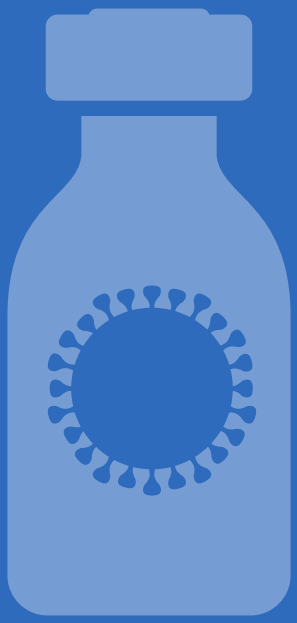
Promoting the **QUALITY OF MEDICINES+**



A Proposed Model to Build Capacity for Emergency Use Authorization for Vaccines

Guidance for National Regulatory Authorities

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About PQM+

The Promoting the Quality of Medicines Plus (PQM+) program is a five-year cooperative agreement between USAID and USP to sustainably strengthen medical product quality assurance systems in low- and middle-income countries. The program works to improve medical product quality through cross-sectoral and systems strengthening approaches and the application of international quality assurance standards across the pharmaceutical system. By sharing scientific expertise and providing technical support and leadership, PQM+ helps create resilient and robust local health systems that address diseases such as HIV/AIDS, tuberculosis, malaria, and neglected tropical diseases, as well as improve maternal, newborn, and child health.

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Acronyms

COVID-19	Corona Virus Disease 2019, also known as SARS-CoV-2
CTD	Common Technical Document
EMA	European Medicines Agency
EUA	Emergency Use Authorization
EUL	Emergency Use Listing
FAQ	frequently asked questions
FDA	Food & Drug Administration
GMP	good manufacturing practice
HHS	Health & Human Services
LMIC	low- and middle-income countries
ML	WHO Global Benchmarking Tool Maturity Level
MRA	Medicines Regulatory Authorities
NCL	National Control Laboratory
PQ	Prequalification
PQM+	Promoting the Quality of Medicines Plus
UK	United Kingdom
USAID	U.S. Agency for International Development
VAERS	Vaccine Adverse Event Reporting System
WHO	World Health Organization

A. Executive Summary

Medicines Regulatory Authorities (MRAs) around the world have undertaken an unprecedented effort to rapidly review the safety, efficacy, and quality of Coronavirus Disease (COVID-19) vaccines. Many MRAs have adopted and implemented various forms of expedited approval pathways for COVID-19 vaccines and other medical products, such as conditional market approvals and emergency use authorizations (EUA). The procedures used by MRAs have varied widely, MRAs must now manage ongoing submission, and safety monitoring processes for multiple COVID-19 vaccines granted expedited approval.

This guidance:

- Is designed to provide practical instruction to MRAs on adopting, implementing, and managing expedited approval pathways for vaccines, with a focus on EUAs for COVID-19 vaccines
- Is based on a rapid assessment of COVID-19 vaccine approval processes in 17 countries participating in the U.S. Agency for International Development (USAID) Promoting Quality of Medicines Plus program (PQM+)
- Emphasizes the importance of 11 considerations and provides examples of different approaches MRAs have taken to address these considerations (**Box 1**).

This guidance also includes recommendations for developing communication plans and products to facilitate transparent communication with the public regarding vaccine decisions. The recommendations include the following communication products: MRA vaccine-specific web pages; review or decision memoranda/assessment reports; letters of authorization; press releases; fact sheets for health care providers; fact sheets for vaccine recipients and caregivers; frequently asked questions (FAQs); and suggested content for social media.

Practical considerations for strengthening operational policies and procedures are also presented, including establishing clear review timelines, allowing for rolling

Box 1. Practical Considerations for Managing Vaccine EUAs

1. Define criteria for granting EUAs in legal and regulatory frameworks.
2. Standardize expedited review pathways.
3. Assign vaccines to review pathways based on preliminary risk-benefit assessment.
4. Impose conditions on approvals to ensure ongoing evaluation of safety and efficacy.
5. Monitor condition compliance closely to facilitate conversion reviews.
6. Require clear safety monitoring and risk management plans.
7. Manage modification requests for vaccine EUA decisions.
8. Leverage reliance mechanisms for lot release.
9. Embrace communication and community engagement to build trust in vaccine regulatory reviews.
10. Use a phased planning approach to prioritize finite resources.
11. Update operational policies and procedures to find efficiencies and facilitate collaborative review.

Tools and Checklists to Facilitate Management of Vaccine EUAs

- Appendix A. Checklist for Strengthening Management of Vaccine EUAs
- Appendix B. Illustrative Workflows for Processing EUA Applications
- Appendix C. Illustrative Application Checklist for Vaccine EUAs
- Appendix D. Preliminary Risk-Benefit Assessment Tool to Inform Pathway Assignment
- Appendix E. Communication Product Guidance
- Appendix F. Template Vaccine EUA Review Memorandum Report/Assessment Report

submissions, using standardized application forms and checklists, and investing in electronic regulatory information systems. Tools and checklists are presented as appendices to facilitate efficient management of vaccine approvals during public health emergencies **(Box 1)**.

B. Introduction

The COVID-19 pandemic has presented one of the greatest challenges to global public health and health care in the past century. The World Health Organization (WHO) declared COVID-19 a pandemic on March 11, 2020, and as of November 9, 2021, more than 250 million confirmed cases of COVID-19, including 5.05 million deaths, had been reported to WHO.[1] The pandemic has also caused severe social and economic disruption and placed enormous strain on health systems around the world. During the course of the pandemic, the SARS-CoV-2 virus has mutated, leading to the circulation of COVID-19 variants. As of September 13, 2021, WHO identified four COVID-19 Variants of Concern and two current COVID-19 Variants of Interest.[2]

In response to the pandemic, governments, pharmaceutical companies, and other organizations around the world launched a historic effort to develop and deploy COVID-19 vaccines. As of November 9, 2021, WHO reported that there were 130 COVID-19 vaccines in clinical development and 194 COVID-19 vaccines in pre-clinical development.[3] As of September 2021, WHO issued Emergency Use Listing (EUL) decisions for vaccines manufactured by Pfizer-BioNTech, AstraZeneca, Serum Institute of India, Janssen/Johnson & Johnson, Moderna, SinoPharm, and Sinovac. As of November 8, 2021, more than 7.08 billion vaccine doses have been administered globally. Unfortunately, not all populations have had equal access to these vaccines. As of July 7, 2021, approximately 51 percent of individuals in high-income countries had received at least one dose of COVID-19 vaccine, whereas only 1 percent, 14 percent, and 31 percent of the populations in low-income, lower middle-income, and upper middle-income countries, respectively, had received at least one dose.[4]

MRAs around the world have undertaken an unprecedented effort to rapidly review the safety, efficacy, and quality of COVID-19 vaccines. Many MRAs have adopted and implemented various forms of expedited approval pathways for COVID-19 health products, such as conditional market approvals and EUA. Some MRAs relied on pre-existing expedited pathways, while others adopted procedures specifically in response to COVID-19. The procedures used to implement these expedited pathways have varied and often include reliance or recognition of decisions made by other MRAs or the decisions issued by the WHO under its EUL procedure.

The United States Food and Drug Administration (FDA), for example, had a pre-existing EUA mechanism to facilitate the availability and use of medical countermeasures, including vaccines, during public health emergencies.[5] Another example is the European Medicines Agency (EMA) process for granting a conditional marketing authorization for medicines on fewer comprehensive clinical data than are normally required, where the benefit of immediate availability of the medicine outweighs the risk inherent in the fact that additional data are still required.[6] This EMA process is intended for use during a public health emergency and certain

other situations. A 2021 rapid assessment of vaccine EUA regulatory frameworks in selected low-and middle-income countries (LMICs) found that 13 out of 17 assessed LMICs had some form of emergency use pathways for COVID-19 vaccines.

C. Purpose and Scope

The **purpose** of this guidance is to provide practical guidance to MRAs on adopting, implementing, and managing expedited approval pathways for vaccines, with a focus on emergency use authorizations for COVID-19 vaccines. Additionally, the considerations in this report may also be useful for reviewing or strengthening review procedures for other types of vaccines in response to future public health emergencies. In this guidance, we use the term Emergency Use Authorization to refer to any expedited review pathway adopted by a MRA to facilitate broad access to a medical product during a public health emergency, and prior to the product meeting all requirements for full registration and market approval.

The **primary audiences** for this report are MRAs and other stakeholders in countries that have yet to reach Maturity Level 4 (ML4) based on the WHO Global Benchmarking Tool.[7] This guidance should be useful to MRAs without a current EUA pathway and to MRAs looking to strengthen their existing vaccine EUA framework. The goal of this report is to facilitate greater international collaboration, harmonization, and data sharing between MRAs to reduce duplication and facilitate rapid access to safe, effective, and quality vaccines in response to public health emergencies.

This guidance is also intended to help **improve communication and transparency** to the public to maintain trust in the rigor of the regulatory review process and confidence in the safety, effectiveness and quality of approved vaccines.

D. Methods

PQM+ prepared this guidance based on the following methodology: First, the PQM+ team conducted a desk review of EUAs and other expedited approval pathway policies and regulations. This review identified a wide range of expedited approval pathways using varying terminology and procedures. **Table 1** (on the following page) presents an illustrative list of EUA guidance issued by selected MRAs identified in this desk review.

Second, PQM+ developed and sent a questionnaire to PQM+ points of contact in the following countries to identify the current state of COVID-19 vaccine processes for approval in these countries and any of those countries' expedited approval pathways: Democratic Republic of Congo, Bangladesh, Benin, Burkina Faso, Ethiopia, Ghana, Guinea, Kenya, Liberia, Mali, Mozambique, Nepal, Pakistan, Nigeria, Rwanda, Senegal, and Uzbekistan. The findings from this data collection phase were synthesized into a report titled *Rapid Assessment of Existing Emergency Use Authorization Regulatory Processes and Procedures for COVID-19 Vaccines in PQM+ Countries*.[8]

Table 1. Illustrative List of EUA Guidances	
Country	**Title of EUA Guidance**
India	Draft Regulatory Guidelines for Development of Vaccines with Special Consideration for COVID-19 Vaccine
Canada	Guidance for market authorization requirements for COVID-19 vaccines (adopted 20 Nov 2020)
Ethiopia	Guideline for Emergency Use Authorization of COVID-19 Vaccine (Jan. 2021)
Kenya	Guidelines for Emergency and Compassionate Use Authorization of Health Products and Technologies (April 2020)
Pakistan	Circular No.F.1-28/2020-AD/BD – Emergency Use Authorization for COVID-19 Vaccines
South Africa	Information and Guidance on Application for Registration of Candidate COVID-19 Vaccine – Communication to Industry (v1 Nov 2020)
Nigeria	Guidance on Regulatory Preparedness for Licensing or Access to COVID-19 Vaccines (Oct 2020)
European Medicines Agency	Guideline on the scientific application and the practical arrangements necessary to implement Commission Regulation (EC) No 507/2006 on the conditional marketing authorization for medicinal products for human use falling within the scope of Regulation (EC) No 726/2004 (25 Feb 2016)
Japan	Principles for the Evaluation of Vaccines Against the Novel Coronavirus SARS-CoV-2 (Sept 2 2020)
United States	Emergency Use Authorization for Vaccines to Prevent COVID-19 – Guidance for Industry (25 May 2021)

Following this data collection phase, the team reviewed the EUA policies and guidance and other relevant guidance from WHO and international MRAs for expedited and emergency approval pathways. PQM+ then synthesized the components of these various guidance documents and policies into this guidance with an emphasis on practical considerations for MRAs that have yet to reach WHO ML4. PQM+ then shared a draft of this guidance for review and comments and held a consultative webinar on October 18, 2021. The PQM+ team prepared and submitted this final version in November 2021.

The guidance in this report should be viewed as presenting considerations and illustrative procedures and a step-by-step framework for operationalizing vaccine EUAs. Each vaccine candidate and country context may require modifications to the procedures and tools presented in this guidance. Every country will also have its own policy and legal framework, which should be reviewed to ensure alignment between EUA procedures and national policy and legal

requirements. Therefore, this guidance should be reviewed critically by policymakers, subject matter experts, civil society representatives, and other key stakeholders in each country and adapted as appropriate for the national context.

E. Practical Considerations for Managing Vaccine EUAs during Public Health Emergencies

This section summarizes practical considerations for MRAs when developing and implementing EUA procedures for vaccines, with a focus on vaccines for COVID-19. Many of the considerations in this section may be applicable to review of medicines and vaccines in non-emergency settings, but the considerations herein are especially relevant for public health emergencies when a vaccine has not yet obtained full marketing approval in a given country. The considerations described in this section have been combined into a Checklist for Strengthening Management of Vaccine EUAs and is included as Appendix A. An illustrative workflow for processing initial EUA applications and modifications to EUA decisions is included as Appendix B.

1. Define Criteria for Granting Vaccine EUAs in the Legal and Regulatory Framework

The first step in operationalizing an EUA process is ensuring there is a legal framework that grants the national MRA the legal authority to deviate from required medical product registration and marketing authorization requirements when faced with certain types of public health emergencies. Countries should have statutory laws and regulations in place that regulate the marketing of vaccines and medicines. EUAs should be a legally recognized exception to this requirement. Countries will need to carefully assess how much detail on EUAs to include in statutes, versus delegating authority to other authorities within appropriate agencies. For example, the criteria for issuing an EUA in the United States is defined in U.S. statutory law, but the Secretary of Health and Human Services (HHS) is also granted discretion under the statute to adopt implementing regulations for EUAs.[9]

Statutory provisions provide a strong legal foundation for EUAs, but can also be the most time consuming to amend in the future. In many settings, adopting regulations can also be a multi-month process due to notice and comment requirements. In contrast, policies, guidelines, and circulars are often the quickest to adopt and amend. Often a country's statutory environment will influence whether a statutory law or regulation may be required. For example, if an EUA process would conflict with an existing statutory law, a country may be forced to revise the statutory law prior to operationalizing an EUA framework. Often a combination of a statutory provision with implementing regulations and/or policies can be useful framework for establishing a strong legal foundation for EUAs, while granting the MRA flexibility to adopt and amend regulations or policy guidance that lay out the criteria and specific requirements for EUAs.

Laws, regulations, and policies establishing EUA processes vary regarding the criteria that must be met to issue an EUA. Below is a list of criteria that countries can consider adopting to clarify when EUAs are appropriate:

a. Emergency Declaration

Many EUA pathways require an emergency declaration by a governmental authority in order to issue an EUA. Consultation with other governmental authorities can be required prior to issuance of the emergency declaration. The law or policy establishing the EUA can also prescribe the standards that must be met to declare the emergency, such as the emergence of a disease that is contagious and imminently life threatening or threatens national security and for which there is no approved, adequate, and available product to diagnose, treat, or prevent the disease or condition.[10]

The emergency declaration that opens an EUA pathway can be different from emergency declarations issued by other governmental authorities. For example, in the United States, an emergency must be declared by the secretary of HHS to open the EUA pathway. Yet, the emergency declaration issued by the secretary of HHS that activates the EUA pathway for COVID-19 vaccines was different from emergency declarations issued by the president of the United States relating to COVID-19. This is an important distinction, because the grounds for declaring and rescinding an emergency declaration relating to EUAs can be different from the basis for declaring and rescinding other types of public health emergency declarations and allows the governmental authority overseeing EUAs more discretion regarding when to declare and end the EUA emergency declaration.

b. EUA Issuance Criteria

Laws, regulations, and policies for EUAs should clearly establish the criteria for issuing EUAs. Following is a list of illustrative issuance criteria, adapted from the U.S. EUA statute, that countries can consider adopting to guide EUA decisions:

- The agent/virus/bacteria (hereinafter referred to as agent) is the subject of an emergency declaration issued pursuant to national law.
- The agent can cause a serious or life-threatening disease or condition.
- Based on the totality of scientific evidence available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing such disease or condition.
- The known and potential benefits of the product, when used to diagnose, prevent, or treat such disease or condition, outweigh the known and potential risks of the product, taking into consideration the threat posed by the disease or condition.
- That there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating such disease or condition.

Note that the last issuance criterion above requires that there not be an alternative product that is adequate, approved, and available. Therefore, a vaccine candidate may still be eligible for an EUA even after multiple other vaccines have been approved for the same agent (e.g., COVID-19) if the combination of previously approved vaccines is not adequate and sufficiently available to meet the public health

emergency. In addition, a new vaccine that has significantly superior attributes compared to already-approved vaccines may be eligible for an EUA if already-approved vaccines are not "adequate" to respond to the agent.

Harmonizing issuance criteria among countries can be important to facilitate reliance and recognition pathways for EUAs. Significant differences between issuance or review criteria can undermine an MRA's ability to rely on or recognize the decision of other competent authorities if review or issuance criteria among countries conflict. Therefore, countries should strongly consider aligning EUA issuance criteria with MRAs with which they plan to establish reliance or recognition relationships to facilitate rapid reliance and recognition reviews during public health emergencies.

2. Standardize Expedited Review Pathways

MRAs in countries that plan to import vaccines should carefully consider reliance on the vaccine evaluation decisions made by other MRAs and review authorities, such as WHO. Establishing ongoing relationships and data-sharing agreements with ML4 MRAs can help facilitate access to information and reports about vaccines, including post-approval safety data. Collaborating with other MRAs for joint regional reviews of vaccine candidates can be another mechanism for international collaboration that can reduce duplication among MRAs. WHO has established a procedure for collaborative marketing authorization of prequalified vaccines, which could be used as a model for regional COVID-19 vaccine reviews.[11,12]

The WHO has proposed a regulatory pathway framework for influenza pandemic preparedness that may present a useful framework for considering expedited EUA pathways for COVID-19 vaccines.[13] At least one country, Nigeria, has adopted a similar version of this pathway framework for use in COVID-19 vaccines, with some modifications.[14]

An expedited review pathways framework for COVID-19 modeled on the WHO pandemic influenza framework could consist of the following five pathways: (1) Full Review; (2) Fast-Track Review of Basic Documentation; (3) Reliance; (4) Recognition; and (5) Strain/Variant Change Procedure. Each of these potential pathways is discussed below. Appendix C includes an illustrative application checklist that can be used to facilitate reviews of EUA applications based on pathway assignment.

a. Full Review

Full review refers to the MRA's regular review process as determined by the MRA's legal and regulatory requirements and internal policies and procedures. Full review can include optional fast-track procedures that establish shorter review timelines for priority products. WHO has published guidance on the dossier content for full reviews of vaccines.[15,16]

The minimum clinical follow-up data required for vaccine EUAs are often shorter in duration than full market authorization applications. For example, Ethiopia's EUA guidelines state that "Phase IIb and Phase III studies should include a median follow-up duration of at least two months."

Canada's policy on COVID-19 vaccines states, "The median duration of safety follow-up to support authorization should be at least 2 to 3 months after all doses in the schedule have been given."[17] Singapore's minimum data requirements to access its Pandemic Special Access Route calls for "Safety data from phase III studies with a median follow-up of at least 2 months."[18]

b. Fast-Track Review of Basic Documentation

Fast-track review of basic documentation is an expedited review process based on available information. Information will often be submitted in batches to and reviewed by the MRA on a rolling basis as it becomes available. Documentation to be reviewed under this pathway could include:

- Whether the vaccine has been approved by the WHO, the evidence/certificate of WHO prequalification (PQ), or EUL with assessment report
- Whether the vaccine has been approved by a stringent MRA, the Common Technical Document (CTD) Module 2, and assessment report by the MRA
- Whether the vaccine has not been approved by WHO or stringent supporting MRA, or the reviewing MRA does not have access to the reports issued by licensing MRAs, the CTD Module 2 quality, nonclinical and clinical overviews, and full dossier to the extent available
- Evidence of quality (certificate of analysis or lot release) and good manufacturing practices (GMP) compliance (GMP certificate)

c. Reliance

Reliance is a pathway that reviews the EUA or marketing authorization report(s) and decisions issued by a supporting MRA or WHO (e.g., EUL or PQ). This pathway depends on access to the report issued by the supporting MRA or WHO. It will include a technical review by the MRA, but the technical review will generally be limited to the report issued by the authority being relied upon. Any approval through a reliance pathway usually involves accepting the conditions and limitations on the use of the vaccine included in the decision being relied upon. Additional information or documentation can be requested of the applicant if deemed necessary by the MRA's technical review committee. The documentation reviewed under this pathway could include:

- Certificate of the responsible MRA's or WHO's decision
- Assessment reports of the responsible MRA(s) or WHO

d. Recognition

Recognition is a pathway that accepts the decision of another MRA or WHO PQ or EUL decision without further technical evaluation by the MRA. As with reliance, an approval through a recognition pathway usually involves accepting the conditions and limitations on the use of the

vaccine included in the decision being relied upon. Recognition is the most expedited review pathway and will generally be limited to a review of the following component:

- Certificate of the responsible MRA's decision or WHO assessment report

e. Strain/Variant-Change procedure

MRAs can consider establishing a strain/variant-change procedure that provides expedited review of strain/variant changes to a vaccine that has been previously approved by the MRA. A number of COVID-19 variants have been identified, and vaccines that have already been approved may be modified to respond to new strains/variants. Therefore, it may be beneficial for MRAs to establish a variant-change procedure that allows for expedited review of these modified vaccines when deemed appropriate by the MRA. Many countries have already established accelerated review procedures for seasonal influenza vaccines. WHO has identified a number of factors for considering whether a seasonal influenza vaccine strain change procedure should be used, which may be a useful model for evaluating whether variant change procedures should be used for COVID-19 vaccines (**Box 2**).[19]

Box 2. Factors for Deciding Whether Seasonal Influenza Strain Change Procedure Should be Used

- The candidate monovalent pandemic influenza vaccine has an antigen content similar to that of the corresponding single component in a licensed trivalent or tetravalent seasonal influenza vaccine containing the same subtype; *and*
- The excipients in the candidate vaccine are the same as those in the licensed vaccine; *and*
- The manufacturing technology (for example, eggs, inactivant, purification process) and controls are the same as those of the licensed vaccine.

3. Assign Vaccines to Review Pathways Based on Preliminary Risk-Benefit Assessment

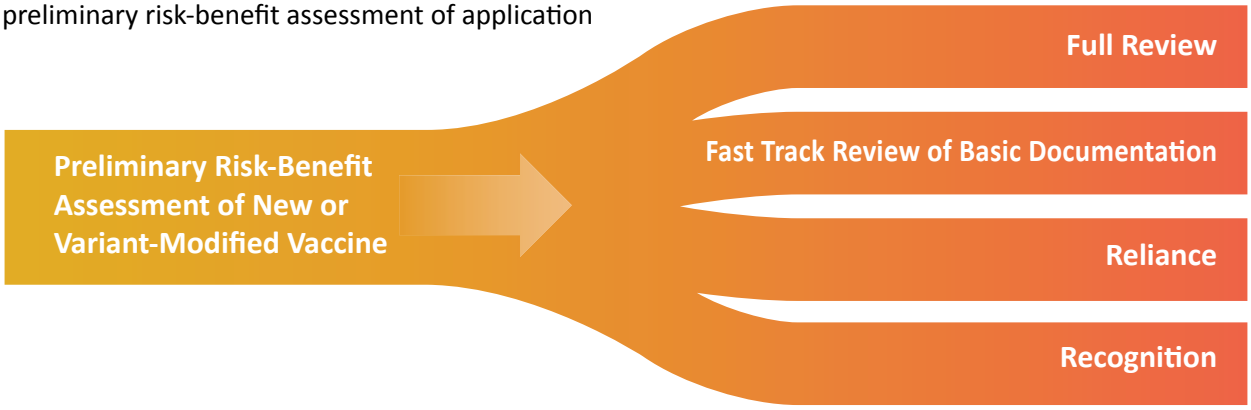
The WHO's influenza guidance includes a proposed decision-making framework for assignment to various review pathways based on the status of the vaccine and the continuum of pandemic phases. Due to the plethora of COVID-19 vaccines developed and still under development and finite MRA resources, MRAs may need to use a multi-criteria risk-benefit assessment approach to determine the appropriate review pathway for each vaccine candidate. Appendix D presents illustrative criteria that an MRA could consider using to inform its decision-making on pathway assignments. The criteria in Appendix D are illustrative only and MRAs can adapt these criteria or develop their own criteria based on the review priorities of the MRA. Establishing explicit risk-benefit criteria prior to the analysis can help ensure that the various categories of risks and benefits are considered.

MRAs can allow applicants to propose an expedited pathway and justify their rationale by

providing written responses to questionnaires structured to align with the criteria selected by the MRA. However, MRAs should consider retaining the right to assign an application to the pathway determined most appropriate by the MRA. For example, Ghana's reliance policy allows the Ghana FDA to "activate the reliance pathway to facilitate regulatory decisions either on a case-by-case basis or at the explicit request of the Applicant."[20]

Figure 1. Illustrative EUA Assignment Pathways Framework

Showing the four pathways that could result from a preliminary risk-benefit assessment of application



4. Impose Conditions on Approvals to Ensure Ongoing Evaluation of Safety and Efficacy

MRAs have imposed a range of conditions on COVID-19 vaccines approved via expedited pathways to ensure ongoing evaluation of vaccine safety and efficacy. These conditions can vary, including the completion of ongoing Phase III clinical trials. For example, the UK imposed a range of conditions on the Pfizer vaccine relating to quality, instructions for use, and deployment, but also included general conditions requiring the manufacturer to provide the MRA any additional relevant information obtained by the manufacturer relating to the safety, efficacy or quality of the vaccine (**Box 3** on next page). The US FDA imposed a number of conditions on the EUA of the Janssen vaccine, including requiring ongoing observational studies and reporting of adverse events to the U.S. Vaccine Adverse Event Reporting System (VAERS).

Box 3. General Condition Placed by UK on Pfizer BioNTech Temporary Authorization

- Pfizer/BioNTech must promptly provide to MHRA any further data that is generated by them, or which otherwise come into their possession, which is relevant to the risk / benefit profile of the product;
- Pfizer/BioNTech must respond in a timely manner to any requests for further supple mentary data relating to product.

Countries should consider placing conditions on vaccine EUA relating to the following areas:

- Conditions to ensure that health care providers administering the product areaware of the product emergency use status, its significant known benefits and risks, and any alternatives
- Conditions to ensure that patients are made aware of its emergency use status, known significant benefits and risks, and any alternatives, and option to accept or refuse the product
- Conditions for monitoring, analyzing, and reporting adverse events
- Conditions for the manufacturer regarding recordkeeping and reporting
- Conditions on distribution of the product regarding who may distribute the product and means of distribution
- Conditions on collecting and analyzing safety and effectiveness data
- Conditions relating to advertising the product during the period of emergency use
- Condition requiring the applicant to submit an application for full approval once adequate data is available and/or within a certain amount of time after the vaccine obtains full approval from a ML4 MRA.

5. Monitor Condition Compliance Closely to Facilitate Conversion to Full Approval Reviews

MRAs should consider the implications of transitioning vaccines from conditional market approval or EUA to full approval. There are some substantial differences among EUAs that implicate transitioning to full approval. First, many EUAs are effective only for the duration of the public health emergency. For example, the FDA guidance on EUAs for COVID-19 vaccines states, "this policy is intended to remain in effect only for the duration of the public health emergency related to COVID-19 declared by the Secretary of Health and Human Services…."[21] The Kenya EUA guidance states that, "the emergency use authorization shall terminate upon declaration of end of public health emergency." In contrast, EMA[22] and South African Health Products Regulatory Authority[23] have elected to use a conditional market authorization approach for COVID-19 vaccines. The conditional market authorizations issued by EMA and South Africa do not automatically expire with the end of a COVID-19 emergency declaration. The UK elected to initially use a temporary authorization approach, which allowed use of the COVID-19 vaccine in the UK under certain conditions on a temporary basis, which was not explicitly linked to a formal emergency declaration.[24]

EUAs that link authorization to the duration of a declared public health emergency should establish processes to facilitate transitioning EUAs into full approvals. As discussed in Section 4, the emergency declaration relating to EUAs can be distinct from other types of emergency declarations issued by other government officials. MRAs should provide manufacturers that receive EUAs with advance notice prior to termination of the emergency declaration. The amount of advance notice should allow sufficient time for the manufacturer to submit an application to the MRA for full marketing approval.

As noted above, MRAs can also consider placing a condition on the EUA that requires the manufacturer to submit an application for full approval when adequate data are available and/or within a certain amount of time after the vaccine obtains full marketing approval from an ML4 MRA. This condition may help facilitate converting EUAs into full approvals on a rolling basis, as opposed to having to process numerous full marketing applications at the same time at the end of an emergency declaration. The expedited pathways framework adopted by the MRA can also be used to process conversions to full approval or remove conditions on conditional approvals. If a sponsor achieves full approval by an ML4 MRA or obtains WHO PQ, the MRA can process those conversions using the expedited reliance or recognition procedures. Transitioning conditional authorizations to regular authorizations as soon as appropriate will help prevent a backlog in conversions which could unintentionally allow EUAs to lapse.

EUA legal and regulatory frameworks can also address compassionate use or other types of continued use following the cessation of an EUA. For example, Kenya's EUA policy states, "For cases affecting individuals following a public health emergency, the use of products shall continue under the compassionate use authorization clause."[25] The statute authorizing EUAs in the United States allows for continued use of a medical product approved with an EUA following the cessation of the public health emergency when the patient received the medical product during the period of the EUA and the patient's attending physician deems continued use necessary.

6. Require Safety Monitoring & Risk Management Plans

MRAs should ensure that clear safety monitoring and risk management plans are in place for vaccines approved for public health emergencies and for emergency use and consider the role of data sharing and communication among MRAs. The WHO *Global manual on surveillance of adverse events following immunization* provides helpful guidance on establishing safety monitoring and risk management approaches for vaccines.[26] Other resources on vaccine safety monitoring include WHO's COVID-19 vaccines: safety surveillance manual,[27] Global Vaccine Safety Blueprint,[28] and the Council for International Organizations of Medical Sciences Guide to Active Vaccine Safety Surveillance.[29]

Nigeria's COVID-19 EUA policy references a number of post-marketing risk management and surveillance steps that may be required for COVID-19 vaccines (**Box 4** on the following page). Ghana's EUA policy references the EMA risk management plan requirements and states that a risk management plan should at least comply with the Module V of the EMA risk management systems guidelines.[30] Passive surveillance programs are critical, but active surveillance programs should also be considered during the EUA period. A number of countries have established and widely promoted passive surveillance and reporting systems, including VAERS in the United States. Adverse events of special interest reporting should be addressed within safety monitoring plans. MRAs should consider what post-marketing studies are being conducted in other countries and consider whether there are existing gaps in knowledge that would warrant additional post-marketing studies in the country of the MRA or whether sharing data from post-marketing studies from other countries is sufficient.

Box 4. Components of Post-Marketing Surveillance Plan that may Be Required under Nigeria EUA Policy

- Submission of reports of specific adverse events of interest in an expedited manner beyond routine required reporting;
- Submission of adverse event report summaries at more frequent intervals than specified for routine required reporting;
- Ongoing and/or extended safety follow-up for vaccine associated ERD of subjects enrolled in pre-licensure clinical studies;
- A pharmacoepidemiologic study to further evaluate (an) important identified or potential risk(s) from the clinical development program, such as vaccine associated ERD or other uncommon or delayed-onset adverse events of special interest;
- A pregnancy exposure registry that actively collects information on vaccination during pregnancy and associated pregnancy and infant outcomes

7. Manage Modification Requests for Vaccine EUA Decisions

EUA decisions will be based on the information included in the submitted application. Key aspects of the application will often be identified in the EUA decision letter as conditions. These can include manufacturing location(s), eligible criteria (e.g., age), manufacturing processes, formulations, education materials, and other key aspects of the approval. Material changes to information included in the EUA application, such as vaccine formulation, manufacturing location(s) or processes, or patient eligibility criteria, should be approved by the MRA prior implementation. For example, the EUA authorization letter issued by the FDA for the Pfizer COVID-19 COMIRNATY vaccine in October 2021 stated, "No changes will be implemented to the description of the product, manufacturing process, facilities, or equipment without notification to and concurrence by FDA."[31]

Managing these EUA modification requests can require significant MRA resources, especially if multiple vaccines have received EUAs, such as has occurred for COVID-19. MRAs can conduct risk-benefit assessments to determine the appropriate level of review or pathway to process supplemental applications that seek to change or add new manufacturing sites. Depending on the nature of the proposed changes, the appropriate pathway to process the supplemental filing could be the same pathway used to review the original application (e.g., reliance or recognition), or the risk-benefit assessment may indicate that a different pathway is more appropriate. The risk-benefit assessment can help ensure that the appropriate level of review occurs for supplemental filings seeking to make material changes to the EUA decision letter.

8. Leverage Reliance Mechanisms for Lot Release

Reliance and recognition processes can also play an important role in lot release. WHO has issued guidelines for lot release of pandemic influenza vaccines by MRAs and/or national control laboratories (NCLs) of vaccine importing countries[32] and for lot release of COVID-19 vaccines.[32] This guidance emphasizes the importance of leveraging reliance and recognition mechanisms to facilitate timely access to vaccines from quality-assured sources. The WHO's guidance for COVID-19 vaccine lot release states, in part:

> **WHO advises that receiving countries do not conduct lot release test again on vaccines procured from assured sources, e.g., vaccines that are WHO prequalified, listed under WHO EUL, or approved by SRAs, as they have been tested and released already by NRAs with stable, formal approaches for vaccine approval. In other words, in order to expedite the deployment of the EUL listed vaccines as rapidly as possible, WHO's recommended lot release strategy is to rely on the lot release certificates issued by the responsible NCL that are provided with each batch of PQ/EUL vaccines… For self-procured or donated COVID-19 vaccines, review of the summary lot protocol by the procuring/receiving NRA/NCL is essential for assuring the safety and quality of these products. This is additional to the lot release that should have been performed in the country of manufacture. Recognition/acceptance of lot release certificates from the NRA/NCL of the country where the vaccine is manufactured, or from another competent NRA/NCL, should be considered as a strategy.**

9. Embrace Transparent Communication and Community Engagement to Build Trust in Vaccine Regulatory Reviews

Open and transparent communication builds public trust in vaccine regulatory review processes. This is particularly important in this era of concerns over vaccine hesitancy. MRAs should develop a comprehensive communication strategy that provides information to a wide range of audiences. A number of MRAs have developed vaccine-specific web pages to share information broadly on specific vaccines. Others are taking advantage of opportunities presented by social media channels to improve communication with the public. MRAs should consider developing a standardized communication plan for key regulatory decisions. These communication plans should consider language and disability access to ensure that materials are accessible to the entire population in the country. Some of the components of a standardized communication package could be:

- Decision memorandum/assessment report explaining rationale for the regulatory decision

- Letter of authorization
- Press release
- Fact sheet for vaccine recipients and caregivers
- Fact sheet for health care providers
- FAQs page/document

The WHO has issued communication guidelines for outbreak responses and pandemic influenza that provide helpful principals and approaches for managing communication with all stakeholder about vaccine review and deployment (**Box 5**).[34,35,36] The WHO Regional Office for Europe has also developed a vaccine safety communication library with a wide range of resources for supporting public communication relating to vaccination and immunization programs.[37]

Box 5. WHO Outbreak Communication Guidelines (2005)

Understanding the public is critical to effective communication. It is usually difficult to change pre-existing beliefs unless those beliefs are explicitly addressed. And it is nearly impossible to design successful messages that bridge the gap between the expert and the public without knowing what the public thinks.

Appendix E contains more detailed guidance on the content for each of the following communication products:

- MRA vaccine-specific web pages
- Review or decision memorandum/assessment report
- Letters of authorization
- Press releases
- Fact sheet for health care providers
- Fact sheets for recipients and caregivers
- FAQs
- Social Media Content

10. Use a Phased Planning Approach to Prioritize Finite Resources

Anticipating the needs and opportunities of the different phases of public health emergencies can help improve the preparedness and efficiency of vaccine reviews. WHO's *Guidelines on regulatory preparedness for provision of marketing authorization of human pandemic influenza vaccines in non-vaccine-producing countries* categorizes influenza pandemics into four phases: interpandemic phase, alert phase, pandemic phase, and transition phase. The guidelines present steps to be taken during these different phases and how procedures may need to be modified depending on the phase.

WHO's EUL procedure uses a three-phased approach consisting of pre-emergency phase, emergency phase, and post-listing phase. Kenya's COVID-19 EUA guidance adopts a similar phased framework as pre-emergency phase, emergency phase, and post-authorization phase.[38]

MRAs can consider adopting a phases framework to optimize allocation of resources during different phases of a public health emergency. **Table 2** provides an overview of key activities to consider during pre-emergency, emergency, and post-emergency phases focusing on vaccines.

Table 2. Key EUA activities for MRAs in the pre-emergency, emergency, and post emergency phases.

Pre-Emergency Phase
Establish legal and regulatory frameworks and clear issuance criteria for EUAs
Strengthen and streamline MRA application policies and procedures
Consider adopting electronic regulatory information systems to facilitate remote reviews
Establish technical working groups with needed technical expertise to facilitate rapid EUA review when emergencies arise
Establish reliance and recognition arrangement and data sharing agreements with ML4 MRAs and regional MRAs
Emergency Phase
Process EUA applications
Activate TWGs to provide technical guidance on EUA applications
Monitor compliance with EUA conditions
Maintain reliance and recognition arrangements, including data sharing agreements with other MRAs
Post-Emergency Phase
Work with manufacturers to convert EUAs into full marketing authorizations
Conduct after-action review of processes and identify opportunities for improvement
Continue oversight of post-marketing surveillance programs

11. Update Operational policies and Procedures to Find Efficiencies and Facilitate Collaborative review

Processing EUAs during a time of public health emergency can put significant strain on the administrative and operational capacity of MRAs. To streamline EUA reviews, an MRA can review their operational policies and procedures to identify ways to improve the efficiency of reviews and adopt mechanisms that facilitate collaborative reviews.

a. Establish Clear Review Timelines

Given the seriousness of the COVID-19 pandemic, many MRAs have established expedited review timelines for COVID-19 vaccines. Our rapid assessment found that only six countries met the

COVID-19 vaccines submission dossiers timeline of a maximum of 15 working days as indicated in the COVID-19 vaccine introduction readiness assessment tool sections on regulation and safety surveillance (VIRAT/VRAF 2.0).[39] Kenya's policy states that abridged reviews and WHO Emergency Use List products shall be evaluated within seven calendar days. Ghana's policy states that an EUA application will be "acted upon within 15 working days."[40] South Africa's policy states that COVID-19 vaccines will receive "priority/expedited review" but does not include a specific number of days.

b. Allow for Rolling Submissions

Rolling reviews can allow for expediting vaccine regulatory reviews while late-stage clinical trials are still ongoing. The amount of clinical trial data required before submitting an initial application may vary, but, for example, South Africa's[41] and Canada's[42] EUA policies lay out the minimum data that should be included in an application (**Box 6**). Encouraging pre-submission meetings with applicants can help clarify expectations for rolling submission applications to ensure alignment between data availability and the needs of MRA reviewers. Minutes of pre-submission meetings should be prepared and agreed to between the MRA and applicant for transparency and recordkeeping purposes.

Box 6. Minimum Requirements for Rolling Submissions in South Africa & Canada

South Africa

- Non-clinical and clinical trials phase 2 data that demonstrate promising evidence of safety and efficacy
- Written confirmation that phase 3 trials have started and there are enough people enrolled to provide evidence of safety and efficacy within a reasonable amount of time (expected to be within 6 months from initial filing)
- Evidence which shows that manufacturing of the candidate vaccine is in compliance with good manufacturing practices (GMP) and that product quality and consistency are well controlled
- A submission plan giving the anticipated timelines for submitting the various components of the application. A preliminary submission should be included in the initial filing.

Canada

- Non-clinical and clinical trials phase 2 data that demonstrate promising evidence of safety and efficacy
- Confirmation that phase 3 trials have started and there are enough people enrolled to provide evidence of safety and efficacy within a reasonable amount of time (expected to be within 6 months from initial filing)
- Evidence that manufacturing is in compliance with good manufacturing practices (GMP) and that product quality and consistency are well controlled
- Sponsors must also file a plan giving the anticipated timelines for submitting the various components of the application.

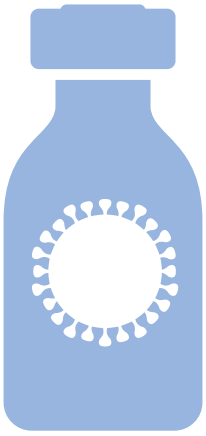
c. Use Standardized Application Forms & Checklists

Making standardized application forms and checklists will help ensure that the submitted applications have the information needed by the MRA. MRAs dossier requirements can vary based on the risk assessment and views of different MRAs. However, much of the information in MRA applications is the same across countries. MRAs should consider

harmonizing vaccine application forms to facilitate manufacturer submission to multiple MRAs. MRAs can still require supplemental forms for information, which is not part of the standardized application. For example, the Common Technical Document (CTD) format is accepted for WHO prequalification of vaccines. An electronic version of the CTD (eCTD) has also been developed.[43] EUA policies in Ghana, Nigeria and Ethiopia allow for submissions using the CTD format.

d. Invest in Electronic Regulatory Information Systems

Electronic application systems can facilitate timely review of EUA applications. Paper-based application systems present a number of barriers to expedited reviews, including challenges with sharing key documents with reviewers and processing delays. Electronic application systems can also help facilitate remote review by reviewers who are not physically located at the same location. Facilitating remote review can be especially important when technical experts are located throughout the country or when MRA staff are not able to work in person or travel to the MRA office due to the public health emergencies. Ideally, electronic applications systems would be established and fully implemented in a pre-pandemic phase to facilitate remote access and communication during a public health emergency. Implementing a software system during a pandemic phase may be challenging and divert attention from more urgent priorities.



Appendix A. Checklist for Strengthening Management of Vaccine EUAs

- ☐ Establish clear criteria for issuing EUAs in legal and regulatory framework
- ☐ Adopt a EUA application form that facilitates rapid review and pathway assignment of vaccine EUA applications containing the following information:
    a. Applicant and manufacturer information;
    b. Basic information about the vaccine product and intended population;
    c. Information about submissions to other MRAs or WHO and associated decisions;
    d. Proposed pathway;
    e. Risk assessment justifying pathway assignment; and
    f. Proposed post-marketing surveillance plan
- ☐ Adopt standardized pathways for expedited review of vaccines during public health emergencies and clear review expectations for each pathway
- ☐ Require applicants seeking EUA to complete a risk assessment to inform pathway assignment; a risk assessment tool can be included in the EUA application
- ☐ Establish MRA review timeline expectations and monitor performance against these timelines for continuous process improvement
- ☐ Establish and maintain technical review committee with technical expertise needed to review quality, clinical, and non-clinical study data
- ☐ Allow for vaccine quality and study data reports to be submitted in CTD format
- ☐ Adopt online application processes for EUA applications to facilitate submission and coordinate MRA staff reviews
- ☐ Develop and maintain post-marketing surveillance information monitoring system to aid in monitoring PMS data
- ☐ Develop and maintain system to monitor compliance with conditions placed on EUAs (e.g., supplemental data submission requirements)
- ☐ Ensure that each approved vaccine has a designated point of contact within MRA responsible for monitoring supplemental submissions, including post-marketing surveillance and safety monitoring data
- ☐ Establish and maintain community engagement mechanisms to receive real-time feedback from key stakeholders and affected communities about vaccine decisions and monitoring
- ☐ Establish public website for each approved vaccine with key information about each approved vaccine (e.g., recipient fact sheet, FAQs, assessment report, decision letter)
- ☐ Share key decisions and information about approved vaccines on social media channels to facilitate public awareness and understanding of MRA decisions

Appendix B. Illustrative Workflow for Processing EUA Applications

Initial EUA Applications

- ☐ Vaccine application file opened by MRA
- ☐ MRA point of contact for application designated
- ☐ Minutes from pre-submission meeting(s) prepared and added to application file
- ☐ Vaccine application received and added to application file
- ☐ Written acknowledgment of application receipt sent to applicant
- ☐ MRA management team conducts initial review of application to assess whether application contains the information required to conduct pathway assignment analysis
    a. If application is found to lack information needed for pathway assignment, a letter should be sent to applicant requesting missing information
- ☐ MRA review team conducts risk-benefit assessment and documents pathway assignment decision
- ☐ MRA review team reviews application to determine whether application contains sufficient information for assigned pathway
    a. If application is found to lack information needed for assigned pathway, a letter should be sent to applicant requesting missing information
- ☐ Application assigned to application review team with targeted review completion date
    a. Composition of review team determined by MRA pathway framework (e.g., internal MRA staff, external technical review committee)
- ☐ Application review team reviews application and documents analysis and decision in decision memorandum/report
- ☐ MRA prepares decision letter, including any conditions on the authorization
- ☐ Decision letter and review memorandum/report added to MRA application file
- ☐ Decision letter and review memorandum/report sent to applicant
- ☐ Decision letter, review memorandum/report, and key associated documents (e.g., provider fact sheet, patient fact sheet) posted on MRA website

EUA Modification Requests

- ☐ Request for modification received by MRA
- ☐ Written receipt of request sent to applicant
- ☐ MRA team reviews request to determine if information sufficient to conduct risk-benefit analysis to inform pathway assignment
    a. If application is found to lack information needed for pathway assignment, a letter should be sent to applicant requesting missing information
- ☐ MRA review team conducts risk-benefit assessment and documents pathway assignment decision

- ☐ Application assigned to review team with targeted review completion date
    a. Composition of review team determined by MRA pathway framework (e.g., internal MRA staff, external technical review committee)
- ☐ Review team reviews modification request and documents analysis and decision in decision memorandum/report
- ☐ MRA prepares decision letter modifying original decision letter, or explaining rationale for rejecting the modification request
- ☐ Modified decision letter and review memorandum/report added to MRA application file
- ☐ Modified decision letter and review memorandum/report sent to applicant
- ☐ Modified decision letter and review memorandum/report posted to MRA website

Appendix C. Illustrative Application Checklist for Vaccine EUAs

Application Package Contents	Required by Pathway*			
	Recognition	Reliance	Fast-Track Abbreviated Review	Full Review
EUA Application Form	Yes	Yes	Yes	Yes
Minutes from pre-submission meeting	Yes	Yes	Yes	Yes
Proposed package insert	Yes	Yes	Yes	Yes
Proposed fact sheet for vaccine recipients and caregivers	Yes	Yes	Yes	Yes
Proposed fact sheet for health care providers	Yes	Yes	Yes	Yes
Proposed post-marketing surveillance plan	Yes	Yes	Yes	Yes
Certificate of the responsible MRA's or WHO's decision	Yes	Yes	Yes	Yes
Assessment reports of the responsible MRA(s) or WHO	No	Yes	Yes	Yes
Evidence of quality and good manufacturing practices compliance (GMP certificate)	No	No	Yes	Yes
CTD Module-2 quality, nonclinical and clinical overview	No	No	Yes	Yes
Full dossier as required by national law/ or and regulations (e.g., CTD Modules 2-5)	No	No	No	Yes

*Note that if required information is not available please explain the absence in the cover letter (e.g., if the vaccine product has not had any previous reviews by the WHO or another MRA)

Appendix D. Preliminary Risk-Benefit Assessment Tool to Inform Pathway Assignment

Applicant Name	
Vaccine Product Name	
Application No.	
Application Receipt Date	
Preliminary Review Team	
Criteria	**Narrative Discussion of Risks & Benefits**
Prior Review Decisions (e.g., Outcomes of reviews conducted by other MRAs and stringency of those MRAs and/or WHO pre-qualification or Emergency Use Listing)	
Quality (e.g., whether vaccine manufacturer has other WHO pre-qualified or stringent regulatory authority approved vaccines, stringency of MRA providing lot release certification)	
Safety (e.g., consider important identified or potential risk(s) from the clinical development program or other uncommon or delayed-onset adverse events of special interest)	

Need (e.g., ability of already approved vaccines to meet near-, medium-, and long-term demand for different populations in the country, reported efficacy of the vaccine relative to other products on the market)	
Access (e.g., the extent to which the country will be able to access the vaccine if approved, which may be influenced by manufacturer's capacity, access channels through international mechanisms such as COVAX, planned donations, cost)	
Deployment Feasibility (e.g., cold chain requirements, number of doses required)	

Appendix E. Communication Product Guidance

a. MRA Vaccine-Specific Webpages

An MRA's website presents a space for the MRA to share key information about a vaccine regulatory review with the public. Some MRA's publish a specific webpage for each vaccine to help with sharing information about each vaccine. The webpages can include a document repository that includes all versions of key documents relating to the vaccine regulatory process, including safety updates, news, review reports, MRA letters, etc. Examples of MRA webpages for specific vaccines include the EMA website for the AstraZeneca COVID-19 vaccine[44] and the US FDA website for the Pfizer COVID-19 vaccine.[45] The vaccine-specific webpage can be structured in different ways, but below is a list of components that MRAs could consider including on a webpage dedicated to a particular vaccine:

- Vaccine Overview Section
- Downloadable Package Insert
- FAQs
- Fact Sheets for Caregivers and Patients
- Fact Sheets for Health Care Providers
- Letters of Authorization (and amendments thereto)
- Review Memorandum/Assessment Reports
- Press Releases
- Links to Webcasts of MRA Press Conferences and Video Interviews

b. Review or Decision Memorandum/Assessment Report

The purpose of a Review Memorandum (also referred to as a Decision Memorandum or Assessment Report) is to collect and synthesize the MRA's analysis and rationale underlying the MRA's decision. The format of the decision memorandum may vary depending on the level of review (e.g., full review, review of basic documentation, reliance, and recognition). Appendix F includes an illustrative template of a Review Memorandum/Assessment Report. Some MRAs have published their Review Memoranda for COVID-19 vaccines on their websites, which may present useful examples for other MRAs.[46,47,.48]

c. Letters of Authorization

A Letter of Authorization is usually written by the MRA to the applicant documenting the decision of the MRA. These letters can be published on MRA website to increase awareness and transparency regarding the scope and conditions of the authorization. An EUA Letter of Authorization could include the following sections:

- Criteria for Issuance of Authorization
- Scope of Authorization
- Product Description
- Conditions of Authorization
- Duration of Authorization

d. Press Releases

Publishing press releases can be an important mechanism for communicating with the public and specifically with mass media, such as news websites, TV, and radio. Press releases are generally summaries of key information and will frequently include quotes from key MRA officials, which can then be used in media reports. The WHO Regional Office for Europe has published guidance titled *How to prepare a press release* that includes guidance on the elements of a press release, strategies for media engagement, and model press releases as examples.[49] This guidance specifically focuses on press releases relating to vaccine and immunization programs and is a helpful resource for strategizing how to structure a press release to optimize uptake and dissemination through a broad range of media.

e. Fact Sheet for Health Care Providers

Fact Sheets for health care providers should be structured to deliver the most critical information for health care providers about a vaccine. The fact sheet should provide key step-by-step instructions, such as information relating to storage and handling, dosage and scheduling, administration, contraindications, warnings, and adverse reactions. The health care provider fact sheet should also summarize information to be provided to vaccine recipients/caregivers. The fact sheet can also list the mandatory requirements/conditions on the vaccine due to its EUA authorization status and include the full prescribing information insert as an attachment to the fact sheet.

f. Fact Sheet for Vaccine Recipients and Caregivers

Fact sheets for vaccine recipients and their caregivers are summaries of the most important information for patients and caregivers to inform their decision-making about the vaccine and instructions for post-vaccination. The fact sheet can be formatted in different ways, but a question and answer (Q&A) format can be a useful format for recipient/caregiver fact sheets. The fact sheet should present the risks and benefits of the vaccine and instructions regarding communications with health care providers and contraindications. The fact sheet should also provide the recipient and caregiver contact information if the recipient suffers from side effects, including reporting information to any passive surveillance systems. For example, the FDA fact sheet for recipients and caregivers for the Pfizer COVID-19 vaccine includes the information for reporting adverse reactions to the FDA/CDC Vaccine Adverse Event Reporting System (VAERS).

g. Frequently Asked Questions

An FAQ page and/or document can be a useful tool for communicating with the public about a vaccine approved under an EUA. The FAQ format is helpful for delivering information succinctly and can be updated regularly to respond to new concerns or questions. FAQs can also be a helpful tool for responding to concerns or rumors circulating on social media, in part, because FAQs can easily be converted into social media messages and shared by the MRA on social media to respond to rumors or misinformation circulating online. You can find an example of a FAQ responding to social media rumors on the US FDA FAQ page for the Pfizer-BioNTech COVID-19 vaccine.[50]

h. Social Media Content

Posting key regulatory documents online is important for building public trust in vaccine regulatory decisions, but it is also important to ensure that key information is shared with the public using social media and other channels where many people receive their news and information. MRAs should strongly consider mapping the landscape of social media being used by their population and sharing key regulatory information on social media accounts on those platforms. Often this will require converting regulatory decisions into different formats (e.g., shorter statements, infographics, photo boards, or videos). These abbreviated communications can then link to full documents to provide the public easy links to the full documentation prepared and published by the MRA.

The time investment to publicize key information, especially FAQs, via social media can be well worth the cost to ensure that the public is adequately educated about the scientific evidence underlying vaccine regulatory decisions and the rigor of underlying clinical trials. Community advisory mechanisms, such as community advisory boards, can be helpful for identifying active social media platforms and early identification of rumors that are circulating on social media. Community advisory and engagement boards can also help with designing and providing feedback on social media content that maximizes circulation on social media platforms.

Appendix F. Template Vaccine EUA Review Memorandum/Assessment Report

An EUA Review Memorandum/Assessment Report could include the following sections:

A. Executive Summary
B. Background
    a. Outbreak background
    b. Available therapies
    c. Applicable regulatory requirements
C. Vaccine Overview
    a. Vaccine Composition
    b. Dosing Regimen
    c. Proposed Use
D. Review of Clinical Safety and Effectiveness Data
    a. Overview of Clinical Studies
    b. Analysis of Specific Studies
        i. Design
        ii. Assessment of Follow-up Duration
        iii Subject Disposition and Inclusion in Analysis Populations
        iv. Demographics and Other Baseline Characteristics
        v. Vaccine Efficacy
        v Safety
E. Review of Other Information Submitted in Support of Application
    a. Plan for Continuing Blinded, Placebo-Controlled Follow-up
    b. Pharmacovigilance Activities
    c. Non-Clinical Studies
    d. Chemistry, Manufacturing and Control Information
    e. Clinical Assay Information
    f. Inspections of Clinical Study Sites
    g. Prescribing Information and Fact Sheets
F. Benefit/Risk Assessment in the Context of Proposed Indication and Use Under EUA
    a. Known Benefits
    b. Unknown Benefits & Data Gaps
    c. Known Risks
    d. Unknown Risks & Data Gaps
G. Review Meeting Summary
H. Overall Summary and Recommendations
I. References

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