Emergency Use Authorization procedure and conditions for Deployment of COVID-19 Vaccines

DRA-G-D3-RP-08

Drug Regulatory Authority

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1. Introduction

Since its emergence in 2019, the SARS-Cov-2 virus has spread to almost every country making the COVID-19 pandemic a global health crisis. COVID-19 vaccines once available are expected to play a major role in the control of the pandemic.

In the context of the current public health emergency, the emergency regulatory procedures for a COVID-19 vaccine are put in place to expediate the timely access to the vaccine. The expedited assessment could be based on reliance approaches to facilitate the approval and provision of import permits in the shortest time possible.

The Medicines Act and the Bhutan Medicines Rules and Regulation 2019 provide legal basis and regulatory frameworks for regulation of medicinal products including vaccines. As per the Section 5.12 of the Act, "*the Board may at its own discretion revise the conditions under which any medicinal product is registered"*. Further, as per Section 5.13 of the same Act, *"The Board may exempt registration requirement of any medicinal product or group of products for reason, which shall be specified by the Board while granting exemption."*

Accordingly, the term "Emergency Use Authorization (EUA)" has been adopted to facilitate access of therapeutic product or vaccine in a market during a declared emergency. As of 9 January 2020, there are four covid-19 vaccines granted emergency authorization by the National Regulatory Authorities in the world.

Acknowledging the unprecedented speed at which the COVID-19 vaccines are developed and complexity involved in performing a complete, independent assessment of the safety, efficacy and quality of COVID-19 vaccines and in keeping with WHO recommendations of reliance and recognition, the Drug Regulatory Authority will leverage the scientific assessment conducted by stringent National Regulatory Authorities.

This document is intended to provide clarity on regulatory requirements and conditions for emergency use listing, importation, storage, distribution and handling of the vaccines under EUA.

2. Scope

This document provides an overview of the activities the DRA will conduct in relation to emergency use listing, importation, lot release and post-marketing surveillance of COVID-19 vaccines.

3. Objectives

To introduce Emergency Use Authorization and clarify regulatory process of DRA with respect to emergency listing, importation and post-marketing surveillance of COVID-19 vaccines.

4. Normative Reference

The following documents, in whole or in part, are normatively referenced in this guideline and are indispensable for its application.

i. The Medicines Act of the Kingdom of Bhutan 2003.
ii. Bhutan Medicines Rules and Regulation 2019.

5. Definitions

5.1 **Act:** It refers to The Medicines Act of the Kingdom of Bhutan 2003.

5.2 **Emergency Use Authorization:** It refers to special authorization for releasing a therapeutic product or vaccine in a market during a declared emergency based on the emergency use listing mechanism adopted by WHO or Stringent National Regulatory Authorities.

5.3 **Regulation:** It refers to The Bhutan Medicines Rules and Regulation 2019.

5.4 **Stringent National Regulatory Authorities:** It refers to list of WHO designated regulatory authorities which are the members of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), an ICH observer, a regulatory authority associated with an ICH member through a legally-binding, mutual recognition agreement. The list of Stringent Regulatory Authorities is attached as Annexure 1.

5.5 **WHO Emergency Use Listing:** It refers to a risk-based procedure for assessing and listing unlicensed vaccines, therapeutics and in vitro diagnostics with the aim of expediting the availability of these products in a public health emergency

6. Acronyms

6.1 AEFI: Adverse Events Following Immunization.
6.2 DoPH: Department of Public Health
6.3 DRA: Drug Regulatory Authority
6.4 EUA: Emergency Use Authorization
6.5 EUL: Emergency Use Listing
6.6 MoH: Ministry of Health
6.7 NRA: National Regulatory Authority
6.8 VPDP: Vaccine Preventable Disease Program
6.9 SRA: Stringent Regulatory Authorities
6.10 WHO: World Health Organization

7. General Principles

7.1 In order to establish the necessary processes for timely accessibility of the vaccine, DRA shall grant Emergency Use Authorization (EUA) of COVID-19 vaccines relying on and/or recognize the decision of WHO and other NRAs with stable formal approaches for such authorization.

7.2 Emergency Use Authorization shall not be treated as vaccine registration but an interim authorization.

7.3 Emergency Use Authorization shall be valid for such time during the emergency and may be cancelled if quality, safety and efficacy data suggests that the benefits of the vaccine no longer outweigh the risks during an emergency or when the emergency has ceased or when there is adequate quality, safety and efficacy data to support a registration application and transition the emergency vaccine to a registered vaccine.

7.4 Emergency Use Authorization shall reflect the same conditions of the reference NRA or WHO including the scope and duration of the authorization and post-approval changes, if any.

7.5 There shall be an effective communication and cooperation between DRA and relevant stakeholders including MoH, customs authorities, procurement and deployment entities.

7.6 Considering the risk of substandard and falsified products entering the market, only government procurement agencies and international organizations identified by the government will be allowed to apply for listing and importation of vaccines.

7.7 DRA shall monitor that vaccine administration takes place in a manner and in an environment to ensure safety, quality or efficacy of the product is not compromised and products administration instructions of the manufacturers are duly adhered to.

7.8 DRA shall publish summary product information of the vaccines listed on the DRA's website for reference by the healthcare professionals and public. The product information will include the information on dosage and administration Storage and Handling, Dosing and Schedule, Adverse Reactions, contra-indications and conditions of use.

7.9 DRA shall make amendments of any post approval changes or updating any information corresponding to the National Regulatory Authority who has granted the emergency authorization or WHO.

7.10 Turnaround time for listing, issuance of import authorization and lot release certificates, has been substantially lowered to enable rapid access to the vaccine and to minimize risk of any loss of safety and efficacy resulting from delayed regulatory approval.

7.11 The DRA has a regulatory role in following four key areas:

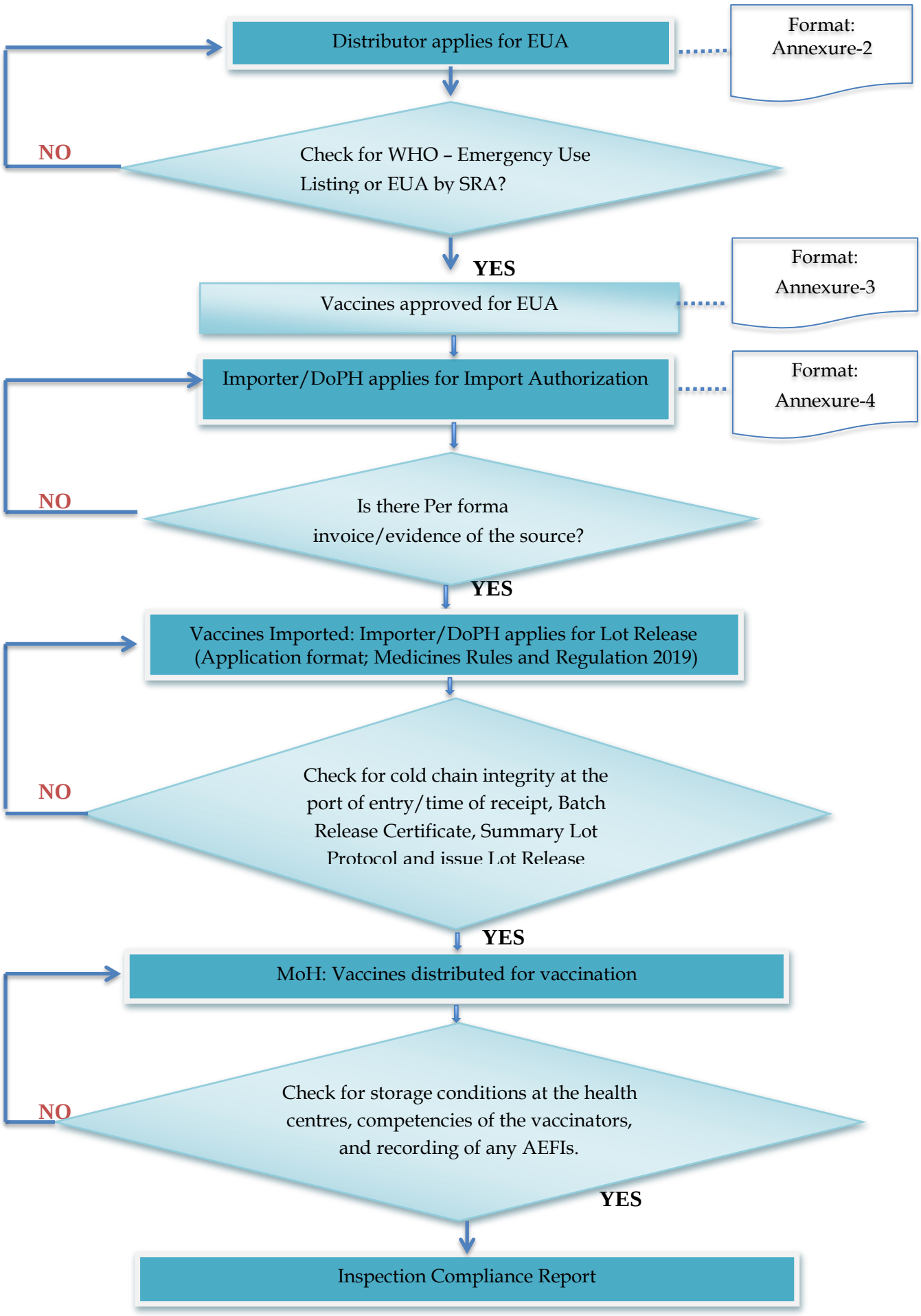
7.11.1 Emergency Use Authorization

7.11.2 Import Authorization

7.11.3 Lot Release

7.11.4 Post-Marketing Surveillance

The process map for Emergency Use Authorization and Post-Marketing Surveillance is presented in the figure below:



8. Emergency Use Authorization

8.1 For grant of Emergency Use Authorization, the applicant has to be an importer or manufacturer approved by the Ministry of Health.

8.2 The vaccines should be either listed for emergency use by the WHO or granted Emergency Use Authorization or special access by any Stringent Regulatory Authorities (as per the Annexure 1).

8.3 The following documents are required at the time of application (as per the format Annexure 2)

a) Copies of Artworks of package label and insert (The product labelling must be in English).
b) Product information and instructions for the storage, distribution and usage of the product including the conditions of use.
c) Evidence of approval/authorization from the listed by the SRA.

8.4 The Application fee is exempted for such authorization during emergency.

8.5 EUA will be issued in a prescribed format (Annexure 3) within seven days from the date of application.

8.6 The details of the vaccines granted EUA will be published on the DRA's website.

9. Import Authorization

9.1 As per section 22 of the Act, COVID-19 vaccines will require import authorization prior to their importation.

9.2 Following documents will be required for importation of a COVID-19 vaccine:

a) Application for Import Authorization (Annexure 4)
b) Pro-forma invoice or evidence of the source of vaccines.

9.3 Import authorization will be issued within two working days from the date of application.

9.4 Importation for personal use shall be highly discouraged considering logistics and safety concerns.

10. Lot Release

10.1 As per section 240 of the Regulation, DRA will conduct lot release of the vaccine at time of arrival, prior to distribution for use.

10.2 Lot release is carried out by reviewing the manufacturers' summary protocol, or through recognition of the decision of another regulatory authority.

10.3 Following documents will be required for lot release:

a) Application for lot release of vaccines (form in the Regulation)
b) Batch Release Certificate
c) Shipping Documents
d) Summary Lot Protocol

10.4 DRA will visit the cold chain facility and verify the consignment of the vaccines for lot release.

10.5 DRA will issue lot release certificate within two days from the date of application.

11. Post-Marketing Control Surveillance

11. 1 Storage, distribution and handling of vaccines

11.1.1 DRA will conduct regular cold chain facility inspections to monitor storage conditions.

11.1.2 All Vaccination providers must administer the vaccine in accordance with the Authorization and comply with the terms and training provided by the MoH.

11. 2 AEFI

11.2.1 DRA shall conduct post-market monitoring of the vaccine to ensure that it continues to be safe for use by relying on network of healthcare professionals and international regulatory counterparts to enable us to detect early safety signals.

11.2.2 The AEFI reporting shall be as per the existing practice wherein VPDP, MoH shall collect and analyze AEFI data and inform DRA of any serious AEFI requiring regulatory action.

11. 3 Suspension of Use and Product Recall

11.3.1 The vaccines use maybe suspended or vaccines maybe recalled when there is substantial product quality issue arising out of breakage in the cold chain, or due any serious life-threatening AEFI or upon voluntarily recall by the manufacturers.

11.3.2 The VPDP shall inform the DRA in case of serious any life-threatening AEFI that would entail suspension or recall of the vaccine from the market.

11.3.3 Upon receipt of notification of serious AEFI from VPDP, DRA will issue recall notification and initiate product recall within 72 hours.

12. Reference

12.1 Emergency Use Authorization for Vaccines to Prevent COVID-19 Vaccines, US FDA.

12.2 Guidance on National Deployment and Vaccination Plan for COVID-19 Vaccines, WHO.

12.3 Pharmacovigilance Plan for the EU Regulatory Network for COVID-19 Vaccines, EMA.

12.4 Consideration on core requirements for RMPs of COVID-19 Vaccines, EMA.

12.5 Emergency Use Listing Procedure, WHO.

13. Annexures

13. 1 Annexure 1: List of Stringent Regulatory Authorities

13. 2 Annexure 2: Format for Application for Emergency Authorization Use.

13. 3 Annexure 3: Format for Emergency Use Authorization Letter

13. 4 Annexure 4: Application for Authorization to Import Vaccines

Annexure 1: List of Stringent Regulatory Authorities

(As designated by WHO @www.who.int/medicines/regulation/sras/en/)

1. Australia
2. Austria
3. Belgium
4. Bulgaria
5. Canada
6. Cyprus
7. Czech Republic
8. Denmark
9. Estonia
10. Finland
11. France
12. Germany
13. Greece
14. Hungary
15. Iceland
16. Ireland
17. Italy
18. Japan
19. Latvia
20. Liechtenstein
21. Lithuania
22. Luxembourg
23. Malta
24. Netherlands
25. Norway
26. Poland
27. Portugal
28. Romania
29. Slovakia
30. Slovenia
31. Spain
32. Sweden
33. Switzerland
34. United Kingdom
35. United States of America

Annexure 2: Application Form for Emergency Use Authorization of Medicinal Products

I/We……hereby apply for the grant of Emergency Use Authorization for the following medicinal product:

1. Name of Vaccine: ……
2. Brand Name (if any): ……
3. Manufacturer: ……
4. Reference NRA by which the vaccine is granted Emergency Use Authorization:
   i. ……
   ii. ……

Please attach following documents:

1. Evidence of EUA listing by WHO or referenced National Regulatory Authority (NRA)
2. Artworks of package, label and insert
3. Product Information Product information and instructions for the storage, distribution and usage of the product including conditions of use. (Fact sheets about the product).

Declaration:

- I, hereby declare that all information provided on this application is complete, true and correct to the best of my knowledge and will be liable for any consequences if any information provided is proven to be false or misleading.'

- I, hereby declare that any updates related to safety and efficacy the product will be communicated as part of post authorization changes.

- I, hereby declare that vaccine to be supplied is same as the one listed on WHO-EUL list or reference NRA

Signature of applicant

Name:

Address:

Date:_____

Annexure 3: Format for Emergency Use Authorization Letter

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Royal Government of Bhutan

Drug Regulatory Authority

Thimphu, Bhutan; Post Box No. 1556

DRA/D4b/01-Gen/20-21 …… 2021

The ……

……

Subject: Emergency Use Authorization of Covid-19 Vaccine

Dear Sir/Madam,

This is in response to your application dated dd/mm/yyyy requesting the Drug Regulatory Authority to issue an Emergency Use Authorization (EUA) for emergency use of …..manufactured by….

We are pleased to grant the Emergency Use Authorization with the following specification and conditions which is being referred from the reference National Regulatory Authority:

Product Name: (Ingredients)	
Reference National Regulatory Authority/WHO EUL:	
Criteria of Authorization:	Emergency use of ….. COVID-19 Vaccine for the prevention of COVID-19 meets the criteria for issuance of an authorization under this guidance document.
Scope of Authorization:	The manufacturer/distributor will supply to Ministry of Health …… COVID-19 Vaccine. Vaccine covered by this authorization will be administered by healthcare professionals in individuals ages 16/18 and older.
Product Description:	…..Vaccines is supplied as a frozen suspension in multiple dose or single dose vials; (if accompanied by

	diluents), dose, its contents, Vial label contents. Storage conditions etc.
Conditions of Authorization:	Fact Sheets to be made available to the vaccination providers, recipients, and caregivers. Vaccines shall be stored at appropriate storage conditions and cold chain is maintained until delivered to receipt sites. Any instructional and educational materials that are inconsistent with the authorized labeling are prohibited.
Vaccination Providers:	Vaccination providers will administer the vaccine in accordance with the authorization and will participate and comply with the terms and training required by the Vaccination Program. The vaccination providers to report any Vaccines AEFI.
Duration of Authorization	This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency the vaccine during the COVID-19 pandemic is terminated or EUA is revoked under Section 5.15 of the Act.

Yours sincerely,

(Wangdi Gyeltshen)
Drug Controller

Copy to:

1. Hon'ble Chairperson, Bhutan Medicines Board, Thimphu for kind information.

Annexure 4: Application for Authorization to Import vaccines

I/we…… hereby apply for import of the following vaccines:

Product Name:	EUA No.	Manufacturer:	Pack size:	Quantity

Port of entry:

(Please attach the following Documents)

a. Copy of Proforma invoice or evidence for the source of distribution

- ☐ I, hereby declare that all information provided on this application is complete, true and correct to the best of my knowledge and will be liable for any consequences if any information provided is proven to be false or misleading.'

- ☐ I, hereby declare that vaccine to be supplied is same as the one listed on WHO-EUL list or reference NRA

Signature of applicant

Name:

Address:

Date:_____

Drug Regulatory Authority

Promoting availability of quality, safe and efficacious medical products for consumers

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