the government will ensure equitable access to all drugs, including essential drugs, at all levels by taking drug safety, efficacy, and affordability into account. All drugs required for the prevention, control, and eradication of Malaria, Kalaazar, Nipah virus, SARS, tuberculosis, AIDS, and Dengue, as well as other contagious diseases, will be made accessible. Access to all types of vaccines and other drugs required for better maternal and child health care will be ensured on an equitable basis.

On May 17, 2020, the Bangladesh Government issued a gazette notification to include action to combat the COVID-19 pandemic in Clause 4.2 of the National Drug Policy 2016. This gazette notification authorized DGDA as a licensing authority to issue NOC/EUA in the event of a need for manufacturing, importing, distributing, and ensuring access to essential drugs, investigational drugs, and medical devices in the country for detection of Corona virus and other emerging infectious diseases and diagnosis, treatment, and prevention of COVID-19 (Government Gazette Notification No: 45.00.0000.182182.99.017.08-110). As per Clause 4.5 (L) of National Drug Policy 2016, DGDA/Government can enforce the registered manufacturers to produce any medicine in case of public health emergency, and manufacturers will be obliged to obey the order of the government.This is included in the proposed Drug and Cosmetics Act 2023.

The Ministry of Health and Family Welfare (MOHFW) established a technical committee on June 4, 2020, for the evaluation of medicines, investigational drugs, vaccines, and medical devices related to the treatment/prevention of the COVID-19 public health emergency by a gazette notification. The Public Health Emergency Committee (PHEC) makes recommendations to the director general (DG) of DGDA and DGDA officials regarding medical products, including vaccines, to be used/authorized for treatment and prevention related to the COVID-19 pandemic.

In future preparation, readiness for any other endemic, pandemic, fatal infectious diseases like NIPA , Chikungunya etc or any other public health emergency, DGDA will issue NOC/ EUA as fitted. The public health emergency committee will remain valid and will support DGDA to evaluate / recommending for issuing NOC/EUA .

To ensure the quality, safety, and efficacy of vaccines and medical products in Bangladesh, the Government formed a committee, the Quality Assurance Committee for Vaccines, on December 14, 2020, headed by the DG of DGDA. This committee is enabled to take necessary measures to ensure the quality, safety, and efficacy of vaccines and medical products in Bangladesh.

According to the Government Notification No: 45.00.0000.182.89.001.21.93, dated April 24, 2021, the Vaccine must have EUA/EUL from the United States, United Kingdom, Switzerland, Germany, France, Australia, Japan, and/or the European Medicine Agency (EMA), or WHO to issue the EUA/NOC. But in special cases, the DGDA can issue EUA/NOC of the medicines, vaccines, investigational drugs, and medical devices having EUA at other countries/regulatory bodies than those mentioned above prior to evaluating the dossier—clinical and chemistry, manufacturing, and controls (CMC) data—by the PHEC.

In general, the DGDA performs as Bangladesh's National Pharmacovigilance Center and is linked to the WHO-Upsala Monitoring Center, a global pharmacovigilance (PV) platform. Since the government's COVID-19 vaccination campaign began, the DGDA has devised a 'Pharmacovigilance Protocol for COVID-19 Vaccine with the goal of ensuring its safety, quality, and efficacy. This protocol has been approved by MOHFW. After receiving EUA from the DGDA, this protocol provides instructions for passive and active PV activities in Bangladesh relating to reporting, investigation, causality assessment, and management of adverse events following immunization (AEFI) from vaccines/ medical products. For effective regulatory decision making, the protocol describes the monitoring, evaluation, and management of AEFI and serious adverse events cases following

immunization. DGDA, DGHS and EPI consulted the district or city corporation AEFI Committee, Divisional AEFI Casualty Assessment Committee.

The Bangladesh MOHFW formulated a National Deployment and Vaccination Plan (10) for vaccines with an aim to present the Bangladesh plans for the deployment, implementation, and monitoring of potential Vaccine(s). The National Deployment and Vaccination Plan emphasizes the following areas: planning and coordination; regulatory preparedness; advocacy, communication, and demand promotion; vaccine deployment; human resources, vaccine, cold chain, and logistics planning; vaccine safety; and monitoring and evaluation. Planning and coordination committees oversee the planning, implementation, and monitoring of the deployment and introduction of Vaccine(s) in the country. The Government has established vaccination working groups at different levels to support development of a deployment plan— planning, implementing, monitoring the implementation of vaccine deployment— in coordination of various sectors as per national guidelines. The DGDA is responsible for establishing regulatory pathways of vaccines and medical products authorization and utilizing the necessary regulatory instruments and resources ahead of time for regulatory decision making and safeguarding vaccines. The approval and import procedures are based on the origin of vaccines and the purchasing methods. An RMP has been put in place to protect against any potential adverse effect from vaccine use. The Government, along with the National Immunization Technical Advisory Group, has developed a deployment plan to ensure equitable allocation of limited doses. Initially focusing on high -risk groups, a phase-by-phase rollout of vaccines and medical products has been implemented.

3. Scope of EUA Guideline of Vaccines and Medical Products

This document is intended to establish eligibility criteria, essential information requirements, and procedures for evaluating Vaccines based on a critical set of quality, safety, efficacy/immunogenicity/performance data, regardless of whether Vaccines are imported or produced locally. It is also intended to adapt global best practices and guidelines in a national context thr ough aligning with the national regulatory framework.

This guideline is intended to assist manufacturers, importers (local agents/distributors), and other interested parties in submitting applications to the DGDA in order to get an EUA for applicable Vacci nes in Bangladesh.

4. Eligibility Criteria of vaccines and medical products for EUA

In context of the vaccines and medical products, the imported/locally manufactured vaccines shall be eligible for an EUA in Bangladesh if they meet the following criteria:

- All Phases of clinical trials (Pre-clinical, Phase-I phase-II & phase-III/non-inferiority trial) as appropriate to be determined by DGDA should have been completed for local production. Manufacturer should submit further trial data on rolling basis, when available.

- Must have registration/EUA by the NRA of the country of origin with satisfactory clinical and pre-clinical data and complete CMC data evaluated and recommended by PHEC; or

- Registration/EUA in any of the seven countries—United States, United Kingdom, Switzerland, Germany, France, Australia, Japan—and/or the EMA or WHO EUL.

- The EUA of vaccines and medical products is applicable based on decision from PHEC or DGDA. The decision will depend on the end of pandemic (following declaration from WHO), sufficiency of supply versus demand, transition from EUA system to full marketing authorization in other countries, or any guidance from WHO.

5. EUA Pathways

One of the key challenges in ensuring access to life-saving vaccines in Bangladesh is establishing pathways for authorizing vaccines and medical products for emergency use in a timely manner. Vaccines and medical products EUA will be carried out following a critical review pathway, either adopting reliance and recognition or through critical review. In Bangladesh, DGDA has two distinct regulatory EUA pathways, which are depicted below:

5.1. Reliance and recognition pathways

Regulatory reliance has emerged as an exciting and viable way to avoid duplication of review efforts, ease the burden on under-resourced regulatory agencies, and still deliver new medicines to patients who need them. DGDA may totally or partially rely upon the evaluations performed by another NRA or trusted institution in reaching its own decision. The DGDA remains responsible and accountable for decisions taken even when it relies on the decisions and information of others. With strong collaboration among regulatory agencies, it may be possible to build upon existing frameworks and global standards, building trust and sharing resources and experiences. The basis of applying this pathway for those imported vaccines and medical products that got

EUA/conditional marketing authorization (CMA) registration in any of the seven countries (United States, United Kingdom, Switzerland, Germany, France, Australia, and Japan) or EMA and/or WHO EUL. Imported bulk for fill-finish or for technology transfer pre-clinical and clinical parts of dossier will go under reliance pathway with the aforementioned criteria. The reliance and recognition pathways require submission of satisfactory evidence of required documents as per requirements of DGDA.

5.2 Critical review pathway

The PHEC will review the submitted documents (Referred to section 7) and make a recommendation to DGDA. Based on this recommendation, the PHEC and the DG of DGDA will take the decision of EUA, regardless of whether the application will be granted. The proposed Vaccines or bulk for vaccine or master cell bank for vaccines should go through the critical review pathway:

a) The imported Vaccines/ medical products that are not listed by the aforementioned regulatory bodies/countries or WHO EUL
b) Local manufacturing through imported bulk
c) Local manufacturing through technology transfer (either from bulk or master seed)
d) Indigenous Vaccines/ medical products development and local production

6. Registration and Marketing Authorization Department for Vaccines and Biologics and Public Health Emergency Committee

Upon receipt of an application from applicant, Registration and Marketing Authorization Department of Vaccines and Biologics will process the application, and the evaluation report will be reviewed by PHEC if the DG of DGDA decides.

6.1. Registration and Marketing Authorization Department for Vaccines and Biologics

For the evaluation of vaccines, the Registration and Marketing Authorization Department for vaccines and biologics" will:

- ✓ Scrutinize the EUA application and communicate through official letter to the applicant if any further documents required
- ✓ Prepare a summary report based on the review of the submitted common technical document (CTD) dossier

The Registration and Marketing Authorization Department for Vaccines and Biologics may invite members of the following departments and experts from relevant fields to review the respective part of the CTD dossier:

- Clinical trial oversight
- NCL-Vaccine Wing
- Regulatory Inspection

- PV

6.2 Public Health Emergency Committee for evaluation of vaccines and medical products

The PHEC will review technical documents and provide its recommendation to the DG of DGDA on the conditions under which the vaccines and medical products may be granted under the EUA procedure or may not be granted. PHEC will adopt a proactive search, review, and use of the published evidence on vaccines and medical products with the aim of supporting regulatory decisions. The PHEC will:

- ✓ Review the summary report of the eligible vaccine from Registration and Marketing Authorization Department for Vaccines and Biologics
- ✓ Review the published guidelines, requirements/recommendations, and international guidance materials available from WHO and any other regulatory authorities relevant to the evaluation of vaccines and medical products
- ✓ Explore relevant publications that support scientific consensus on a product's safety, immunogenicity, or clinical efficacy
- ✓ After evaluation of the applied vaccine, the PHEC will evaluate the risk-benefit ratio for issuance or rejection of the EUA application and will recommend to the DG of DGDA.
- ✓ Members of the PHEC will sign "confidentiality undertaking and declaration of interest (DOI)."

7. Submission and Review Processes

7.1. Essential data requirements for EUA

Imported finished vaccines and medical products (For reliance and recognition)	Imported finished vaccines and medical products (For full/critical review)
1. Evidence of EUA by the NRA in the country of origin 2. Evidence of EUA/EUL/CMA any of the 7 countries (USA, UK, Switzerland, Germany, France, Australia, and Japan, and/or EMA or WHO EUL. The CTD dossier to be submitted to DGDA (if it is required by DGDA) with following data: 3. The review report of the referring regulatory authority for reliance	Dossier in CTD format with following data: 1. Pre-clinical study report 2. Phase I, phase II, and phase III full study report (if applicable) 3. Complete CMC data 4. Evidence of EUA/registration by the NRA in the country of origin 5. RMP for applied vaccines and medical products to be submitted by local agent/manufacturer 6. Proper labeling and PIL 7. SmPC should be submitted

Imported finished vaccines and medical products (For reliance and recognition)	Imported finished vaccines and medical products (For full/critical review)
4. RMP for applied vaccines and medical products to be submitted by local agent/manufacturer 5. Proper labeling and product Information leaflet (PIL) 6. Summary of product characteristics (SmPC) should be submitted	

Note: In case of importing same finished vaccine from same company but different source of production/ same finished vaccine from different company, the importer should submit a new application for EUA.

Vaccines and medical products from imported bulk (for critical review)
1. Source validation certificate Dossier in CTD format with following data: 2. Evidence of EUA/registration by the NRA in the country of origin 3. Lot release certificate from NRA/NCL of country of origin 4. Pre-clinical study report 5. Phase I, phase II, and phase-III full study report 6. Complete CMC data 7. RMP for applied vaccines and medical products to be submitted by the manufacturer. 8. Proper labeling and PIL 9. SmPC should be submitted

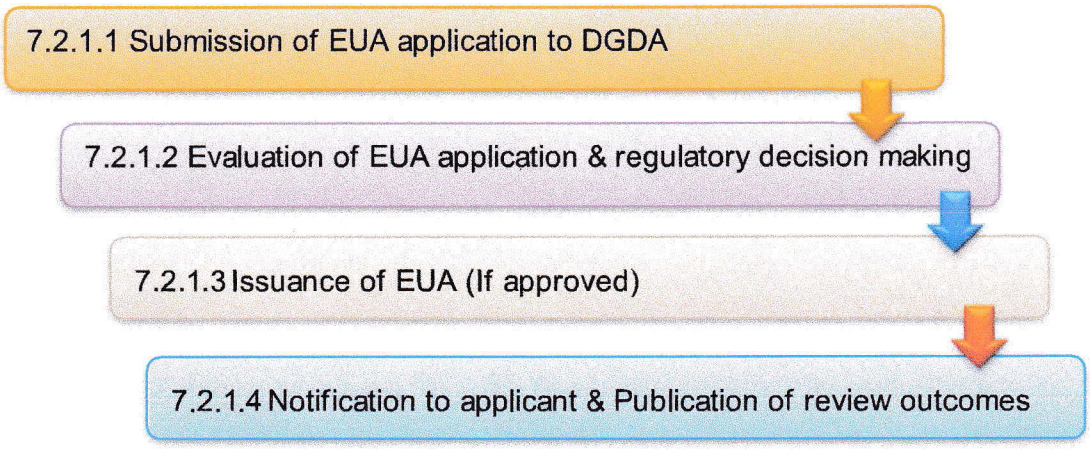
Locally produced vaccines and medical products from Master Cell Bank (MCB) which is approved in other countries with WHO Maturity Level 3 in terms of vaccine manufacturing capacity
1. Agreement copies of Master Cell Bank (MCB) transfer between innovator & receiving manufacturer. 2. Research license from DGDA for developing vaccines using master cell bank. 3. Permission documents (NOC) for importing master seed/ cell line for target vaccine. Dossier in CTD format with following data: 4. Evidence of EUA of the vaccine (Reference Vaccine) by the NRA which contains same Cell Line 5. Preclinical study report of the MCB provider/ Innovator/ carried out by local developers 6. Clinical trial protocol to be approved by DGDA, having prior ethical clearance from BMRC. 7. Comparative Immunogenicity Clinical Trial between Reference vaccine vs Locally produced vaccine (non-inferiority study design) 8. Complete CMC data 9. RMP for applied vaccines and medical products to be submitted by the receiving manufacturer

10. Proper labeling and PIL 11. SmPC should be submitted
Indigenous vaccines and medical products (for critical review)
1. Permission documents (NOC) for importing master seed/cell line for target vaccine 2. Research license of the manufacturer from DGDA (Form 17 of Bengal Drug Rule 1946) Dossier in CTD format with following data: 3. Pre-clinical study report. 4. Clinical trial protocol to be approved by DGDA, having prior ethical clearance from Bangladesh Medical Research Council 5. Phase I, phase II, and phase III satisfactory full study report 6. Complete CMC data 7. RMP for applied vaccines and medical products to be submitted by the manufacturer. 8. Proper labeling and PIL 9. SmPC should be submitted

Note: In case of age group extension and changing dose regimen after approval of EUA with specific dose for specific age group, the EUA holder should submit safety and efficacy data for claimed age group in favor of applied new dose.

7.2. Submission procedure and processing of the EUA application

7.2.1. General steps involved in submission and process of issuing EUA[11]



7.2.1.1. Submission of EUA application

- The manufacturer/importer must submit an application to DGDA as per Annex 1 along with proof of the submission of government fees.
- The application letter should be submitted along with required essential documents mentioned in Section 7.1.
- Applicant must submit the documents following CTD format.

7.2.1.2. Evaluation of EUA application and regulatory decision making

7.2.1.2.1. Screening by Registration and Marketing Department of Vaccines and Biologics of DGDA

- The Registration and Marketing Authorization Department for Vaccines and Biologics of DGDA will scrutinize the EUA application.
- The Registration and Marketing Authorization Department for Vaccines and Biologics will communicate through official letter to applicant if any EUA application, whether rejected or any further documents are required to be submitted.
- Relevant department of DGDA will review the relevant section of the CTD application.
- This department will also prepare a summary report to present to the DG of DGDA.

7.2.1.2.2. Determination of regulatory approval pathway

- The head of Registration and Marketing Authorization Department for Vaccines and Biologics will present the summary report of the proposed vaccines and medical products for EUA to the DG of DGDA.
- Based on the submitted documents (according to section 7.1), the DG of DGDA will instruct the pathway of EUA approval toward either reliance and recognition pathway or critical review pathway.

7.2.1.2.3. Review, evaluation, and recommendation

- For the critical review pathway, Registration and Marketing Authorization Department for Vaccines and Biologics will place the documents and summary report to the PHEC. PHEC will review the documents along with summary report and will submit its recommendation to DG of DGDA.
- In case of reliance and recognition pathway, DG of DGDA may award EUA of the vaccine with the intimation to the PHEC.

7.2.1.2.4. Decision of DGDA

- Based on the recommendation of PHEC, the decision (approval/rejection) for EUA will be taken by the DG of DGDA.
- In case of approval, DGDA will issue EUA.
- In case of rejection, DGDA will communicate the decision to the applicant with necessary justification.

7.2.1.3. Issuance of EUA (If approved)

- DGDA will issue EUA for vaccines and medical products upon satisfactory review.
- DGDA may impose conditions along with the issuance of EUA, such as rolling safety and effectiveness data submission or any other risk-based conditions.
- The EUA holder will be bound to follow and comply with the imposed conditions.
- If any non-compliance is evidenced after issuance of EUA, DGDA may cancel, revoke, and/or suspend the EUA.
- Tentative time need to execute up to EUA certificate issuance is 15 days. Calculation of tentative time depends on as per submission of applicant's consecutive deficient documents.

7.2.1.4. Notifications to manufacturer and publication of review outcomes and communications

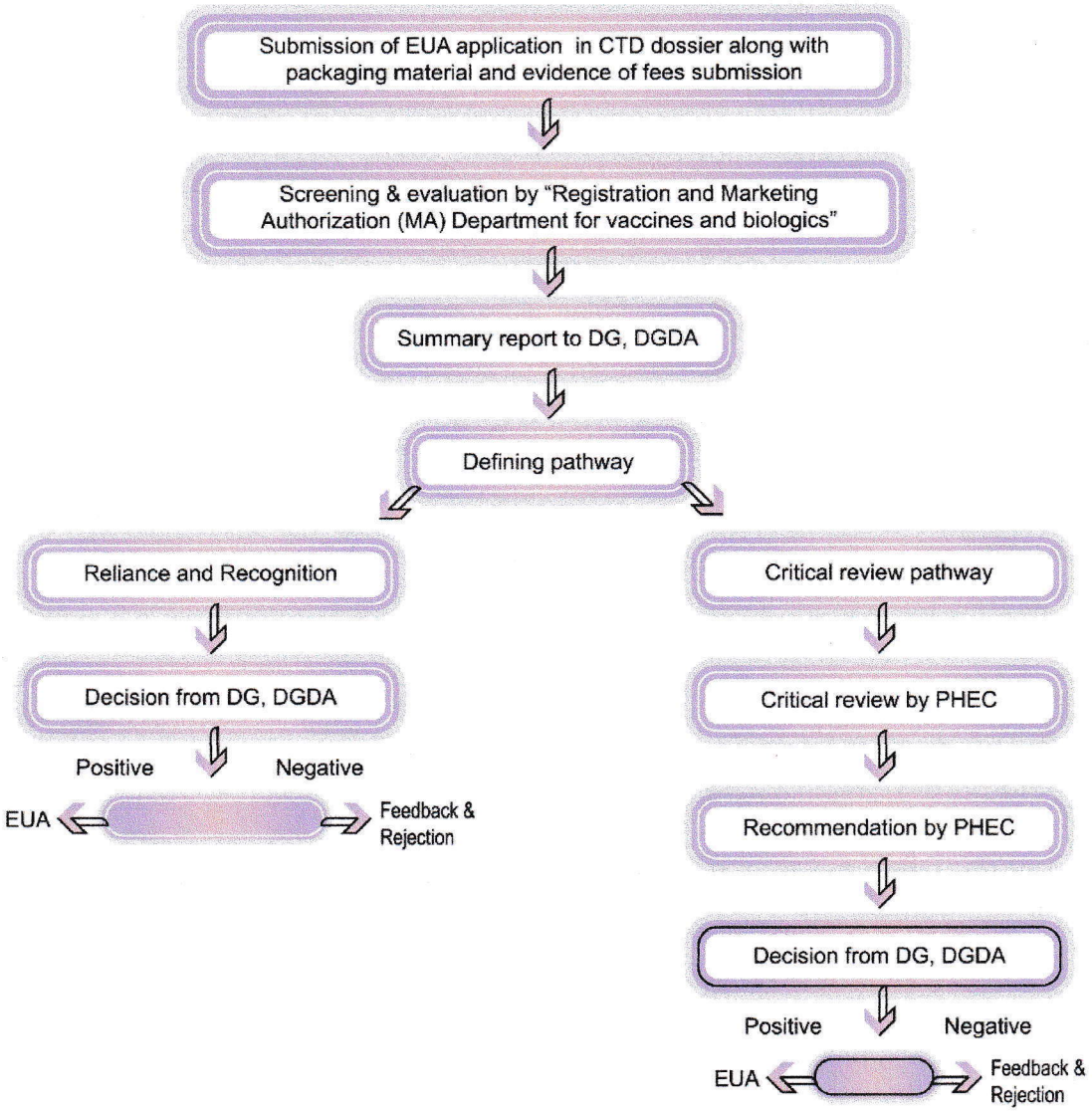
- Upon issuance of EUA, DGDA will notify the applicant and publicize through its website and other relevant media.

7.3. Specific steps involved in submission and evaluation of EUA

7.3.1. **Imported finished** vaccines and medical products

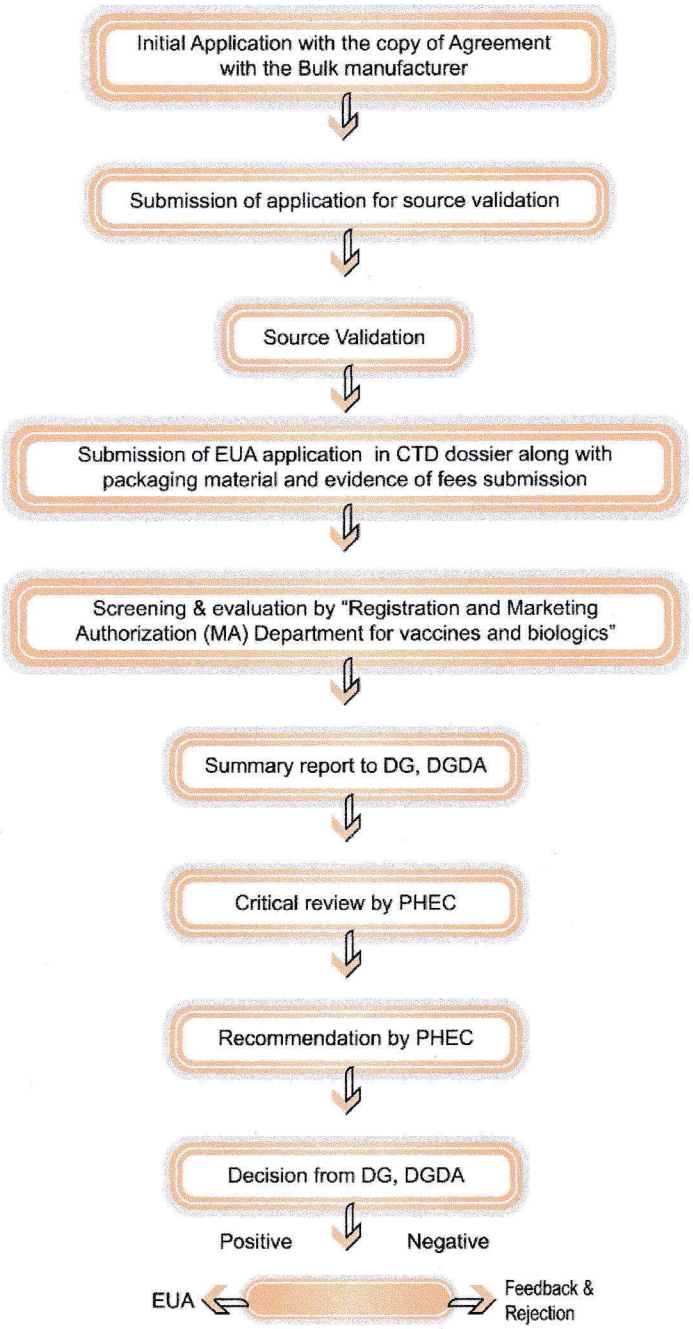
Criteria for finished vaccines and medical products importers:

- If an innovator/manufacturer by itself applies for EUA in Bangladesh, it must have a registered local office in Bangladesh.
- The innovator/manufacturer may appoint a local agent to apply for EUA. The local agent must be a registered entity in Bangladesh.
- If any registered local company/agent applies for EUA of a vaccines and medical products in Bangladesh, it must have a valid agreement with the innovator/manufacturer.
- The importer/manufacturer/local agent must have a proper cold chain system and distribution facility across Bangladesh.



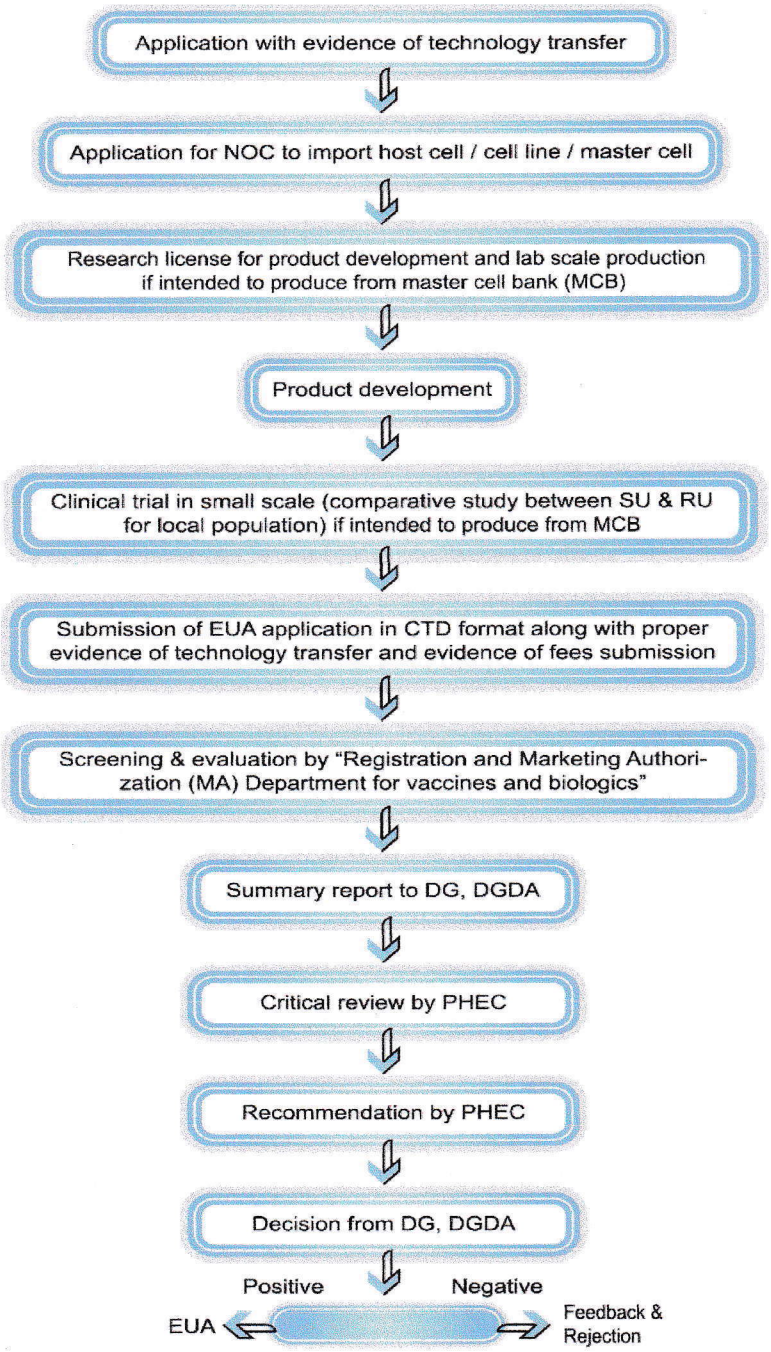
7.3.2 Local manufacturing of vaccines and medical products from imported bulk

After making an agreement with the manufacturer, an applicant must submit an initial application to DGDA to initiate further steps under an expedited EUA procedure. The application for source validation must be submitted as per the checklist of required documents (Annex 6) prior to applying for EUA. Upon completing the source validation, the applicant can submit an EUA application to DGDA, along with evidence of paid submission fees. The steps involved in the regulatory pathway for local manufacturing of vaccines and medical products from imported bulk are given below:



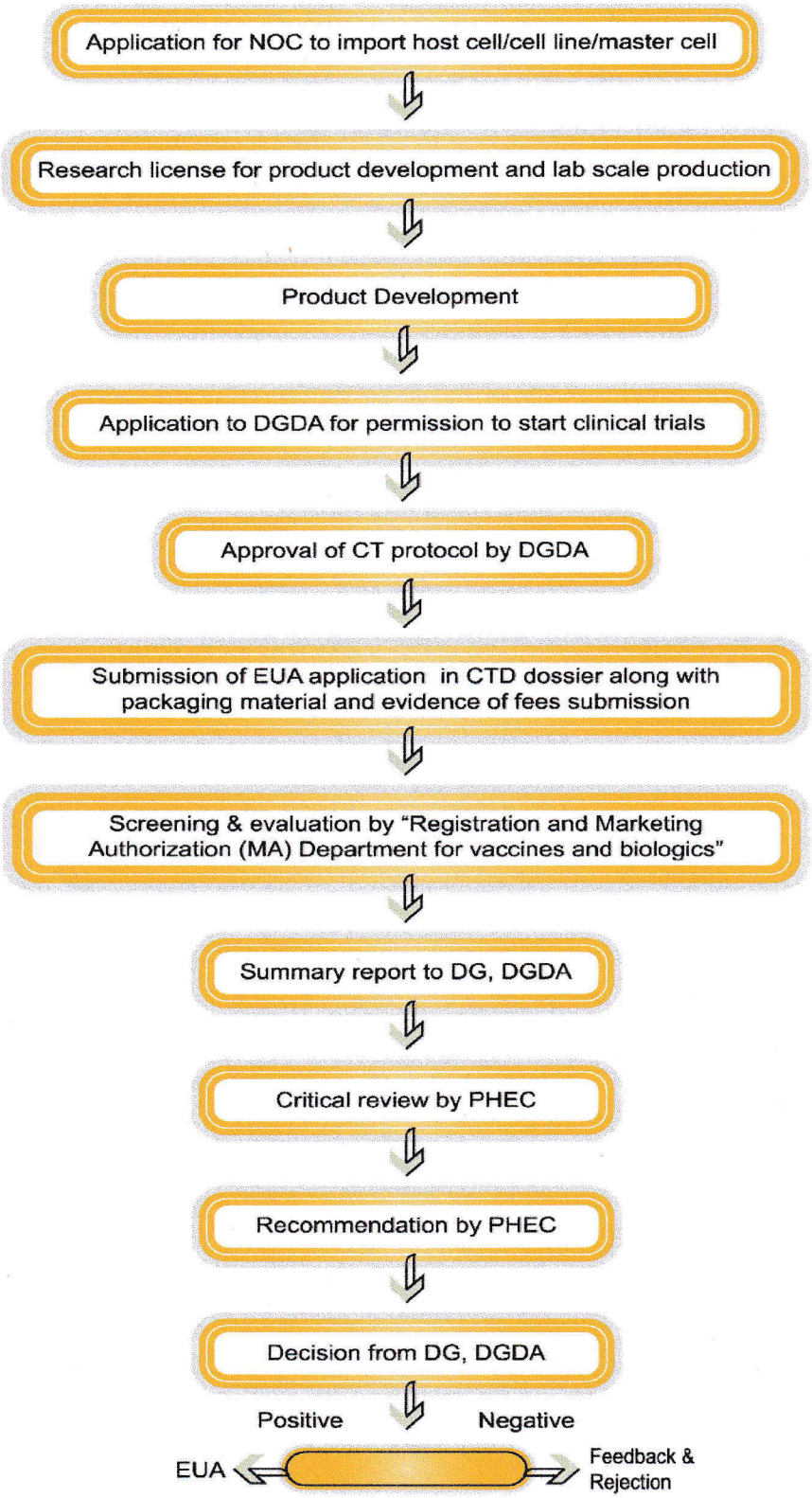
7.3.3. Local Manufacturing of vaccines and medical products through technology transfer

Generally, a technology transfer should include relevant documentation, information, and knowledge from the sending unit in order to enable the receiving unit to effectively execute the specified process or procedure in, for example, production and quality control. A successful transfer of technology should result in documented evidence that the receiving unit can routinely reproduce the transferred product, process, or proceed in compliance with a predefined set of specifications as agreed between the sending unit and the receiving unit. In the case of technology transfer of vaccines and medical products in Bangladesh, an applicant is required to submit appropriate evidence of technology transfer as per required documents mentioned in Section 7.1 during the submission of an EUA application to DGDA.



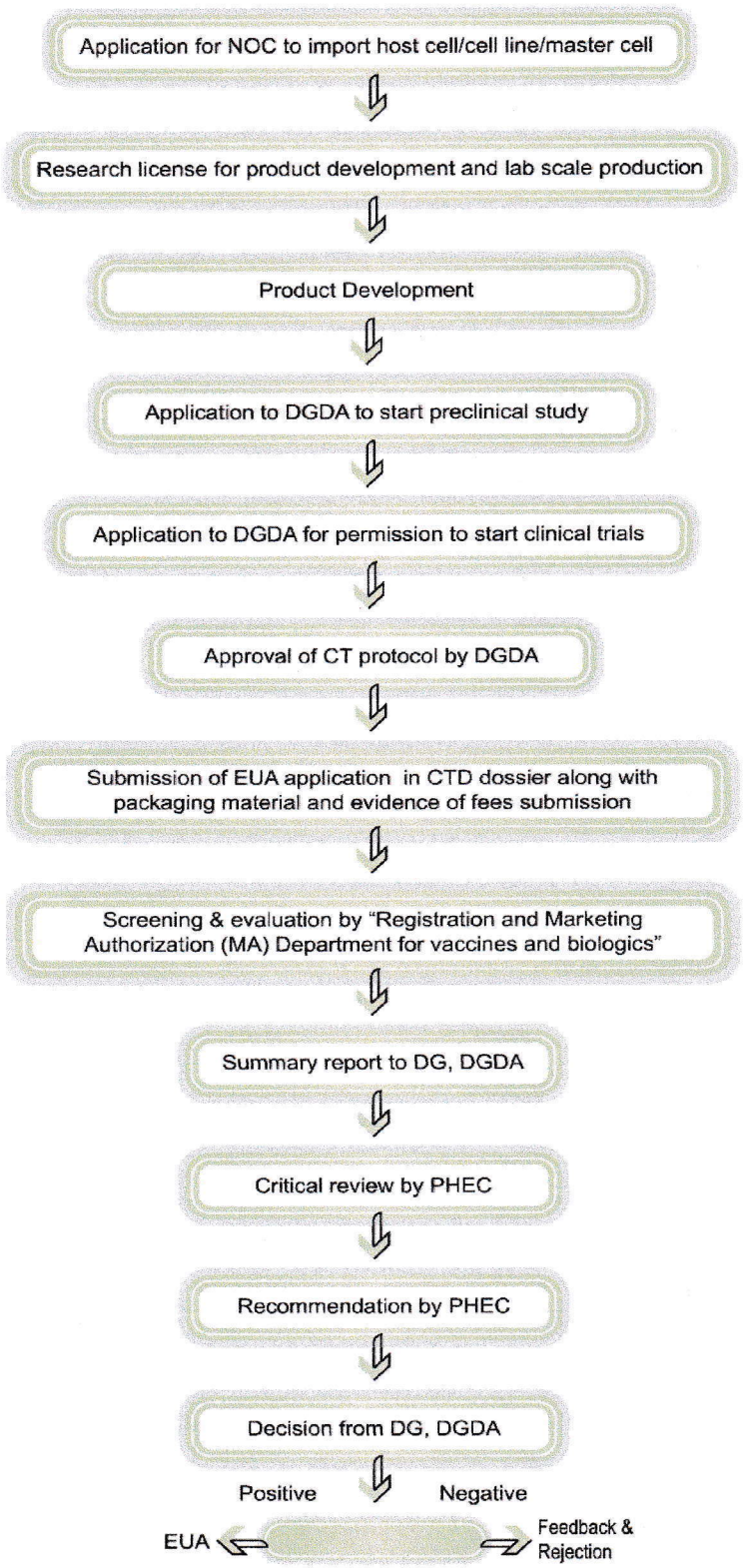
7.3.4 Locally produced vaccines and medical products from Master Cell Bank (MCB) which is approved in other countries

The steps involved in the regulatory pathway for locally manufactured vaccine produced from Master Cell Bank (MCB) which is approved in other countries are given below:



7.3.5 Indigenous or locally developed vaccines and medical products

The steps involved in the regulatory pathway for indigenous or locally developed vaccines and medical products are given below:



8. Risk-based Approach of Applying Regulatory Cooperation Mechanism upon Issuing EUA

If it is required, any neighboring NRA/WHO listed authorities or any other regulatory network that is willing to cooperate with DGDA in establishing an integrated regulatory cooperative mechanism/link for jointly evaluating the vaccines and medical products or task sharing, it is also required to establish the mechanism through a cooperation agreement between/among DGDA and cooperating NRA(s).

9. Risk-based Approach of Determining Validity of EUA

- The EUA of vaccines and medical products will have the validity until the date after 6 months of transition from EUA to full marketing authorization. After the transition of EUA to full marketing authorization notice, the EUA holder should apply for full marketing authorization, to get within 6 months.
- The transition decision will depend on the end of the pandemic (following declaration from WHO), sufficiency of supply versus demand, transition from EUA system to full marketing authorization in other countries, or any guidance from WHO even during the pandemic period.
- The validity of EUA may be ended upon decision of DGDA at any time based on guidelines from WHO, WHO listed authorities/SRA/other NRA to be relied on.

10. Withdrawal and Suspension of Emergency Use Authorizations

EUA of a vaccines and medical products may be canceled, revoked, or suspended based on following issue(s):

- ❑ Unacceptable post-EUA safety and efficacy data as recommended by the relevant committee(s)
- ❑ Decision of WHO for delisting the vaccine from WHO EUL
- ❑ Published safety/alert/signal by the WHO
- ❑ Any other relevant data that supports the cancelation, revocation, and suspension.

11. Criteria for the Evaluation of vaccines and medical products

General Considerations

Format and content of an application	The application should be formatted according to the International Council for Harmonization CTD guidelines.
Screening of applications	A vaccine's CTD is expected to contain sufficient information to support the product's quality, effectiveness, immunogenicity, and safety, as well as evidence that such information justifies the vaccine's wide use. At this point, queries may be issued to the applicant, and acceptance of the application for review will be conditional upon satisfactory responses.

Additional non-clinical information

The CTD dossier requires the presentation of a summary table of non-clinical studies. Additional information on non-clinical studies may be requested by the clinical reviewers whenever necessary, and if this is anticipated by the applicant, such information should be included in the application. If novel adjuvants are used, relevant non-clinical data, as recommended in the WHO guidelines on the non-clinical evaluation of vaccine adjuvants, must be submitted.

Assays for vaccines with multiple components or adjuvants should be measured with either a multiplex assay or separate single assays. The assays used for immunogenicity evaluation should be validated for their intended purpose and calibrated against WHO international standards where available.

Clinical Assessment

Clinical development program	The applicant should provide a tabulated summary of the clinical development study in one or more table(s) in the CTD dossier. A tabular synopsis of the clinical development study in one or more tables should be included in the CTD dossier by the applicant.
Requirement for the protocols of clinical trials that support application	The English version of the protocols of the clinical trials supporting the application must be provided by the applicant. The protocols should be the final approved versions, incorporating all amendments.
Evidence of Ethical Committee approval of clinical trials	The summary is expected to include evidence of the clinical trial's approval by competent ethical committees, as well as information regarding their contact information in CTD. If the clinical trial has been conducted in

	Bangladesh, it is required to provide sufficient evidence of approval from DGDA and ethical clearance from the Bangladesh Medical Research Council.
Evidence of good clinical practices (GCPs) for each trial conducted	In absence of a certificate of GCP compliance from the responsible NRA, applicants must submit evidence of GCP compliance for each trial, such as independent monitoring of trial conduct, sponsor audits, available NRA inspection reports, or Data and Safety Monitoring Board reports, as well as information regarding their contact information. If the clinical trial has been conducted in Bangladesh it is required to provide the sufficient evidence of compliance of GCPs and/or a certificate from DGDA regarding GCP compliance.
Evidence for registration of each clinical trial	Each clinical study supporting an application must have been registered in one of WHO's International Clinical Trials Registry platforms. The registry's name as well as the registry number must be provided. If this is not practicable, an explanation should be given. If the clinical trial is conducted in Bangladesh, it is necessary to provide appropriate evidence/reference of DGDA approval.
Clinical trial design	Randomized, blinded, active-controlled Phase III efficacy trials are required. The most efficient study design for showing vaccine efficacy is an individually randomized controlled trial with 1:1 or 2:1 randomization between vaccine and placebo groups. Other types of randomizations, such as cluster randomization, may be acceptable if there is evidence that potential biases have been avoided. Randomized, blinded, active-controlled Comparative immunogenicity & safety clinical trials against Reference vaccine will be also acceptable in relevant cases. Study design can be non-inferiority or superiority.
Statistical considerations	The primary efficacy end-point, point estimate for a placebo-controlled effectiveness trial should be at least 50%, and the statistical success criterion should be that the lower bound of the suitably alpha-adjusted confidence interval around the primary efficacy end-point point estimate is >30%. A lower bound $\leqslant$30% but >0% may be acceptable as a statistical success criterion for a secondary efficacy endpoint, provided that secondary endpoint hypothesis testing is dependent on success of the primary endpoint. The lower bound of the appropriately alpha-adjusted confidence interval around the primary relative efficacy or immunological marker (Neutralizing Antibody) (for future option) point estimate should be >10 percent for non-inferiority comparisons based on efficacy.

Clinical trial endpoint assays—relevance, validation, and accreditation	o Any serological correlate of protection used in the analyses must be justified and supported with the best scientific evidence available. o Assays should consider the assessment of a functional antibody response along with immunoglobulin serum titer unless the immunoglobulin measured is clearly demonstrated as an immune correlate of protection. o Evidence should be provided of endpoint immunogenicity assay relevance and standardization. o Assay results should be reported in international units wherever possible. o The laboratory should be identified and evidence of competence or accreditation to conduct these assays should be provided. o The assays should be validated and run in a central laboratory, if possible.
Vaccine lots used in clinical studies and lot-to-lot consistency studies	Manufacturing consistency for vaccine candidate lots used in clinical trials should be shown and documented thoroughly. CMC consistency data must be submitted if clinical lot-to-lot consistency has not been shown.
Follow-up in clinical trials	As immune responses to the vaccine wane, study participants should be followed for COVID-19 outcomes for as long as possible (at least one to two years), to assess duration of protection and the potential for vaccine-associated enhanced disease. The condition for immunogenicity outcomes follow-up usually covered by protocol approval process and decision for the timeline "at least one to two years" is provided by clinical trial advisory committee of DGDA.
Requirement for RMP, or equivalent document as part of the CTD	RMPs, including PV plans, are part of modern risk management strategies required for vaccines. This plan should include actions designed to address all important identified and potential risks.
Specific data should be submitted to answer the questions	Please find the list of questions in Annex 8.

Manufacturing and Quality Control

Information on CMC: a list of each site where the product is manufactured, including relevant information about each site and the current status of the manufacturing site(s) with respect to current good manufacturing practice (GMP) requirements should be provided.

Information during application	The complete information of CTD Module 3 must be submitted during the application.
Drug substance	○ Manufacturer(s) - The manufacturer and manufacturing sites ○ Description of manufacturing process and process controls - A flow diagram depicting the manufacturing process from starting materials (Master and Working Cell Banks, Master and Working Seeds, and biologically derived starting materials) to the drug substance should be provided. - Relevant information for each stage of the upstream and downstream processes should be included. Critical steps and critical intermediates for which specifications are established should be identified. A description of each process step in the flow diagram should be provided, including major equipment and process controls, including in-process tests and operational parameters, with acceptance criteria. Information on procedures used to transfer material between steps, equipment, areas, and buildings, as appropriate, and shipping and storage conditions should be provided. If applicable, reprocessing procedures with criteria for reprocessing of any intermediate or the drug substance should be described. A description of the filling procedure for the drug substance, process controls (including in process tests and operational parameters), and acceptance criteria should be provided. ○ Cell banking system, characterization, and testing - A complete characterization of the cell banks should be supplied, including viral safety tests, in accordance with applicable WHO guidelines and should include viral safety studies. Information on the cell banking system should include quality control activities and cell line stability during production and storage (including procedures used to generate the Master and Working Cell Bank(s). ○ Characterization of master and working seed

Information during application	The complete information of CTD Module 3 must be submitted during the application.
	- Full characterization of master and working seed and complete history of the virus used to prepare the virus seed. o Controls of critical steps and Intermediates - Tests and acceptance criteria for all critical steps (with justification including experimental data) should be provided for all critical steps of the manufacturing process to ensure that the process is controlled. o Process validation and/or evaluation - Process validation (based on quality risk-based approach) and demonstration of consistency of production at the production scale used for the lots to be distributed should be provided. - Sufficient information should be provided on validation and evaluation studies to demonstrate that the manufacturing process is suitable for its intended purpose and to substantiate selection of critical process controls (operational parameters and in-process tests) and their limits for critical manufacturing steps (e.g., cell culture, harvesting, purification, and modification). o Analytical method validation - If novel test methods have been developed for potency tests and other critical assays, full description of the test development and qualification/validation must be provided. - The analytical procedures and corresponding validation should be cross-referenced or provided as part of justifying the selection of critical process controls and acceptance criteria. o Manufacturing process development - A description and discussion should be provided of the significant changes made to the manufacturing process and/or manufacturing site of the drug substance used in producing nonclinical, clinical, scale-up, pilot, and, if available, production scale batches. o Control of drug substance - The specification for the drug substance should be provided and justified. - Analytical procedures for testing of the drug substance should be validated and standard testing procedures must be provided.

Information during application	The complete information of CTD Module 3 must be submitted during the application.
	- Description of batches and results of batch analyses should be provided to demonstrate lot consistency. o Reference standards or materials - Information on reference standards or reference materials should be provided. o Container closure system - A description of the container closure system(s) should be provided, including the identity of materials of construction of each primary packaging component, and their specifications. o Stability - This section should include a summary of the studies undertaken (conditions, batches, analytical procedures) and a brief discussion of the results and conclusions, the proposed storage conditions, retest date or shelf-life, where relevant. The post-approval stability protocol should be included.
Drug product	o Manufacture - Manufacturer(s) of drug product, filler/packagers must be indicated for the vaccine that will be submitted for EUA. o Pharmaceutical development - The pharmaceutical development section should contain information on the development studies conducted to establish that the dosage form, the formulation, manufacturing process, container closure system, microbiological attributes, and usage instructions are appropriate for the purpose specified in the application. The studies described here are distinguished from routine control tests conducted according to specifications. - This section should also identify and describe the formulation and process attributes (critical parameters) that can influence batch reproducibility, product performance, and drug product quality. o Components of the drug product - Drug substance

Information during application	The complete information of CTD Module 3 must be submitted during the application.
	▪ The compatibility of the drug substance with excipients/stabilizers/adjuvants listed should be discussed. ▪ If the manufacturer of the drug substance is different from the manufacturer of the drug product, it should be indicated. - Excipients, stabilizers, adjuvants ▪ The choice of excipients/stabilizers/adjuvants listed, their concentration, and their characteristics that can influence the drug product performance should be discussed relative to their respective functions. o Formulation development - A brief summary describing the development of the drug product should be provided, taking into consideration the proposed route of administration and usage. o Manufacturing process development - The selection and optimization of the manufacturing process, in particular its critical aspects, should be explained. Differences between the manufacturing process(es) used to produce pivotal clinical batches and the process described in finished product that can influence the performance of the product should be discussed. o Container closure system - The suitability of the container closure system used for the storage, transportation (shipping) and use of the drug product should be discussed. o Compatibility of diluents - If the vaccine is lyophilized, the compatibility of the drug product with reconstitution diluent(s) or dosage devices—if applicable—should be addressed to provide appropriate and supportive information for the labeling. o Batch formula - A batch formula should be provided that includes a list of all components of the dosage form to be used in the manufacturing process, their amounts on a per batch basis, including overages, and a reference to their quality standards.

Information during application	The complete information of CTD Module 3 must be submitted during the application.
	○ Description of manufacturing process and process controls - A flow diagram should be presented giving the steps of the process and showing where materials enter the process. The critical steps and points at which process controls, intermediate tests, or final product controls are conducted should be identified. A narrative description of the manufacturing process, including packaging, that represents the sequence of steps undertaken and the scale of production should also be provided. Novel processes or technologies and packaging operations that directly affect product quality should be described with a greater level of detail. - Equipment should, at least, be identified by type and working capacity, where relevant. - Steps in the process should have the appropriate process parameters identified. ○ Controls of critical steps and intermediates - Tests and acceptance criteria should be provided (with justification, including experimental data) performed at the critical steps of the manufacturing process, to ensure that the process is controlled. Information on the quality and control of intermediates isolated during the process should be provided. ○ Process validation and/or evaluation - Process validation (based on quality risk-based approach) and demonstration of consistency of production at the production scale used for the lots to be distributed should be provided. In relevant cases, Process validation protocol with commitment letter should be submitted to conduct process validation of first 03 commercial lot (after getting EUA/annexure approval with condition). - Use of multiple sites for production of drug product should be supported by demonstration of analytical comparability. ○ Control of drug product - The specification(s) for the drug product and the analytical procedures used for testing the drug product should be provided.

Information during application	The complete information of CTD Module 3 must be submitted during the application.
	- Justification for the proposed drug product specification(s) should be provided. o Control of excipients, stabilizers, adjuvants - The specifications for excipients and the analytical procedures used for testing the excipients should be provided, where appropriate. - Analytical validation information, including experimental data, for the analytical procedures used for testing the excipients should be provided, where appropriate. - Justification for the proposed excipient specifications should be provided, where appropriate. - For excipient(s) and adjuvants used for the first time in a drug product or by a new route of administration, full details of manufacture, characterization, and controls, with cross references to supporting safety data (nonclinical and/or clinical) should be provided according to the drug substance format. o Reference standards or materials - Information on the reference standards or reference materials used for testing of the drug product should be provided. o Stability - The types of studies conducted, protocols used, and the results of the studies should be summarized. The summary should include, for example, conclusions with respect to storage conditions and shelf-life, and, if applicable, in-use storage conditions and shelf-life. - Generated complete stability data with commercial lots should be submitted after EUA. o Post-approval stability protocol and stability commitment - The post-approval stability protocol and stability commitment should be provided. As data for real-time stability will be limited at the time of submission, updated information will be part of the post-listing commitments.

Information during application	The complete information of CTD Module 3 must be submitted during the application.
Changes	If changes in the manufacturing process are introduced before the assessment is finalized or after the listing, these must be reported and all information provided for evaluation before the final report is prepared. Post-listing changes must also be reported.
Inspection reports	Inspection report(s) from the responsible NRA showing compliance with GMP requirements should be provided. In cases where an inspection was deemed not required, a valid GMP certificate for the facility should be provided.
Labeling	Vial label, carton label, and package insert should follow the models provided by WHO. 1. Summary of product characteristic (information for health care 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 health care providers are adequately informed about the uncertainties regarding both the potential benefits and risks 6. Storage condition should be mentioned on the vial and packaging

12. Post-authorization Activities for vaccines

12.1. Lot release

Vaccines should be manufactured in accordance with GMP and tested by the vaccine manufacturer for quality and safety. Such vaccines should also undergo quality control testing (with a certificate of analysis) and be released by the responsible NCL in accordance with WHO's Guidelines for Independent Lot Release of Vaccines by Regulatory Authorities (and should be accompanied by lot release certificate).

DGDA will adopt a reliance-based approach in case of vaccines coming from reliable sources and will only test physical parameters and review basic required documents. The lot release certificate of the responsible NRA/NCL of the producing country shall be duly recognized. The required documents for expedited lot release are:

- Summary lot protocol
- Q-tag or data logger reading

- Certificate of Analysis
- Lot release certificate of NCL or Official Medicines Control Laboratory from country of origin

In case of local manufacturing from bulk and indigenous vaccine/tech transfer vaccine, a full laboratory test report from any WHO functional laboratory is required for the first three batches or numbers of batches decided by DGDA/NCL, and physicochemical parameters, sterility, and endotoxin tests will be performed by the DGDA NCL vaccine wing. Further full laboratory testing will be decided on a case-by-case basis, based on the outcome of the risk-based assessment. The procedures adopted should ensure that vaccines are deployed as quickly as possible.

12.2. Monitoring of vaccine storage facilities

DGDA will form the following vaccine monitoring teams to monitor vaccines and medical products storage conditions:

- An inspection team to inspect the storage facilities where the vaccine will be stored
- An inspection team to receive vaccines and check the data logger and physical parameter of the vaccines at the airport
- Formation of a team with DGDA officers on a risk-based approach at the district level to receive/monitor vaccine and data logger

12.3 Post-authorization monitoring

12.3.1 Risk management plan

To safeguard against any harm linked with the usage of products, an RMP should be in place. The manufacturer will submit the RMPs, which outline a series of activities aimed at identifying, characterizing, preventing, or minimizing the risk associated with the product; evaluating the vaccination's effectiveness; and communicating the risk information to the national EPI program and other relevant stakeholders. Based on available adverse events of special interest, the RMP could be developed and implemented.

12.3.2 Pharmacovigilance and safety surveillance

In general, the DGDA performs as Bangladesh's National Pharmacovigilance Center and is linked to the WHO-Upsala Monitoring Center, a global PV platform. Every MA holder of EUA for vaccines and medical products has to submit AEFI/ADR report to PV Cell of DGDA. PV cell is responsible for causality assessment and signal generation. DGDA will take regulatory decision as per signal.

12.4 Post-authorization data submission requirement

Emergency Use Authorization (EUA) once authorized with limited data in specific area of requirements like clinical trial, safety surveillance & pharmacovigilance, process validation of three consecutive production batches and real time study report, the EUA holder should submit following data to DGDA on timely manner:

12.4.1 Further clinical trial study data (if conducted)

12.4.2 Continuous safety monitoring data

12.4.3 Real time stability data

12.4.4 Evidence data/ document due to change control

Bibliography

1. World Health Organization. Operational Guidance : Legal and Regulatory Framework Facilitating Vaccine Deployment, Jan. 2021. Accessed Nov. 17, 2021, at https://apps.who.int/iris/handle/10665/339391

2. World Health Organization. Emergency Use Listing Procedure. V. 14, Dec. 2020, pp. 1–62.

3. U.S. Food and Drug Administration. Emergency Use Authorization of Medical Products and Related Authorities: Guidance for Industry and Other Stakeholders, 2017, pp. 1–45 Accessed Nov. 17, 2021, at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities

4. Food and Drug Department of Laos. Guideline on the Issuance of Emergency Use Authorization, 2021.

5. Health Canada. Guidance for Market Authorization Requirements for COVID-19 Vaccine, 2021. Accessed Nov. 17, 2021, at https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/guidance-market-authorization-vaccines.html

6. Directorate General of Drug Administration. Guidelines on the Evaluation of Biosimilar Products, 2017.

7. DCVMN. Workshop by CEPI: Best Practices for Tech Transfer. Accessed Oct. 19, 2021, at https://www.dcvmn.org/Workshop-by-CEPI-Best-Practices-for-Tech-Transfer

Annexes

Annex 1: Application Format for Emergency Use Authorization

[Must be Submitted in Official Pad with full address]

Reference no: ..... Date: .....

To
Director General
Directorate General of Drug Administration
Aushad Bhaban, Mohakhali, Dhaka-1212

Subject: Application for Emergency Use Authorization of vaccines and medical products [name of vaccine] in Bangladesh

vaccines and medical products: [name of the vaccine]

Dear Sir,
We ..... hereby submit our applications for the below:

Name of vaccines and medical products:
Type of the vaccine and presentation:
The target indication for [name of vaccine] is:
Description of intended use of Vaccine:

Category of applied vaccine for EUA application-

- ☐ Imported finished vaccines and medical products
- ☐ Indigenous vaccines and medical products development and local production
- ☐ Local manufacturing of vaccines and medical products from imported bulk
- ☐ Local manufacturing of vaccines and medical products through technology transfer
- ☐ Local production of vaccines and medical products from Master Cell Bank (MCB) which is approved in other countries

The following documents need to submit:

Imported finished vaccines and medical products (for reliance and recognition)

Documents	Yes	No
Evidence of European Medicine Agency (EUA) by the NRA in the country of origin		
Evidence of EUA/EUL/CMA any of the 7 countries (USA, UK, Switzerland, Germany, France, Australia, and Japan and/or EMA or WHO EUL		
The review report of the referring regulatory authority for reliance		
The CTD dossier to be submitted to DGDA (if it is required by DGDA).		
RMP for applied vaccines and medical products to be submitted by local agent/ manufacturer.		
Proper Labeling and PIL		
SmPC should be submitted		

Imported finished vaccines and medical products (for critical review)

Documents	Yes	No
Dossier in CTD format with following data:		
Preclinical study report		
Phase I phase II, and phase-III full study report		
Complete CMC data		
Evidence of EUA /Registration by the NRA in the country of origin.		
Risk Management Plan (RMP) for applied vaccines and medical products to be submitted by local agent/ manufacturer.		
Proper labeling and PIL		
SmPC should be submitted.		

Indigenous or locally developed vaccines and medical products

Documents	Yes	No
Permission documents (NOC) for importing master seed/ cell line for target vaccine.		
Research license of the manufacturer from DGDA. (Form 17 of Bengal Drug Rule 1946)		
Clinical trial protocol to be approved by DGDA, having prior ethical clearance from BMRC.		
Dossier in CTD format with following data:		
Pre-clinical study report.		
Phase-I phase-II & phase-III satisfactory full study report.		
Complete CMC data		
Risk Management Plan (RMP) for applied vaccines and medical products to be submitted by the manufacturer.		
Proper labeling and PIL		
SmPC should be submitted		

Local Manufacturing through bulk

Documents	Yes	No
Source validation certificate		
Evidence of EUA by the NRA in the country of origin		
Lot release certificate from NRA/NCL of country of origin.		
Dossier in CTD format with following data:		
Preclinical study report		
Phase I, phase II, and phase III full study report		
Complete CMC data.		
Risk Management Plan (RMP) for applied vaccines and medical products to be submitted by the manufacturer.		
Proper labeling and PIL		

SmPC should be submitted		

Locally produced Vaccine from Master Cell Bank (MCB) which is approved in other countries

Documents	Yes	No
Agreement copies of Master Cell Bank (MCB) transfer between innovator & receiving manufacturer		
Research license from DGDA for developing vaccines using master cell bank		
Permission documents (NOC) for importing master seed/ cell line for target vaccine.		
Evidence of EUA of the vaccine (Reference Vaccine) by the NRA which contains same Cell Line		
Dossier in CTD format with following data:		
Preclinical study report of the MCB provider / Innovator/carried by local developer		
Clinical trial protocol to be approved by DGDA, having prior ethical clearance from BMRC.		
Comparative Immunogenicity Clinical Trial between Reference vaccine vs Locally produced vaccine (Non-inferiority study design)		
Complete Dossier in CTD format with full CMC data		
Risk Management Plan (RMP) for applied vaccines and medical products to be submitted by the manufacturer.		
Proper Labelling and Product Information Leaflet (PIL).		
Summary of product characteristics (SmPC) should be submitted.		

Other Documents

sl	Documents	Yes	No
1	Proof of deposit of applicable fees as per DGDA requirements		
3	Contact person: [name of applicant's contact person] Title Tel: Email:		

Signature:

Name:

Title:

Date: