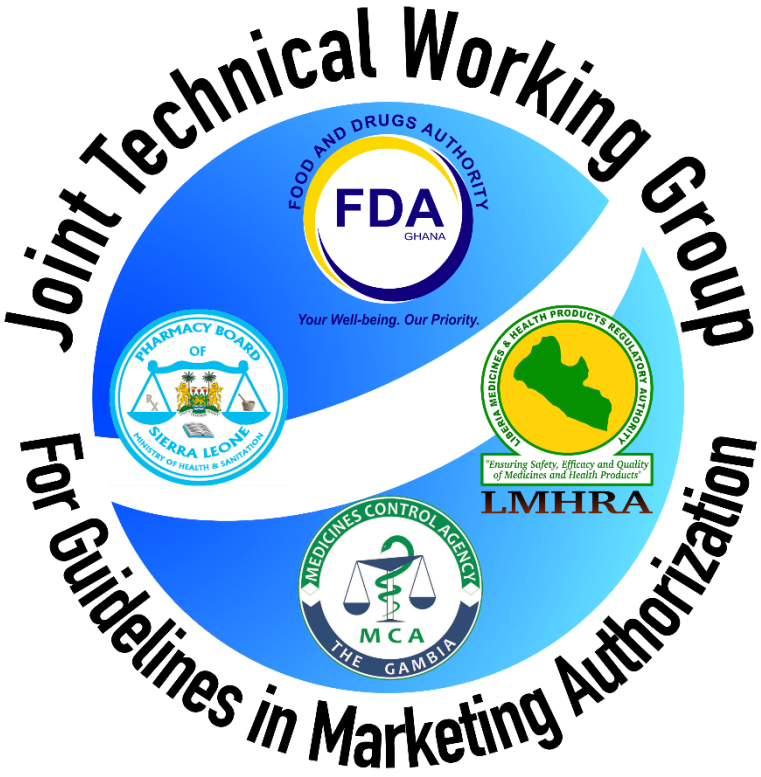

Guideline on

Emergency Use Authorization

For the National Medicines Regulatory Authorities of Ghana, Liberia, Sierra Leone, and The Gambia

Updated December 2, 2022

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<02 December 2022>
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Guideline on Emergency Use Authorization, Version 1.0, Updated December 2, 2022

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Date of coming into effect	<DD Month YYYY>[4]

This guideline replaces '<guideline>' (NMRA/…/…).[5]

Comments should be provided using the template for submission of comments. The completed comments form should be sent to <as appropriate (NMRA's Email)>

Keywords	***emergency, fast-track, non-routine, accelerated, expedited***

[1]Last day of relevant Committee meeting.
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[4]First day of coming into effect. Latest 3 months after adoption.
[5]If this supersedes a previous guideline – otherwise delete.

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An agency of the <……>.
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Guideline on Emergency Use Authorization, Version 1.0, Updated December 2, 2022

Table of contents

Style notes for this draft version:

[ ] Comments to be removed with finalization

< > Placeholder to be filled with specific information or to be decided if kept or deleted.

Acknowledgements

We duly thank the US Food and Drugs Authority (USFDA), and Food and Drugs Authority Ghana (FDA), and the World Health Organization publishing their guidelines that contributed in several aspects relevantly to the development of this guideline.

Executive summary

The development of this guideline is based on the outcomes and consensus of the meetings convened in January / February 2020 by GHPP-PharmTrain Project team of the Federal Institute for Drugs and Medical Devices (BfArM, Germany) with participants from the national medicines regulatory authorities (NMRA) of Liberia (LMHRA, Liberia Medicines and Health Products Regulatory Authority), Sierra Leone (PBSL, Pharmacy Board of Sierra Leone), and The Gambia (MCA, Medicines Control Agency).

This document has been discussed and adapted in exchange between LMHRA, PBSL, The Gambia MCA, Ghana (FDA, Food and Drugs Authority) and the GHPP-PharmTrain project team from November 2021 to September 2022.

From January 2022 the Joint Technical Working Group for Guidelines in Marketing Authorization (TWG-MAG), with the above-mentioned members, was established to continue the successful development of regulatory guidelines.

<This document should be read in conjunction with the accompanying notice and the relevant sections of other applicable guidance.>

1. Introduction (background)

This guideline gives clarity on the regulatory requirements for an emergency use authorization of a medicinal product during a declared public health emergency (PHE) involving (amongst others) a heightened risk of attack on the general public's life, health, safety or a significant potential to affect national security. This guideline should be read along with other guidance documents concerning information and application requirements on the <NMRA website>, such as the <Guideline on Donation> and <Guideline on Registration>.

The Emergency Use Authorization (E.U.A.) is granted by the legal provision <quote title of national medicines Act if applicable>. The E.U.A. empowers the <NMRA> to permit the approval of an unregistered medicinal product in a PHE. This procedure takes into consideration whether the known and potential benefits outweigh the known and potential risks of the product when used to diagnose, treat, or prevent serious or life-threatening diseases or conditions, when there are no approved adequate, and available alternatives.

The <NMRA> expects that a Government Ministry, Department or Agency (MDA) or any other recognized agency (e.g., the Ministry of Health or the Ministry of Defence, Ministry of Interior, an entity appointed by a Government MDA, etc.) shall submit the request for consideration for an E.U.A. to the <NMRA>. The <NMRA> may seek additional data and information on a case-by-case basis to ensure that the statutory criteria for issuance of an E.U.A. are met. In the event of a PHE an applicant may apply for an E.U.A. directly to the <NMRA> or, a request for consideration may also be submitted by a MDA or any other recognized agency.

1.1. Objectives:

This Guideline on Emergency Use Authorization seeks to expedite access to quality, safe and efficacious medicinal products to the public during a PHE.

2. Scope

This document provides guidance to industries, government agencies, and the general public on the general recommendations and procedures on the issuance of E.U.A. process for the use of a medicinal product during a PHE. This can be a repurposed medicinal product (approved product but unapproved use), a novel medicinal product (unapproved product) as well as a medicinal product that has been approved by a

reference institution. Vaccines do not fall into the scope of this guideline. The E.U.A. is a special procedure for fast-track approvals of medicinal products in the event of a PHE when the community/public health authorities may be willing to tolerate less certainty about the efficacy and safety of products, given the morbidity and/or mortality of the disease and the lack or paucity of treatment, diagnosis/detection or prevention options. To establish eligibility of unlicensed medicinal products for assessment under this procedure, this guideline defines the steps that <NMRA> will follow, the essential information required, and the process to be used in conducting the assessment to determine whether an unlicensed product can be approved on a time limited basis, while further data is being gathered and evaluated.

3. Legal basis

In pursuant of legal provision <quote title of national medicines Act if applicable> of <country>, this document provides guidance on the use of medicinal products during a declared PHE.

4. General Requirements

4.1. Declaration of Emergency

The <Minister for Health>/<President> shall declare a national PHE by an Executive Instrument where there is a situation that poses an immediate risk to health or life.

To meet the criteria for a national PHE, the incident should;

- Immediately threaten life or health;
- Have already caused loss of life or health detriments,
- Have a high probability of escalating to cause immediate danger to life or health.

4.2. Eligibility for Emergency Use Authorization

This is when an unapproved medicinal product or an approved medicinal product with unapproved use can be authorized for use during a declared PHE involving a heightened risk of affliction or attack on the safety and security of the general public or a significant potential to affect national security. These products and their uses are not approved, cleared, or registered as per standard registration procedure. After consultation with relevant bodies and/or committees as per national requirements (<see Annex xx (NMRA may add an annex here)>) (to the extent feasible and appropriate given the circumstances of the emergency), the <NMRA> may issue an E.U.A. only if, the <NMRA> concludes that:

1. The agent/pathogen/item specified in the declaration of emergency (in the following called “the agent”) can cause a serious or life-threatening disease or condition.

2. Based on the totality of scientific evidence available, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing

   (a) the serious or life-threatening disease or condition referred to in 1. above;

   or

   (b) a serious or life-threatening disease or condition caused by a product granted emergency use authorization for diagnosing, treating, or preventing the disease or condition referred to in 1. above.

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

4. An approved alternative to the product for diagnosing, preventing, or treating such serious or life-threatening disease or condition is not available or not adequate.

   A potential alternative product may be considered as:

   - “not available” if there are insufficient supplies to meet fully the emergency need.

   - "not adequate" if
     - there are data contraindicating the use of any available alternative for special circumstances or populations (e.g., immunocompromised individuals or individuals with a medicinal product allergy) or
     - if the agent is or may be resistant to available alternative products

5. The product is manufactured in compliance with current Good Manufacturing Practices (GMP).

6. The applicant undertakes to complete the development of the product and apply for full approval. For that purpose, the remaining clinical trials and other testing needed to complete the development of the product must already be underway at the time of the application for an E.U.A..

<NMRA> may consider reviewing a candidate product for an E.U.A. that does not meet all of the requirements. In such situations, the application letter and documentation provided to <NMRA> should justify the application of the product although it does not meet all eligibility requirements.

5. Instructions for the Applicant

5.1. Request for Consideration for an E.U.A.

Although an E.U.A. may not be issued until after a PHE has been declared by the <Minister of Health>/<President>, <NMRA> recognizes that during such exigent circumstances, the time available for the submission and review of an E.U.A. request

may be severely limited. Therefore, the <NMRA> strongly encourages an entity with a possible candidate product, particularly one at an advanced stage of development, to contact the <NMRA> for the candidate product even before a determination of an actual or potential emergency.

This guidance offers recommendations for both "pre-emergency" activities to be conducted prior to the determination of actual or potential emergency and "emergency" activities to be performed once the determination has been issued. In addition, this section of the guidance sets out the information for the <NMRA> to allow an assessment of safety and effectiveness and to make an adequate risk-benefit determination to support issuance of an E.U.A.. Details about the format of submissions are specified in Annex I.

Pre-submission Meeting(s)

A pre-submission meeting is anticipated to facilitate the entire E.U.A. process:

For both pre-emergency and emergency activities, a pre-submission meeting is recommended. These meetings should be scheduled as early as possible. Applicants intending to make submissions for an E.U.A. may face different challenges with respect to their applications. These may vary from complying with the administrative requirements in terms of the format and the availability of data. <NMRA> therefore encourages applicants to schedule a pre-submission meeting with the agency by email to obtain guidance in accordance with the requirements outlined in section 5.2.1.. A pre-submission meeting request form is in Annex II.

A presentation should be prepared detailing the product, the technology used, the data available, specific transport/storage and labelling information. Information on whether the medicinal product has been or is intended to be submitted to WHO, or other regulators for approval and the time frame for submissions should be shared. In advance to the meeting, the applicant should supply a list of questions addressed to the <NMRA> and propose a predefined agenda for an efficient meeting structure. Such meetings are important for discussing the availability of essential data required for specific products, expected timelines for submission and updates, monitoring of safety and effectiveness after deployment, and other relevant information. Additional meetings may be held during the assessment process, as requested.

Before the event of a PHE, the <NMRA> should assign a group of regulators within the NMRA a so-called “Roster of expert”. They are responsible to conduct the pre-emergency and emergency activities; to evaluate the eligibility of an E.U.A. to participate in the pre-submission meetings, to communicate the essential data requirements, to communicate the timelines, to conduct the review in an expedited manner, e.g. as rolling review.

<Please specify in a SOP the roster of experts: who (which profession/function) should be part of it within/outside their NMRA>

Pre-Emergency Activities

Such activities may include discussions with <NMRA> about a prospective E.U.A. of a product and the appropriate procedure for submitting data on the product prior to an emergency declaration. The <NMRA> strongly recommends that an entity submitting data during a "pre-emergency" period, follows the recommendations for data submission outlined in the section "Submission of a Request for Consideration," below. If, prior to the declaration of an emergency, <NMRA> concludes that a candidate product may meet the criteria for an E.U.A. the <NMRA> may share appropriate information on such product with the body declaring the PHE. Prior a declaration of an PHE, the <NMRA> may share information regarding a product candidate with the declaring body if the <NMRA> deemed the product candidate eligible.

Emergency Activities

Once a determination of an actual or potential emergency has been made <Act section XY>, the <Minister of Health>/<President> may declare an emergency justifying the authorization to use an unregistered medicinal product for an unapproved use. The Minister will consult with the <NMRA> and other agencies and private entities, where appropriate, to identify products that may be eligible for an E.U.A. in light of the circumstances of the emergency and to facilitate timely submission of the E.U.A. request by an appropriate entity.

5.2. Submission of a Request for Consideration

A request may be submitted based on the totality of scientific evidence available to the <NMRA> (including data from adequate and well-controlled clinical trials, if available), it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing the serious or life-threatening disease or condition. The exact type and amount of data needed to support an E.U.A. may depend on the nature of the declared emergency and the nature of the candidate product. According to <NMRA> recommendations a request for consideration for an E.U.A. shall include a well-organized summary of the available scientific evidence that evaluates the product's pharmaceutical quality, safety and efficacy.

5.2.1. Summary of required Information

The information below summarizes the type of data that <NMRA> requires to be submitted to support a request for consideration for an E.U.A..

1. A description of the product and its intended use (e.g., identification of the serious or life-threatening disease or condition for which the product may be effective)
2. An identification and an explanation of what unmet medical need(s) would be addressed by issuance of the E.U.A

3. A description of the product's international registration/Marketing Authorization (MA) status, including also, whether the product is prequalified WHO.
4. A list of each site where the product, if authorized, would be (or was) manufactured and the GMP status of the manufacturer.
5. An identification of any approved alternative products, including their availability and adequacy for the proposed use (if known).
6. Available safety and efficacy information for the product (Details see Annex IIIa and IIIb)
7. A discussion of risks and benefits (Details see Annex IIIc)
8. A description of the information for health care providers or authorized dispensers and recipients of the product, (e.g., two separate “Condition of use” documents), and the feasibility of providing such information to health care providers or authorized dispensers and recipients in emergency situations
9. Information on pharmaceutical quality
10. Certificate of Analysis of the E.U.A.
11. Medicinal product instructions for use as E.U.A. product (e.g., if follow-up treatment is required)
12. Proposed labelling (if applicable). Including batch number, manufacturing date and expiry date, legal status and limitations of data
13. The <NMRA> recommends that requests for consideration for E.U.A. include statements on whether the nonclinical laboratory studies were conducted in compliance with applicable Good Laboratory Practice (GLP) requirements and whether the clinical studies were conducted in compliance with applicable Good Clinical Practice (GCP) standards.

These data requirements are discussed in more detail in Annex III. Please note that the <NMRA> may also issue subsequent guidance providing greater detail on these recommendations and procedures for specific medicinal products and/or public health emergencies. <NMRA> requests that the applicant submits any data from any ongoing testing (e.g., longer term stability data) or other data or information that may change the <NMRA>'s evaluation of the product's safety or effectiveness that become available during the period of review or the term of the E.U.A. (to the extent that such data are not required to be submitted under a condition of authorization) to the <NMRA> as soon as such data become available.

6. E.U.A. Instructions for the <NMRA>

6.1. Processing of an E.U.A.

This section discusses <NMRA>'s role in pre-emergency activities for an E.U.A. of a medicinal product, as well as the procedures the <NMRA> will follow in processing a request for consideration for an E.U.A. once the <Minister of Health>/<President> has issued a declaration of emergency.

6.2. Pre-Emergency Submission

To allow <NMRA> evaluation process to begin before a determination of actual or potential emergency, the <NMRA> recommends that a pre-emergency submission be filed using existing processes to the extent feasible and appropriate. The extent of, and timelines for, evaluation of such submissions will be determined on a case-by-case basis and will depend on the nature of the emergency.

Subject to exigent circumstances beyond <NMRA>’s control, the <NMRA> anticipates that pre-emergency submissions for high priority activities may be evaluated in a matter of weeks to months.

6.3. Prioritization of Requests for Consideration for an E.U.A.

The <NMRA> intends to establish priorities for its evaluation of requests to consider an E.U.A., prior as well as during a declared PHE. Such prioritization may be based on the circumstances, such as:

1. the seriousness of the clinical condition;
2. the incidence of the clinical condition;
3. the available information concerning the likelihood that the product may be safe and effective in preventing, treating, or diagnosing the condition ;
4. the effect use of the product may have in ensuring national security;
5. whether the product is included in government strategic stockpiles, if applicable;
6. whether the product could be used by a large population or is limited to subpopulation(s) (unless such use may be critical in managing a public health threat or in protecting a subpopulation with no other suitable measures available);
7. request of another government agency;
8. the extent to which the product would serve a significant unmet medical need in a special population (e.g., pregnant women, infants and children, and immunocompromised persons);

9. the availability and, where known, safety and effectiveness of other countermeasures;
10. the urgency of the treatment need (i.e., the window of opportunity for treatment can vary between different medical conditions);
11. the adequacy of the supporting nonclinical and clinical information; and
12. the quantity of product available.
13. the feasibility of adhering to required storage conditions.
14. the security of the supply chain, if applicable.

<NMRA> intends to establish priorities for its pre-emergency activities at the <Directorate/Program/Department> level or higher and, as appropriate and feasible, will consult with the Ministry and may consult other agencies on its priority setting.

6.4. Consideration for an E.U.A. Request

The <NMRA> will be responsible for the overall disposition of the request and will interact directly with the entity submitting the request for consideration. The <NMRA> will arrange for the consultations with other agencies to the extent that such consultations are feasible and appropriate given the circumstances of the emergency.

The <NMRA> will work with the Ministry depending on the complexity of the issues presented and the nature of the declared emergency, and may seek additional scientific and technical input from outside experts or advisory committees.

<NMRA> recognizes that the exact type and amount of data needed to support an E.U.A. may vary depending on the nature of the declared emergency and the nature of the candidate product. The <NMRA> will evaluate each request in light of the circumstances and the statutory criteria for issuance.

The responsible Department in consultation with other relevant Departments and technical committees (as appropriate and feasible), will perform an evaluation of the information and data included in the request for consideration and make recommendations to the <CEO>/<DG>/<Registrar>. The letter of authorization or otherwise will be issued by the CEO of the <NMRA>.

The letter authorizing the emergency use of a product will include a description of the intended use, the indications and contraindications of the product, as well as the validity of the E.U.A.. The conditions of the authorization for emergency use of an unapproved or approved medicinal product with unapproved use are specified in Annex V.

6.5. Timelines for Evaluation of the Request

The timelines for evaluation and action on a request for consideration for an E.U.A. will depend on the product's profile; the existence, if any, of pending applications for the product; the nature of the emergency; and other relevant factors. Although the length of

time required for action will vary, the <NMRA> recognizes that it is likely that, in a PHE that is occurring or believed imminent, a request for consideration for an E.U.A. will be acted upon with highest priority.

6.6. Validity, Revocation or Termination of an E.U.A.

The validity of an emergency use authorization in the context of a PHE will generally be for 12 months. An E.U.A. will be in effect for the duration of the declaration (as described in section 4.1 Declaration of Emergency), unless the E.U.A. is revoked because the criteria of issuance (as described in section 4.2 Eligibility for an Emergency Use Authorization) are no longer met or revocation is appropriate to protect public health or safety.

1. **Revocation:** The <NMRA> will periodically review the circumstances and appropriateness of an E.U.A, including circumstances that might warrant revocation of the E.U.A.. Such circumstances may include

- significant adverse inspectional findings (e.g., where an inspection of the manufacturing site and processes have raised significant questions regarding the purity, potency, or safety of the E.U.A. product that materially affect the risk-benefit assessment upon which the E.U.A. was based);
- reports of adverse events (number or severity) linked to, or suspected of being caused by, the E.U.A. product; product failure; product ineffectiveness (such as newly emerging data that undermine the <NMRA>'s conclusion that the product "may be effective" against a particular agent);
- and availability of a preferred product.

2. **Termination:** Upon termination of the declaration, an unapproved product or its labelling and product information for an unapproved use must be disposed of pursuant to <quote title of national medicines Act and section XX if applicable> of <country>. A manufacturer may choose to have an unapproved product returned after termination for registration of the <quote title of national medicines Act and section XX if applicable > of <country>. Notwithstanding any such termination, an authorization shall continue to be effective to provide for continued use in any patient who began treatment before termination (to the extent found necessary by the patient's attending physician).

3. **Continued Use:** Any use of an E.U.A. product beyond the term of a declaration is subject to investigational product regulations under clinical trials authorization, except for use by patients who began treatment when the declaration was in effect, to the extent found necessary by such patient's attending physician.

6.7. Publication

<NMRA> will promptly publish a notice of each E.U.A. on the <NMRA> website, including an explanation of the reasons for issuance, a description of the intended use, and any contraindications of the EUA product. <NMRA> also will promptly publish each

termination or revocation of an E.U.A. and an explanation of the reasons for the decision.

By publicly releasing information on an E.U.A., <NMRA> will take necessary steps to protect classified information and information otherwise protected by law, as appropriate.

Disclosures of information by <NMRA> to the Ministry of Health will be consistent with applicable laws protecting trade secrets and confidential commercial or financial information.

7. Post-Authorization Activities

Post E.U.A. monitoring

After a product has been approved and used, <NMRA> will take into consideration reports on safety surveillance, efficacy/effectiveness/performance monitoring, quality complaints and other relevant data that may impact the validity of the E.U.A..

The sources of such information will inter alia be based on existing surveillance mechanisms in <country> and on post-approval surveillance commitments of the manufacturer, set as conditions for the E.U.A.. The applicant must provide a Risk Management Plan considered necessary to identify, characterize and minimize the important risks of a medicinal product.

<NMRA> deems that the emergency use authorization holder is not responding to a post-approval quality/safety issue in a timely and/or scientifically sound manner and if post-approval quality/safety issues are identified and cannot be resolved to <NMRA>’s satisfaction, <NMRA> reserves the right to restrict or revoke the E.U.A. of the product.

Post-E.U.A. changes

The applicant must promptly inform <NMRA> of all changes regarding formulation, manufacturing process, testing methods, specifications, facilities and any other aspects that might result in a change of the safety and/or efficacy and/or performance of the product.

Definitions

Active (Pharmaceutical) Ingredient (API)

An active ingredient is any component that provides pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or animals. Synonym is “active substance”.

Agent

Pathogen/item specified in the declaration of emergency causing a serious or life-threatening disease or condition.

Applicant

A person or entity who has applied for regulatory approval of a product or a change thereof. All applicants are to own the product. Representatives of product owners may not hold themselves as applicants unless they own the product.

In some jurisdictions this term is used in a wider sense (see “Marketing authorization holder)”.

Batch Number

A distinctive combination of numbers and/or letters which specifically identifies a batch or lot and from which the production history can be determined.

Biological (product)

A medicine whose active substance is made by a living organism

Dosage Form

The pharmaceutical form in which the active pharmaceutical ingredient, excipients and physical formulation of a medicinal product is presented e.g. tablet, capsule, solution for injection, cream, inhalation etc.

Excipient

Is any constituent of a pharmaceutical form that is not an active pharmaceutical ingredient.

Finished Pharmaceutical Product (FPP)

Product that has undergone all stages of production, including packaging in its final container and labelling. An FPP may contain one or more active pharmaceutical ingredients.

Manufacturer (GL EUA)

Any person or entity with responsibility in manufacturing activities including implementation of oversight and controls over the manufacture of the medicinal product or active pharmaceutical ingredients or excipients to ensure quality.

Medicinal Product

Any substance or combination of substances prepared, sold or presented for use in the diagnosis, treatment, mitigation or prevention of disease, disorder of abnormal physical state or the symptoms of it or restoring, correcting or modifying organic functions in human beings

The term “medicinal products” in the context of TWG-MAG guidelines includes finished pharmaceutical products (FPPs), biotherapeutics and vaccines. Not included are medical devices, in-vitro diagnostics, blood products and animal products.

Risks

Any known and potential risks relating to the quality, safety or efficacy of the medicinal product as regards patients’ health or public health.

Risk-benefit analysis

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.

References

USFDA. Emergency Use Authorization of Medical Products and Related Authorities. Guidance for Industry and Other Stakeholders. January 2017. FDA/SMC/BPD/GL-EUM/2019/08.

WHO. NEW Emergency Use Listing Procedure (EUL) December 2020, Version 13 December 2020 https://extranet.who.int/pqweb/sites/default/files/documents/EUL-FINAL-13_12_2020.pdf

FDA Ghana. Guidelines For Emergency Use Authorization Of Medical Products February 2021, FDA/GEN/GL-EUA/2021/04.

EMA. Guideline on the scientific application and the practical arrangements necessary to implement Commission Regulation (EC) No 507/2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No 726/2004. 25 February 2016, EMA/CHMP/509951/2006, Rev.1, Committee for Medicinal Products for Human Use.

This guideline template is based on the structure of the Guideline on Guidelines V1, February 2021 developed by the joint working group of Food and Drugs Authority (<NMRA>, Ghana), Liberia Medicines & Health Products Regulatory Authority (LMHRA, Liberia), Medicines Control Agency (MCA, The Gambia), Pharmacy Board of Sierra Leone (PBSL, Sierra Leone), and the Global Health Protection Programme (GHPP) PharmTrain-Project of the Federal Institute for Drugs and Medical Devices (BfArM, Germany)

List of Annexes

Annex I: Format of Submissions

The <NMRA> expects material to be provided in a reviewable form in Common Technical Document (CTD) format and sufficiently complete to permit substantive evaluation.

Submissions shall be made in an electronic format:

1. Two (2) copies, either saved on a USB flash drive or on a CDs, together with an application letter addressed to the Head of the <NMRA>.
2. <NMRA> recommends that the submission begin with a section that describes the contents and organization of the included materials. The applicant or anyone with a right of reference may refer to data or other information previously submitted to the <NMRA> in a registration and/or marketing authorization application.
3. The <NMRA> expects material to be provided in a reviewable form and sufficiently complete to permit substantive evaluation. Nevertheless, the <NMRA> recognizes that, in rapidly developing or unexpected emergency circumstances, or when previously unanticipated or unavailable medicinal countermeasures are being considered, it may not be possible for an entity to provide all of the requested data or to provide it in the format suggested in a timely manner. In such circumstances, the <NMRA> will accept and evaluate the request for consideration for an E.U.A. based on data in the form an entity is able to submit. Missing data and poor documentation may lead to a request for additional information and thus, may cause a delay in the decision-making process or even the decision not to authorize emergency use of the medicinal product.
4. The address for submission of a request for consideration for an E.U.A. is:

<add appropriate address>

Annex II: Pre-submission meeting request form

EUA ASSESSMENTS

Please complete each section of this application form and submit electronically as a Word document to the <NMRA>. Attachments in electronic format that are 8MB or less in size can be sent by email with the completed pre-submission meeting request form, including a proposed agenda for the meeting. Attachments in electronic format that are larger than 8MB should be submitted on CD/DVD, or else be printed and sent by courier or surface mail to the relevant entity of the the <NMRA> <Address>

Applicant (name of manufacturer)	
Contact person responsible for this application	
Contact person's job title/position	
Contact details - postal address:	phone: fax email
Meeting Details	Type of meeting requested Face-to-face / Teleconference
Brief statement of the intended dossier (INN/strength/dosage form), and the expected date for submission to NMRA for E.U.A.	
Specific objectives/outcomes expected from the meeting	
Preliminary proposed agenda including estimated time needed for each agenda item (up to a maximum of 3 hours for the entire meeting) and designated speaker(s)	
List of specific questions by technical are	
List of all individuals (including titles) who will attend the proposed meeting from the applicant’s organization and/or consultants (up to a maximum of 10 proposed participants).	1. 2. 3. 4. 5. 6. 7. 8. 9. 10.

Proposed date(s) and time(s) for the meeting	
Additional information is attached:	Yes/No
Additional information will be forwarded separately: Yes	Yes/No
Completed by	Date

Annex III: Details on required information for submission

In general:

<NMRA> recommends that the request for consideration include the following types of data, as appropriate and to the extent feasible given the exigencies of the circumstances:

1. Well-organized study reports that provide a complete assessment and analysis of available safety and effectiveness data and an interpretation of the findings. If final study reports are not yet available, any available interim study reports should be provided and clearly identified as such
2. Any relevant statistical analyses and source data for clinical studies, nonclinical laboratory studies, and any animal studies demonstrating safety and efficacy of the product in the treatment of the underlying disease or condition or a closely related disease or condition, such as case report tabulations for key studies; case report forms for all patients who died during the clinical studies and for all persons who did not complete the study due to an adverse event, regardless of causality; relevant reports in the published literature; and notarized translations of source materials in a language other than English.

Annex IIIa: Recommended Safety Data

In general:

The amount and type(s) of safety data that <NMRA> recommends to be submitted as part of a request for consideration for an E.U.A. will differ depending upon a number of factors, including whether the product is approved for another indication and, in the case of an unapproved product, the product's stage of development. <NMRA> will interpret safety information in light of the seriousness of the clinical condition, alternative therapies (if any), and the specific circumstances of the emergency. <NMRA> strongly encourages any person or entity with an E.U.A. medicinal product to discuss with the <NMRA> at the earliest possible time (even before a determination of actual or potential emergency) the nature and type of safety data that might be appropriate to submit to <NMRA> (see chapter on pre-submission meetings above).

a) Unapproved uses of approved products

If the new indication uses a similar dose, duration, route of administration, and/or mechanism of action (as appropriate given the nature of the product), and the intended patient population is similar to that for which the product is approved, <NMRA> recommends references of the approved application if the requester submitted the approved application or has a right of reference. If the new use poses a different risk to the patient population (e.g., suggesting the possibility of increased toxicity), the <NMRA> recommends that information from relevant in vitro studies, animal toxicology studies, and (if available) human clinical data and experience be provided to support such a use.

b) Unapproved products

The range of available data for such products will differ widely. <NMRA> recommends that any request for consideration for an E.U.A. include available preclinical testing data, such as in vitro and animal toxicology data. The <NMRA> also strongly encourages that safety information in humans from clinical trials and individual patient experience should be provided, if available. <NMRA> further recommends that data submitted in the request attempt to link the likely patient exposure to any relevant existing preclinical data. Similarly, where animal data are used, sufficient information should be provided to link the results of these data to expected exposures related to the proposed use in humans. Any information on safety associated with use in humans of this or related compounds or devices of a similar design should be also submitted.

c) Approved products by another NMRA or reference institution

For data requirements for this approach reference is made to the “Guideline on Reliance”.

Annex IIIb: Recommended Effectiveness Data

In general for approved medicinal products with unapproved use as well as unapproved medicinal products:

<NMRA> recognizes that comprehensive effectiveness data are unlikely to be available for every E.U.A. medicinal product, and the information necessary to authorize emergency use of a product will depend on the circumstances of the declared emergency, as well as available knowledge about the product's safety profile. <NMRA> plans to assess the sufficiency of the effectiveness data and the risk-benefit profile of each candidate product on a case-by-case basis.

<NMRA> recommends that requests for consideration for E.U.A. include any available relevant scientific evidence regarding the following:

1. The mechanism(s) of the product's action to diagnose, treat, or prevent the disease or condition underlying the request.
2. Preclinical testing data, such as in vitro evidence of effect of the product in preventing or reducing the toxicity of the specified agent.
3. Data to demonstrate effectiveness in diagnosing, treating, or preventing the subject disease or condition in at least one animal species expected to react with a response predictive for humans, where the animal study endpoint is clearly related to the desired benefit in humans (e.g., enhancement of survival or prevention of major morbidity).
4. Evidence of effectiveness in humans (e.g., in published case reports, uncontrolled trials, controlled trials, if available, and any other relevant human use experience)
5. Data to support the proposed dosage (including pharmacokinetics and pharmacodynamic data) for the intended use.

Annex IIIc: Discussion of Risks and Benefits

Products to be used in PHE, in response to recognized health threats, may provide particularly important benefits, therefore higher risks related to the absence of some data may be acceptable. In such cases an E.U.A. can be granted also if preclinical or pharmaceutical data are not comprehensive.

<NMRA> recommends that a request for consideration for an E.U.A. include a discussion of the medicinal product's known and potential risks and benefits, which includes a synthesis of the data and information requested above, including:

1. Measures taken to mitigate risks or optimize benefits (How the anticipated benefits to public health in the context of immediate availability outweigh the risks (also taking into account the as yet missing information))
2. Limitations, uncertainty, and data gaps (Risks inherent in the fact that additional data are still required)
3. A description of circumstances, if any, under which the product should not be used (e.g., contraindications).
4. Benefits to public health of the immediate availability of the medicinal product on the market.

Annex IV: Conditions of Authorization

1. Information relating to the E.U.A. product:

    a. for Health Care Providers or Authorized Dispensers or Pharmacists:

To the extent consistent with other conditions of authorization, information on the E.U.A. of medicinal product should be disseminated to healthcare providers and authorized dispensers through media, videos/DVDs/CD-ROMs, the Internet, and direct communication from the <Ministry of Health>/<President>.

For an unapproved product and for an unapproved use of an approved product, <NMRA> must (to the extent practicable given the circumstances of the emergency) establish conditions to ensure that health care professionals who administer the E.U.A. product are quickly informed:

- That <NMRA> has authorized the emergency use of the product (including the product name and an explanation of its intended use);
- Of the significant known and potential benefits and risks of the emergency use of the product, and the extent to which such benefits and risks are unknown; and
- Of available alternatives and their benefits and risks.

Therefore, <NMRA> recommends that a request for an E.U.A. include a “Condition of Use " document for health care professionals or authorized dispensers that includes essential information about the product. In addition to the required information, this document should include:

- A description of the disease/condition;
- Any contraindications or warnings;
- Dosing information (if applicable), including any specific instructions for special populations; and
- Contact information for reporting adverse events and additional information about the product.

Annex Va provides a template for the “Information for Health Care Providers or Authorized Dispensers Or Pharmacists” as well as “Instructions for use”.

    b. Information for Recipients:

Although informed consent is not required for administration of an E.U.A. medicinal product, the information dissemination requirements are mandatory only to the extent conditions establishing such requirements are practicable. <NMRA> recommends that recipients be given as much appropriate information as possible given the nature of the emergency and the conditions of the authorization. For healthcare provider carrying out

any activity concerning an E.U.A, recipients must be informed that the <NMRA>'s CEO has authorized emergency use of the medicinal product, and has evaluated the potential benefits and risks of the medicinal product. Recipients must have an opportunity to accept or refuse the E.U.A. product and must be informed of any consequences of refusing administration of the product. Recipients also must be informed of available alternatives to the product and of their risks and benefits.<NMRA> requests that some form of written information will be given to recipients in the simplest language possible and using other techniques to improve health literacy. The <NMRA> recommends that the written information include the significant known and potential risks and benefits of the product and the extent to which the potential risks and benefits are unknown, specific instructions for home use (if necessary), and adverse event information, including contact information should adverse events occur. Furthermore, the <NMRA> recommends that the written information for recipients be tested (e.g., by focus groups) for clarity, particularly regarding messages on uncertainty and relative risks. <NMRA> acknowledges, however, that exigent circumstances may dictate the use of other, more appropriate, dissemination methods. Therefore, <NMRA> expects that recipient information would be disseminated in the most effective and expeditious way possible to reach the intended audience. Methods of dissemination may include media (e.g., public service announcements), videos/DVDs, the Internet, and direct communication from health care providers and public health agencies.

Annex Vb provides a template for the "Information for Recipients".

2. Monitoring and Reporting of Adverse Events:

<NMRA> recommends that the Ministry appoint a <Qualified Person for Pharmacovigilance (QPPV) from any established entity> with the experience in adverse event monitoring and reporting for E.U.A.. <NMRA> expects that the primary focus of such conditions will be on capturing serious adverse events and identifying the appropriate mechanism(s) to be used for the collection of follow-up clinical information, the size of the safety database, and the types of data needed. Predefined mechanisms to capture adverse event data are preferred, where feasible. In certain circumstances, other mechanisms also may be considered, such as using postage-paid postcards or stickers added to the product, labelling, and any other information that refers the health care provider or authorized dispenser and recipient to a toll-free number and Internet site to report adverse events such information could be included as part of the recipient information.

3. Records:

<NMRA> requires that records of unregistered product or unapproved use should be maintained and access be granted by the manufacturers to the <NMRA> given the circumstances of the emergency. The <NMRA> may impose comparable record requirements on any person other than a manufacturer who carries out any activity for an unapproved product. The <NMRA> anticipates that such record requirements may relate to the number of doses including lot number of the E.U.A. product; the name and

addresses of the facilities where the E.U.A. product was deployed; monitoring of patients who have been administered with the product under an E.U.A.. The <NMRA> also may impose conditions regarding other matters that the <NMRA> determines are appropriate and practicable given the circumstances of the emergency.

4. Importation authorization

5. Additional Conditions

a. for **Unapproved Products**:

To the extent feasible given the circumstances of the emergency, the <NMRA> may establish additional conditions for unapproved products, such as the following:

- Restricted distribution under the E.U.A.-conditions may be placed on which entities
- may distribute the product and how distribution is to be performed.
- Personnel conditions may be placed on who may administer the product, and on the categories of individuals to whom, and the circumstances under which, the product may be administered.
- Information -- conditions may be placed on the collection and analysis of information on the safety and effectiveness of the E.U.A. product.

The <NMRA> will establish these conditions on a case-by-case basis.

b. for an **Unapproved Use of an Approved Product**:

with respect to an E.U.A. that authorizes a change in labelling of an approved product, but for which the manufacturer chooses not to make such labelling change, the E.U.A. may not authorize a product distributor or any other person to alter or obscure the manufacturer's labelling. However, under such conditions, the <NMRA> must authorize, to the extent practicable under the circumstances of the emergency, any person (other than the manufacturer) acting pursuant to such E.U.A. to provide appropriate information, in addition to the manufacturer's labelling, with respect to the product.

The <NMRA> may establish conditions for distribution and administration of an approved product for an unapproved use that are no more restrictive than those established by the <NMRA> for the distribution and administration of the product for an approved use. Any such additional conditions will be established by the <NMRA> on a case-by-case basis, depending on the circumstances of the emergency and the nature of the approved product authorized for an unapproved use.

6. Compliance with GMPs or Alternative Approaches:

The <NMRA> expects that E.U.A. products will be produced in compliance with GMP; however, limits or waivers may be granted, on a case-by-case basis, after consideration of the circumstances and of any alternative proposed approach.

7. Advertising:

<NMRA> may establish conditions on advertisements and other promotional descriptive printed matter relating to the use of E.U.A. product.

8. Summary of Conditions for Authorization:

The following chart sets out conditions that may be imposed on an E.U.A. for unapproved products and for unapproved uses of approved products, respectively. A condition is identified as "mandatory" to the extent practicable given the circumstances of the emergency, to establish such condition when it is necessary or appropriate to protect the public health. A condition identified as "discretionary" in the chart below is one that the <NMRA> may impose as may be deemed necessary or appropriate to protect the public health. In addition to the conditions described as "mandatory" and "discretionary" in the chart below, the <NMRA> may establish other conditions on an authorization that may be necessary or appropriate to protect the public health.

E.U.A.	Unapproved Product	Unapproved Use of an Approved Product	Approved product by another NMRA
Information for Health Care Providers and Authorized Dispensers	Mandatory for manufacturers and applicant	Mandatory for manufacturers	Mandatory for manufacturers and others
Information for Recipients	Mandatory for manufacturers and applicant	Mandatory for manufacturers	Mandatory for manufacturers and others
Adverse Event Monitoring/Reporting	Mandatory for manufacturers and applicant	Mandatory for manufacturers	Mandatory for manufacturers and others
Recordkeeping/Access	Mandatory for manufacturers and applicant	Mandatory for manufacturers	Mandatory for manufacturers and others
Proof of Compliance with GMPs	Mandatory for manufacturers and others	Mandatory for manufacturers others	Mandatory for manufacturers and others
Advertising	Only after Approval by NMRA	Approval by NMRA	
Distribution	As determined by the NMRA	As determined by the NMRA	Discretionary for manufacturers and others
Post-E.U.A. Data Collection/Analysis	Mandatory for manufacturers and applicant	Mandatory for manufacturers and others	Mandatory for manufacturers and others

Annex Va: Health Care Provider Or Authorized Dispenser Or Pharmacist Information

[PRODUCT for INTENDED USE]

An emergency has been declared by the Minister of Health.

[INCLUDE A BRIEF DESCRIPTION (1-2 sentences) OF THE EMERGENCY].

The <NMRA> has authorized the emergency use of [PRODUCT] for a use [IDENTIFY THE INTENDED USE] that has not yet obtained <NMRA> approval or registration by usual <NMRA> processes. This authorization will terminate on [DATE 1 YEAR FROM THE DATE OF DECLARATION], or when the emergency has ceased to exist, whichever is earlier.

The information in this form is the minimum information necessary to inform you of the significant known and potential risks and benefits of emergency use of [PRODUCT].

The significant known and potential risks and benefits of emergency use of [PRODUCT] are: [LIST]. The extent to which such risks and benefits are unknown is [EXPLAIN].

The available alternatives to [PRODUCT] are: [LIST]. The risks and benefits of [ALTERNATIVES] are: [LIST]. [If there is no alternative, provide an explanation of outcomes of exposure or of any special public health measures (e.g., quarantine or monitoring) that an individual who does not receive the E.U.A product may face.]

INCLUDE NAME, ADDRESS, AND TELEPHONE NUMBER FOR MANUFACTURER.]

As the health care provider or authorized dispenser or pharmacist administering [PRODUCT], please communicate the significant known and potential risks and benefits, and the extent to which such risks and benefits are unknown, to the recipient of [PRODUCT].

Please inform the recipient that he or she has the option to accept or refuse administration of [PRODUCT], and of the consequences of refusing administration. Please inform the recipient of any available alternatives to [PRODUCT], and of their risks and benefits. Please provide the “Recipients Information” to the recipient of [PRODUCT]. <NMRA>/SMC/BPD/GL-EUM/2019/08 26

If providing this information before administration would delay the administration [PRODUCT] to a degree that would endanger the lives of exposed or affected individuals, the information must be provided to the recipient as soon as practicable after [PRODUCT] is administered.

<NMRA> also recommends that E.U.A applicants include the following additional information in the "Conditions of Use" document for Health Care Providers or Authorized Dispensers or Pharmacist if it is available.

Instructions For Use by the Health Care Provider Or Authorized Dispensers

How to administer the product (including dose, route of intake or infusion, how long to use the product, how to take care of the infusion site), how to store the product, how it is supplied/forms that it comes in, how to constitute;

Known major interactions with other products or substances, including drug interactions, cross reactivity for IVDs.

Known efficacy information or performance characteristics (for IVDs)

Contraindications or warnings

Adverse events. Significant known adverse event information (e.g., what are the significant known side effects? Under what conditions should the recipient stop taking product?), instructions for follow up in case of an adverse event, how to report an adverse event, what to do in case of an adverse event (stop using the product? seek treatment?), whom to contact for professional advice if an adverse event occurs or if the product does not work. Health care providers or authorized dispensers or Pharmacist also may report adverse events to the <NMRA>.

Alternatives. If other agents (approved/licensed/cleared products or E.U.A products) may treat or prevent the same or closely related condition for [INTENDED USE], this information should be stated. If available, the relative or expected safety and effectiveness of the alternative should be provided, particularly for use in different populations or settings. Such information may include:

- When an alternative product may be more appropriate, e.g., in the treatment of the pregnant women, infants and children, and immunocompromised individuals, or other special populations.
- For preventive treatments, the time needed for [PRODUCT] to be administered in advance of the exposure to be effective, and alternatives that may be more effective if that time is exceeded.

Significant known and potential risks and benefits may include relevant information about the manufacturer (e.g., a waiver of Good Manufacturing Practices compliance), if known.

Consequences of not taking/using [PRODUCT], including possible health effects and quarantine, and of stopping the use of [PRODUCT] against the recommendation of the health care provider.

New findings. A statement about the fact that any significant new findings observed during or after the course of widespread use will be made available.

Approved products. For approved products being used for unapproved indications, the "Conditions of Use" document also may include critical elements from the package insert.

Contacts. Whom to contact if you have any questions or concerns (other than an adverse event report) about the product.

Annex Vb: Recipients Information

[PRODUCT for INTENDED USE]

An emergency has been declared by the Minister of Health

[INCLUDE A BRIEF DESCRIPTION (1-2 sentences) OF THE EMERGENCY].

The <NMRA> has authorized the emergency use of [PRODUCT] for [IDENTIFY THE INTENDED USE (+ Dosing)]. This authorization will terminate on [DATE 1 YEAR FROM THE DATE OF DECLARATION], or when the emergency has ceased to exist, whichever is earlier.

The information in this condition of use is the minimum necessary to inform you of the significant known and potential risks and benefits of emergency use of [PRODUCT].

The significant known and potential risks and benefits of emergency use of [PRODUCT] are: [LIST]. The extent to which such risks and benefits are unknown is [EXPLAIN].

The available alternatives to [PRODUCT] are: [LIST]. The risks and benefits of [ALTERNATIVES] are: [LIST]. [If there is no alternative, provide an explanation of outcomes of exposure or of any special public health measures (e.g., quarantine or monitoring) that an individual who does not receive the E.U.A product may face.]

[INCLUDE NAME, ADDRESS, AND TELEPHONE NUMBER FOR MANUFACTURER.]

You have the option to accept or refuse administration of [PRODUCT]. The consequences of refusing administration of [PRODUCT] are [LIST].

Available alternatives to [PRODUCT] are: [LIST]. The risks and benefits of these alternatives are: [LIST].

Potential adverse events for [PRODUCT] include [LIST]. Should you experience an adverse event, [INCLUDE INSTRUCTIONS].

Any significant new findings observed during the course of emergency use of [PRODUCT] will be made available [STATE HOW FINDINGS WILL BE MADE AVAILABLE].