Emergency Use Authorizations for Therapeutics: Guidance for National Medicine Regulatory Authorities

During the COVID-19 pandemic, many national medicines regulatory authorities (MRAs) implemented various forms of expedited approval pathways, such as conditional market authorizations and emergency use authorizations (EUA), to review and accelerate the availability of acceptable vaccines, therapeutics, and diagnostics to respond to the pandemic. Many of these expedited review frameworks can be used to review vaccines, therapeutics, and medical devices after the COVID-19 pandemic. However, reviewing and managing EUAs for therapeutics presents some unique considerations for MRAs, particularly those in low- and middle-income countries (LMICs).

In 2021, USAID's Promoting Quality of Medicines Plus (PQM+) program published practical guidance for MRAs on managing EUAs for vaccines titled *A Proposed Model to Build Capacity for Emergency Use Authorization for Vaccines: Guidance for National Regulatory Authorities* and for diagnostics titled *A Proposed Model to Build Capacity for Emergency Use Authorization for Diagnostics: Guidance for National Regulatory Authorities*. The new guidance, *A Proposed Model to Build Capacity for Emergency Use Authorizations for Therapeutics: Guidance for National Medicines Regulatory Authorities*, builds on that work by providing practical guidance to MRAs on adopting, implementing, and managing expedited approval pathways for **therapeutics**—drugs and non-vaccine biological products.

Practical recommendations for strengthening operational policies and procedures for therapeutics EUAs are presented, including establishing clear review timelines, allowing rolling submissions, using standardized application forms and checklists, and investing in electronic regulatory information systems. The following resources are tools and checklists to facilitate efficient management of therapeutics EUAs by MRAs during public health emergencies, and are included as appendices to the guidance.

- **Checklist for Strengthening Management of Therapeutics EUAs**
- **Illustrative Workflows for Processing EUA Applications**
- **Illustrative Application Checklist for Therapeutics EUAs**
- **Preliminary Benefit-Risk Assessment Tool to Inform Pathway Assignment**
- **Communication Product Guidance**
- **Template Therapeutics EUA Review Memorandum Report/Assessment Report**

The guidance emphasizes the importance of 12 recommendations for therapeutics EUAs and provides examples of approaches that MRAs in low-, middle-, and high-income countries have taken to address these recommendations. See these recommendations on p. 2.

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Recommendations for Therapeutics EUAs

1. Define Criteria for Granting Therapeutics EUAs in the Legal and Regulatory Framework: A key step in the process of granting the national MRA the legal authority to deviate from required medical product registration and marketing authorization requirements during public health emergencies.

2. Formalize Collaborative Review Structures and Processes: MRAs in countries that plan to import therapeutics should consider reliance on evaluation decisions that other MRAs and authorities have made, such as through information and work-sharing.

3. Standardize Expedited Review Pathways, Including Recognition and Reliance Pathways: A framework for expedited review pathways can be modeled on the WHO pandemic influenza framework, which consists of the following: 1) full review; 2) fast-track review of basic documentation recognition; 3) reliance; 4) recognition.

4. Assign Therapeutics to Review Pathways Based on Preliminary Benefit-Risk Assessment: A benefit-risk assessment is an important step in deciding which review pathway to use for a particular therapeutic.

5. Impose Conditions on Approvals to Ensure Ongoing Evaluation of Quality, Safety, and Effectiveness: Placing conditions on therapeutics EUAs can mitigate risks associated with EUAs.

6. Monitor Condition Compliance Closely to Facilitate Conversion to Full Approval, Withdrawal, or Revocation of EUAs: MRAs should establish processes to monitor compliance with conditions placed on EUAs and consider new evidence on quality, safety, and efficacy that may inform transitioning therapeutics from conditional market approval or EUA to full approval.

7. Require Risk Management Plans and Periodic Safety Update Reports: This may include information regarding: 1) a medicine's safety profile; 2) how to prevent or minimize risks to patients; 3) plans for studies and other activities to learn more about the safety and efficacy of the medicine; and 4) steps to measure the effectiveness of risk-minimization measures.

8. Monitor Availability of Therapeutics to Guide EUA Decisions and Ensure Equitable Distribution: MRAs can establish availability monitoring systems to help ensure equitable and timely access to therapeutics authorized under EUAs.

9. Manage Modification Requests for Therapeutics EUA Decisions: EUA decisions will be based on the information included in the submitted application, such as manufacturing location(s) and processes, eligibility criteria, formulations, and education materials.

10. Embrace Transparent Communication and Community Engagement to Build Trust in Regulatory Reviews: It is necessary to have a transparent and comprehensive communication strategy that provides information to a wide range of audiences.

11. Use a Phased Planning Approach to Prioritize Finite Resources: Anticipating the needs and opportunities of the phases of public health emergencies can help improve the preparedness and efficiency of EUA reviews.

12. Update Operational Policies and Procedures to Find Efficiencies and Facilitate Collaborative Review: Processing EUAs during a public health emergency can put significant strain on the administrative and operational capacity of MRAs. Hence, the MRA can review its operational policies and procedures to facilitate collaborative reviews.