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# Guideline on regulatory preparedness for the oversight of emergency use authorized medical products 2025

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## 1. Introduction

Regulatory preparedness is the cornerstone of an effective public health response to emergencies, ensuring that safe, effective, and high-quality medical products are rapidly made available to address urgent health needs. In the face of unpredictable public health crises, such as pandemics, natural disasters, or unforeseen events, regulatory agencies must be equipped with robust frameworks and agile processes to authorise the emergency use of unapproved or repurposed medical products. A well-prepared regulatory system can significantly mitigate the impact of these emergencies by facilitating timely access to critical medical interventions while ensuring their safety and efficacy. Emergency use authorisation is a special procedure for expedited approvals of medical products in the event of a PHE when the government may be willing to tolerate less certainty about the efficacy and safety of a product, given the morbidity and/or mortality of the disease and the lack of treatment alternative, diagnosis or prevention options.

This guidance document aims to outline a comprehensive strategy for regulatory preparedness, detailing the processes for the oversight of *Emergency Use Authorised (EUA) medical products*. It underscores the importance of a proactive and coordinated approach involving key stakeholders, including regulatory authorities, healthcare providers, manufacturers, and public health agencies. By establishing clear criteria for EUA, defining submission requirements, and outlining post-authorization monitoring and communication strategies, this document seeks to provide a structured pathway to ensure that EUA products are rigorously evaluated and appropriately managed throughout their lifecycle.

## 2. Scope

2.1. This guideline shall apply to the following category of medical products which are repurposed or unapproved novel medical product;

- 2.1.1. Human Allopathic medicine
- 2.1.2. Veterinary Allopathic medicine
- 2.1.3. Vaccines
- 2.1.4. Biologics and Biotechnology products
- 2.1.5. Medical Devices

## 3. Objectives

3.1. To provide guidance on the regulatory oversight of emergency use authorised medical products during public health emergencies.

3.2. To expedite access to quality, safe and effective medical products during public health emergencies.

## 4. Normative references

4.1. The Medicines Act of the Kingdom of Bhutan 2003
4.2. Bhutan Medicine Rules and Regulations 2019
4.3. Health emergency and disaster contingency plan 2016

## 5. Definitions

5.1. **Act:** It refers to the Medicines Act of the Kingdom of Bhutan 2003.
5.2. **Authority:** It refers to the Bhutan Food and Drug Authority.
5.3. **Batch number:** It refers to a distinctive combination of numbers and/or letters which specifically identifies a batch or lot and from which the production history can be determined.
5.4. **Division:** It refers to the Medical Product Division.
5.5. **Emergency use authorisation:** It refers to an early access mechanism with time limitation used by regulatory authorities to expedite the availability of new investigational/unauthorised medical products during a pandemic or other public health emergency. In principle, this is granted if the known and potential benefits of the vaccine are considered to outweigh the known and potential risks, and upon meeting certain criteria (for example, that no alternative products are approved or available).
5.6. **Emergency use listing:** It refers to a risk-based procedure used by WHO to assess and list unlicensed vaccines with the aim of expediting their availability during a pandemic or other public health emergency. It is expected that a manufacturer that applies for WHO EUL assessment of a vaccine will complete the development of the product prior to its submission for full marketing authorization and WHO prequalification (PQ) in the future.
5.7. **GxP:** It refers to the abbreviation of "Good x Practice". The"x" stands for the various fields to which relevant guidelines and regulations are applicable.
5.8. **Importing country:** It refers to a country that imports a medical product produced in another country.
5.9. **Known risks:** It refers to an untoward occurrence for which there is adequate evidence of an association with the medical product.
5.10. **Potential risks:** It refers to an untoward occurrence for which there is some basis for suspicion of an association with the medical product but where this association has not been confirmed.
5.11. **Post approval variation:** It refers to any modifications made to the details of a medical product after it has been initially approved by a regulatory authority. These changes can be necessary for various reasons, including improvements in the manufacturing process, changes in suppliers, updates based on new scientific information, or adjustments to comply with new regulations.
5.12. **Producing country:** It refers to the country of manufacture and production of the medical product.
5.13. **Public health emergency:** It refers to an occurrence or imminent threat of an illness or health condition, caused by bioterrorism, epidemic or pandemic disease,

or an infectious agent or biological toxin, that poses a substantial risk to humans by either causing a significant number of human fatalities or permanent or long-term disability.

5.14. **Recognition:** It refers to a specific and formalised type of reliance in which an NRA (the relying NRA) accepts the regulatory decision of another NRA (the reference NRA) or the recommendation of a trusted institution (such as WHO). The relying NRA remains responsible and accountable for decisions taken even when it recognizes the regulatory decisions of the reference NRA or the recommendations of a trusted institution.

5.15. **Reference NRA:** It refers to an NRA whose work or decisions are relied upon by the NRA of an importing country for the authorization and life-cycle management of medical products used during a pandemic or other public health emergency.

5.16. **Regulation:** It refers to the Bhutan Medicines Rules and Regulation.

5.17. **Reliance:** It refers to the act whereby a relying NRA takes into account and gives significant weight to assessments performed by another NRA (the reference NRA) or to recommendations given by a trusted institution (such as WHO), or to any other authoritative information, in reaching its own decision.

5.18. **Repurposed medical product:** It refers to the use of existing medical product, originally developed for one medical condition, to be used for a different disease or condition.

5.19. **Risk-benefit analysis:** It refers to the evaluation of the known and potential benefits of the product, when used to diagnose, prevent, or treat the identified disease or condition, in relation to known and potential risks as defined above.

5.20. **Sameness of product:** It refers to two products that have identical essential characteristics (i.e., the product being submitted to the relying authority and the product approved by the reference regulatory authority should be essentially the same).

5.21. **Type III Disaster:** It refers to a severe disaster or public emergency that requires a whole-of-nation approach and mitigation plans for its control as per the Health Emergency and Disaster Contingency Plan 2016.

5.22. **Unapproved novel medical product:** It refers to a medical product that has not received regulatory approval for use in treating a particular medical condition or for any use at all.

5.23. **WHO Listed Authority:** It refers to a regulatory authority globally recognized to be operating at an advanced level of performance, thereby replacing the procurement-oriented concept of "stringent regulatory authority". These NRAs are recognized by WHO to have achieved levels of operation necessary for the regulation of medical products.

## 6. Acronyms

6.1. **BMRR:** Bhutan Medicine Rules and Regulation

6.2. **BFDA**: Bhutan Food and Drug Authority

6.3. **EUA** : Emergency use authorisation

6.4. **IA:** Import authorisation

6.5. **MAH:** Market Authorization Holder

6.6. **MA** : Marketing Authorization

6.7. **NCL**: National control laboratory
6.8. **NRA**: National regulatory authority
6.9. **WLA**: WHO listed authorities
6.10. **WHO:** World Health Organisation
6.11. **PIC/s:** Pharmaceutical Inspection Cooperation scheme
6.12. **PHE:** Public Health Emergency
6.13. **ML:** Maturity Level
6.14. **PQ:** Prequalification
6.15. **EUL:** Emergency use listing
6.16. **GxP:** Good "X" Practices

## 7. General principles

7.1. Regulatory flexibility and a risk based approach to be considered in all aspects of regulating emergency use authorised medical products.

7.2. Considering the complexity involved in performing a complete, independent assessment of the safety, efficacy and quality of the product and in keeping with WHO recommendations, the authority will leverage the scientific assessments conducted by reference NRAs and trusted institutions at the time of issuance of EUA. Recognition and reliance mechanisms where applicable shall be used for the regulation of emergency use authorised medical products.

7.3. Reliance in the context of this guideline will be applied for stable decisions made by the WLAs and WHO.

7.4. In situations wherein decisions for EUA from reference NRAs are not available, the authority may consider the decision made by the NRA of the producing country regardless of its maturity level.

7.5. Considering the risk of substandard and falsified products entering the market, only procurement agencies/institutions identified by the government will be allowed to apply for EUA and importation; and subsequently, the conversion of EUA to full MA. The agency shall be the **local authorised entity** for the product.

7.6. Turnaround time for issuance of EUA, import authorization and lot release certificates, will be substantially lowered to enable rapid access to the product and to minimise the risk of any loss of safety and efficacy resulting from delayed regulatory approval.

7.7. Necessary inspections of manufacturers, packagers/labelers, testing laboratories, importers, distributors and wholesalers of the product may be conducted to ensure that they comply with GxP. Alternatively, available and reliable evidence of compliance with good practice requirements will be leveraged as part of the risk-based inspection process.

## 8. Emergency use authorisation

EUA is issued in the event of declaration of public health emergency or type III disaster by relevant authorities and institutions when it meets the following criteria (not limited to):

- Immediately threaten life and wellbeing of public health
- Have already caused loss of life and health detriments
- Have a high probability of escalating to cause immediate danger to life and public health

### 8.1. Eligibility of EUA for medical products

The criteria for a medical product to be eligible for EUA is as follows but not limited to:

8.1.1. Existing medical products have not been successful in eliminating the disease or preventing the escalation of the emergency;

8.1.2. Repurposed or unapproved medical product may be effective in controlling the escalation of the PHE (Whether diagnose, treat or prevent) based on available scientific evidence;

8.1.3. That the known and potential benefits outweigh the known and potential risks of the repurposed or unapproved product when used to diagnose, prevent or treat the serious or life-threatening disease or condition that is the subject of the declaration; and

8.1.4. That there is no adequate, approved, and available alternative to the repurposed or unapproved product for such serious or life-threatening disease or condition (Unmet medical need).

### 8.2. General conditions of authorisation

**8.2.1.** Information for Healthcare professionals

Any crucial information available on the description and EUA of the medical product along with the instructions for use should be provided so that it may be disseminated to healthcare providers through appropriate communication channels. For any healthcare professional carrying out any activity concerning EUA, they must be informed that such products have been authorised after evaluation of its potential benefits and risks of the product so that proper patient counselling and assurance may be provided to the public receiving the product.

**8.2.2.** Information for recipients

Information dissemination requirements to the general public are mandatory only to the extent where conditions establishing such requirements are practical and must be disseminated in the most effective and expeditious way possible to reach the intended audience. It is recommended that recipients be given as much appropriate information as possible given the nature of the emergency and the conditions of the authorization. Some form of information should be provided to the public

in the simplest language possible to improve health education literacy about the medical product. The information should include:

8.2.2.1. the significant known and potential risks; and benefits of the product and the extent to which some of the potential risks and benefits are unknown;

8.2.2.2. specific instructions for home use (if necessary and where applicable), and;

8.2.2.3. guidance on management of adverse events and whom to contact should adverse events occur.

**8.2.3.** Monitoring and post authorization safety reporting of adverse events

The manufacturer and authorised entities are responsible for monitoring and reporting any adverse events precipitated by the product. The primary focus should be on collection and devising mitigation plans of serious adverse events and identifying appropriate mechanisms to be used for the collection of follow up clinical information.

A risk management plan must also be provided wherein it should contain planning and implementation of risk minimization measures, including the evaluation of the effectiveness of these activities (Risk minimization plan).

**8.2.4.** Accessibility to records

The authority should be able to access the records maintained of such medical products. Such record requirements may relate to the usage pattern and administration of the number of the units/doses including the batch number of the product; the name and address of the facilities from where the medical product was manufactured and deployed; monitoring records of population who have been administered with the product and other GxP related activities.

**8.2.5.** Additional conditions for a **repurposed medical product**

The EUA granted for repurposed medical products should preferably have labelling amendments as per the requirements of the authorisation. However, in cases where the manufacturer chooses not to make such a labelling change, the EUA does not authorise the local authorised entity to alter or obscure the manufacturer's labelling. Under such situations, the local authorised entity must provide appropriate information, in addition to the manufacturer's labelling, with respect to the product.

**8.2.6.** Some additional conditions may also be established on a case-by-case basis. To the extent feasible given the circumstances of the emergency, the following conditions may also be applicable:

**8.2.6.1.** Restricted distribution under the EUA.

**8.2.6.2.** Distribution mechanism of the EUA product.

**8.2.6.3.** Personnel - Conditions may be placed on who may administer the product and on the categories of individuals to whom it may be administered.

**8.2.6.4.** Information - Conditions may be placed on the collections and analysis of information on the safety and effectiveness of the EUA product.

**8.2.7.** Control of advertisement

Advertisement or any other promotional activities relating to the EUA product shall be restricted. Exceptions will be made for educational and safety information on the product and restricted to relevant health institutions so as to promote health education literacy on the EUA product.

8.3. **Issuance of EUA**

Recognition shall be applied to the issuance of EUA wherein it shall be supported by verification of product sameness without further technical review. The decision made by the reference NRA or WHO recommendation for PQ/EUL will be used as the basis of recommendation for authorization and will be accepted based on the use of the evaluation and terms of authorisation from the reference NRA or WHO.

8.3.1. The following documentation shall be required:

8.3.1.1. Application form;

8.3.1.2. Certificate or other evidence of the reference NRA's authorization decision(where the terms and conditions of authorisation has been clearly reflected), or WHO recommendation for EUL;

8.3.1.3. Unredacted assessment and inspection reports of the producing country's NRA or reference NRA preferably or WHO EUL recommendation however public assessment and inspection reports may also be accepted;

8.3.1.4. Specimen of package, label, product information leaflet (where applicable) and the available SmPC of the product consisting of the following minimum information;

8.3.1.4.1. Brand name (where applicable)

8.3.1.4.2. Generic name/type of vaccine

8.3.1.4.3. Method/route of administration

8.3.1.4.4. Strength/dose/concentration

8.3.1.4.5. Storage information

8.3.1.4.6. Lot/batch number

8.3.1.4.7. Name of manufacturer

8.3.1.4.8. Manufacture date

8.3.1.4.9. Expiry date

8.3.1.4.10. Inclusion of statement "For emergency use only" (Optional)

8.3.1.5. cGMP/ISO 13485 certificate(s) of the manufacturing site where applicable;

8.3.1.6. Certificate of analysis or lot release certificate (Evidence of quality);

8.3.1.7. Risk management plan (Refer clause 8.2.3); and

8.3.1.8. Letter of commitment from local authorised entity - Submission of emergency management plan and report thereof and once the medical product becomes eligible for full MA, conversion should be fulfilled.

## 8.4. **Publication -** ***Information to the public***

The authority will publish notifications of each EUA on the website, including an explanation of the reasons for issuance, a description of the intended use, side effects and any contraindications of the EUA product. Any revocation and the reasons for such actions will also be published. As appropriate, the authority will also take necessary steps to protect classified information and information otherwise protected by law.

## 8.5. **Post approval variations**

EUA products usually undergo numerous changes after authorisation for reasons such as but not limited to:

- better understanding of the product and manufacturing process;
- the scale-up of batch quantities;
- additional manufacturing sites;
- extension of shelf life and;
- the availability of additional information resulting from product use in wider populations (Example - extension for use of the product to other groups or populations which were not included in initial clinical indication).

For such variations, the manufacturer and the local authorised entity are requested to provide the updated or latest version of the product information with regards to change. Such changes or amendments should then be made transparently accessible by publishing information on relevant websites and other information sharing platforms.

Recognition/reliance will be used for post-approval variations and the following documents should be submitted:

8.5.1. Evidence of the reference NRAs' approval or WHO PQ/EUL recommendation of the post-approval variation(s);
8.5.2. Assessment reports of the reference NRA or WHO PQ/EUL preferably or public assessment reports of the variation;
8.5.3. Product sample and/or labelling specimen where applicable; and
8.5.4. Documents essentially the same as those submitted to the reference NRA or WHO PQ/EUL for the post approval variation.

## 8.6. **Validity of EUA**

EUA is a temporary conditional authorisation and shall be in effect until:

8.6.1. Upliftment of the status of emergency by national relevant agency or;
8.6.2. Medical product qualifies for routine market authorisation (*Refer section 11*) or;
8.6.3. Revocation of EUA of medical product (*Refer section 8.7*)

8.7. **Revocation of EUA**

The authority is responsible for the periodic review of the circumstances and weighing the appropriateness of the EUA issued including the circumstances that might warrant its revocation. An EUA issued will be revoked in the following cases:

8.7.1. When the medical product no longer meets any of the eligibility criteria as specified in *section 8.1* for which the EUA was issued initially;

8.7.2. When circumstances that warrant revocation occur during periodic review of the EUA by the authority. Such circumstances may include but are not limited to:

8.7.2.1. Repeated significant adverse inspection findings (e.g., where an inspection of the manufacturing site and processes have raised significant questions regarding the purity, potency, or safety of the product that materially affect the benefit-risk assessment upon which the EUA was based on);

8.7.2.2. Huge number of reports of adverse events (number or severity) linked to, or suspected of being caused by the product;

8.7.2.3. Product ineffectiveness (such as newly emerging data that undermine the Authority's conclusion that the product "may be effective" against a particular agent);

8.7.2.4. Availability of a more preferred medical product; and

8.7.2.5. Local authorised entity fail to comply with the conditions of the EUA for the medical product.

However, it must be considered that notwithstanding such revocation, an authorization shall continue to be effective to be provided for “continued use” in any patient who began treatment before termination (to the extent found necessary by the patient's attending physician).

On revocation, the products will be subjected to the existing **Guideline for disposal of medical product waste** for its removal from the distribution chain and consequently, its destruction.

## 9. Importation and import authorisation

Once EUA has been granted for a product, it will be allowed for import in the country wherein the turnaround time for issuance of import authorisation (IA) will be 2 working days to prevent delays in the importation of the product.

9.1. The following documents shall be required for the issuance of IA:

9.1.1. Application form;

9.1.2. Relevant invoice, bill or delivery slip for the batch, including the product name, batch number, quantity, and expiry or manufacture date;

9.1.3. Batch release certificate issued by the manufacturer; and

9.1.4. Lot/batch release certificate issued by the NRA of the producing country.

A record must also be kept of all lots/batches received in the country to facilitate their traceability.

## 10. Lot release of emergency authorised vaccines

For EUA vaccines that have been WHO prequalified or vaccines authorised by a reference authority or NCL, lot release procedure will be conducted based on reliance wherein the lot release certificate from the producing country will be accepted for the release of vaccines.

For EUA vaccines that do not have a WHO PQ/EUL recommendation and are not approved by a reference NRA, the authority may, in the event of a pandemic or other public health emergency, conduct lot release through review of the summary lot protocol.

## 11. Vigilance

Vigilance of medicinal products covered under the scope of this guideline will be handled and managed as per the relevant guideline developed for the purpose. Healthcare professionals, health programs, retailers, manufacturing firms where applicable should share following vigilance reports to the National Vigilance Center, BFDA through the appropriate reporting channels:

11.1. Adverse Drug Reactions
11.2. Adverse Events Following Immunizations
11.3. Medical Device associated Adverse Events
11.4. Substandard and falsified medicinal products

Additionally, the authority will also rely on the safety information received from the relevant international organizations to take necessary regulatory actions.

## 12. Conversion of EUA to marketing authorisation

Once PHE has been declared to be over or the product qualifies for routine market authorisation(whichever comes first), the EUA will no longer be effective and the product will be subjected to conversion from EUA to full market authorisation.

A transition period of six months will be provided for the conversion of EUA to full market authorisation. During this period, importation of the medical product under EUA provisions will be withheld.

The conversion of EUA to marketing authorization will proceed as laid out in the existing effective guideline for registration of medical products.

## 13. References

13.1. Health Emergency and Disaster Contingency Plan 2016
13.2. WHO Guidelines on regulatory preparedness for the oversight of pandemic or other emergency use vaccines in importing countries - TRS1054
13.3. Guideline for Emergency use authorization by Ghana FDA

***Quality Policy of Medical Product Division, BFDA***

*"We commit to provide consistent regulatory operations with risk based planning and continual improvement in compliance with the recognized standards to meet our consumers' satisfaction and confidence"*

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