FOOD AND DRUGS AUTHORITY

GUIDELINES FOR EMERGENCY USE AUTHORIZATION OF MEDICAL PRODUCTS

Document No.	**:FDA/SMC/BPD/GL-EUM/2019/10**
Date of First Adoption	**:15th March, 2019**
Date of Issue	**:15th March,2019**
Version No.	**:01**

1. ACKNOWLEDGEMENT

The Food and Drugs Authority acknowledges the technical support of the United States Food and Drugs Administration (USFDA) in the development of these guidelines.

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1.0 INTRODUCTION

These guidelines publish the regulatory requirements for authorizing the emergency use of a Medical Product (Allopathic Medicines, Biological Medicinal Products and Medical Devices) during a declared public health emergency. Such emergencies shall include, but not limited to, a heightened risk of affliction or attack on the life, health, safety and security of the general public or any incident with a significant potential to affect national security. These guidelines should be read in conjunction with other guidelines on the Food and Drugs Authority's (FDA) website <www.fdaghana.gov.gh>. Those documents provide specific guidance on the labeling requirements.

The Food and Drugs Authority (FDA) shall leverage sections 118, 169, 170, 171,172 and 173 of the Public Health Act (Act 851) during a declared public health emergency to approve the use of an unregistered medical product - under the Emergency Use Authorization (E.U.A) framework - to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by such agents, when there are no adequate, approved, and available alternatives.

These guidelines are intended to inform industries, government agencies, and the general public on the general recommendations and procedures for issuance of an Emergency Use Authorization (E.U.A). The FDA expects that a Government Ministry, Department or Agency (MDA) or any other recognized agency (e.g., the Ministry of Health or the Ministry of Defense, Ministry of Interior, an entity appointed by a Government MDA, etc.) shall submit the request for consideration of an E.U.A. The FDA may seek additional data and information on a case-by-case basis to ensure that the statutory requirements for the issuance of an E.U.A are met.

1.1 SCOPE

In pursuant of Sections 118, 169, 170, 171,172 and 173 of the Public Health Act 2012, Act 851, this document would provide guidance to applicants on the approval for use during a public health emergency of an unregistered medical product.

2.0 GLOSSARY

- **"Authority"** means Food and Drugs Authority
- **"Applicant"** means the product owner or license holder. Representatives of license holders may not hold themselves as applicants unless they own the product.
- **"Accelerated stability studies"** means studies designed to determine the rate of change of vaccine properties over time as a consequence of the exposure to temperatures higher than those recommended for storage. These studies may provide useful support data for establishing the shelf-life or release specifications but should not be used to forecast real time real condition stability of a vaccine. They could also provide preliminary information on the vaccine stability at early developmental stages and assist in assessing stability profile of a vaccine after manufacturing changes.
- **Biological Medicinal Product** means items derived from living organisms (ranging from normal or genetically modified microorganisms to fluids, tissues and cells derived from various animal and human sources) or containing living organisms that are used to;
    - Treat or prevent diseases or manage injury
    - Diagnose medical condition
    - Alter the physiological processes
    - Test the susceptibility to diseases

  Such items include;

    - Products of genetically modified organisms (e.g. insulin etc.)
    - Traditional vaccines (bacterial, viral, combination etc.)

- Immunotherapy products (e.g. cell based tumour vaccines, human cellular vaccines etc.)
- Peptides and Polypeptides (e.g. insulin, cytokine etc.)
- Monoclonal antibodies
- Other human cell based products (e.g. fibroblast, epithelial cells, chondrocytes)

- **“Drug”** means (a) a substance referred to in a publication mentioned in the fourth schedule, (b) a substance or mixture of substances prepared, sold or represented for use in, (i) the diagnosis, treatment, mitigation or prevention of disease, disorder of abnormal physical state or the symptoms of it, in human or animal, or (ii) restoring, correcting or modifying organic functions in man or animal, and (c)nutritional supplements;
- **“Medical Device**” means an instrument or apparatus including components, parts and accessories of it manufactured, sold or represented for use in the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state or the symptom of it in man or animal;
- **“Equivalent”** means equal or virtually identical in the parameter of interest. Small non-relevant differences may exist. Equivalent efficacy of two drug products means they have similar (no better or no worse) efficacy and any observed differences are of no clinical relevance.
- **“ICH” means International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.** ICH is a project that brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration. The purpose is to make recommendations on ways to achieve greater harmonization in the interpretation and application of technical guidelines and requirements for product registration in order to reduce or obviate the need to duplicate the testing carried out during the research and development of new medicines. For more information, see http://www.ich.org/.

- **Lot release:** process for the evaluation of each individual lot of vaccine submitted be used in the market; this means independent control of each lot to guarantee that all the lots produced and used in a country are in compliance with the established quality specifications. This process can be performed by detailed review of Summary Protocols of Production and Quality Control, and includes laboratory testing when it is considered necessary.
- **License:** in some countries it is called registration. Procedure whereby the National Regulatory Authority grants permission for the product in question to be sold and distributed in the country.
- **Master cell bank:** culture of specific cells of known origin that are distributed in a container or packages in a single operation to ensure uniformity and stability in storage. The master bank is usually kept at a temperature of -70°C or less. In some countries, it is called the primary bank.
- **Product development:** all studies to show that the dose, formulation, manufacturing process and packaging system, as well as the microbiological properties, are appropriate for the proposed purpose.
- **Product to be licensed:** both, the document outlining the harmonized requirements for the licensing of vaccines in the Americas and its guidelines for preparation of application, apply to the registration of vaccines in the Americas. The vaccine may be also referred as the product.
- **Raw materials:** any substance used to make or extract the active ingredient but from which the active ingredient is not directly derived. For example, culture media, fetal bovine serum, etc.
- **Starting materials:** any substance of biological origin, such as microorganisms, organs and tissues of plant or animal origin, including cells or fluids of human or animal origin and recombinant cell substrates.
- **Validation:** series of documented procedures or actions, consistent with good manufacturing practices, demonstrating that the processes, equipment, materials, activities and/or systems satisfy the predetermined specifications and quality attributes.

3.0 REQUIREMENTS

3.1 Declaration of A Public Health Emergency

The Minister responsible for Health shall declare a public health emergency by an Executive Instrument when a situation which poses an immediate risk to health, life, property or the environment arise. To meet the criteria for a public health emergency, the incident should;

a) Immediately threaten life, health, property or the environment;
b) Have already caused loss of life, health detriments, property damage or environmental damage; OR
c) Have a high probability of escalating to cause immediate danger to life, health, property and the environment.

3.2 Eligibility for Emergency Use Authorization (E.U.A)

This is when an unregistered medical product can be authorized for use during a declared public health emergency involving a heightened risk of affliction or attack on the health, 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 under section 118 of the Public Health Act (Act 851). However, the FDA may issue an E.U.A only if, after consultation with the Ministry of Health and/or the FDA's Technical Advisory Committees (TACs) for the Safety of Medicines, Vaccines and Biological Products, and Medical Devices (to the extent feasible and appropriate given the circumstances of the emergency), the FDA concludes:

i. that the agent/pathogen/item/ specified in the declaration of public health emergency can cause a serious or life-threatening disease or condition;
ii. that, 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 paragraph (1); or (b) a serious or life-threatening disease or condition caused by a product authorized under section 118, or approved, cleared, or registered for diagnosing, treating, or preventing the disease or condition referred to in paragraph (1) and caused by the agent specified in the declaration of emergency;

iii. that 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; and

iv. that there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating such serious or life-threatening disease or condition.

3.3 Risk-Benefit Analysis:

Products are eligible for Emergency Use Authorization (E.U.A.), if FDA determines that the known and potential benefits of the product, when used to diagnose, prevent, or treat the identified disease or condition, outweigh the known and potential risks of the product. In determining whether the known and potential benefits of the product outweigh the known and potential risks, FDA intends to assess the quality and quantity of the evidence, given the current state of scientific knowledge, of risks and benefits. The FDA intends to use this information to make an overall risk-benefit determination. To accomplish this, FDA plans to look at the totality of the scientific evidence, which could arise from a variety of sources. The Agency intends to evaluate and consider all evidence, including results of domestic and foreign clinical trials, animal data, and in vitro data, available for consideration. FDA anticipates that, for some candidate products, data from controlled clinical trials will be available. For others, the FDA expects to consider clinical study other than a controlled trial if the circumstances

warrant. For others, in vivo efficacy data may only be available from animal models.

3.4 Alternatives to the Product:

The FDA may issue an E.U.A if it determines that there is no adequate, approved, and available alternative to the candidate product. A potential alternative product may be considered as:

a) “unavailable” if there are insufficient supplies to meet fully the emergency need.
b) "inadequate" if there are contraindicating data for special circumstances or populations (e.g., immunocompromised individuals or individuals with a drug allergy) or if the agent is or may be resistant to approved and available alternative products.

3.4 Request for consideration for an E.U.A.

Although an E.U.A. may not be issued until after a Public Health Emergency has been declared by the Minister, FDA 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 FDA strongly encourages an entity with a possible candidate product, particularly one at an advanced stage of development, to contact the FDA for the candidate product even before a determination of 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 types of information FDA believes are important to allow an assessment of safety and effectiveness and to make an adequate risk-benefit determination to support issuance of an E.U.A.

3.5 Pre-emergency activities:

Such activities may include discussions with FDA about a prospective E.U.A product and the appropriate procedure to use, when submitting data on the product prior to a determination of actual or potential emergency. The FDA strongly recommends that an entity submitting data during a "pre-emergency" period follow the recommendations for data submission contained in "Submission of a Request for Consideration," below. If, prior to the declaration of an emergency, FDA believes that a candidate product may meet the criteria for an E.U.A, the FDA may share appropriate information on such product with the ministry of health.

3.7 Emergency Activities:

Once a determination of actual or potential emergency has been made under section 169, the Minister responsible for health may declare an emergency justifying the authorization to use an unregistered medical product for an unapproved use. The Minister will consult with the FDA 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.

3.8 Submission of a request for consideration:

Based on the totality of scientific evidence available to the FDA (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 vary depending on the nature of the declared emergency and the nature of the candidate product. To facilitate FDA evaluation of such data, the Authority recommends that a request for consideration for an E.U.A include a well-organized summary of the available scientific evidence that evaluates the product's safety and effectiveness, including

the adverse event profile when used for diagnosis, treatment, or prevention of the serious or life-threatening disease or condition, as well as data and other information on safety, effectiveness, risks and benefits, and (to the extent available) alternatives.

The information below summarizes the types of data that FDA recommends to be submitted to support a request for consideration for an E.U.A.

For FDA to evaluate a request for consideration for an E.U.A, the following information should be submitted:

i. 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)
ii. identification and an explanation of what unmet need(s) would be addressed by issuance of the E.U.A
iii. a description of the product's international registration/Marketing Authorization (MA) status, i.e., whether the product is prequalified by an international organization such as WHO
iv. a list of each site where the product, if authorized, would be (or was) manufactured and the Good Manufacturing Practices (GMP) status of the manufacturer
v. identification of any approved alternative products, including their availability and adequacy for the proposed use (if known)
vi. available safety and efficacy information for the product
vii. a discussion of risks and benefits
viii. a description of the information for health care providers or authorized dispensers and recipients of the product, (e.g., two separate “Fact Sheets”), and the feasibility of providing such information to health care providers or authorized dispensers and recipients in emergency situations
ix. information on chemistry, manufacturing, and controls
x. Certificate of Analysis of the E.U.A medical product instructions for use as E.U.A product (e.g., if follow-up treatment is required)

xi. Proposed labeling (if applicable). Including batch number, manufacturing date and expiry date

xii. Name of reference substance/material (if applicable).

These recommendations are discussed in more detail below.

3.9 Recommended Safety Data

In general:

The amount and type(s) of safety data that FDA recommends 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. FDA will interpret safety information in light of the seriousness of the clinical condition, alternative therapies (if any), and the specific circumstances of the emergency. FDA strongly encourages any person or entity with an E.U.A drug to discuss with the Authority 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 FDA.

In the case of previously 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, FDA recommends that the request for consideration for an E.U.A reference 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 Authority 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.

In the case of products under development:

The range of available data for such products will differ widely. FDA 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 FDA also strongly encourages that safety information in humans from clinical trials and individual patient experience be provided, if available. FDA 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 also should be submitted.

3.10 Recommended Effectiveness Data

In general:

FDA recognizes that comprehensive effectiveness data are unlikely to be available for every E.U.A drug, 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. FDA plans to assess the sufficiency of the effectiveness data and the risk-benefit profile of each candidate product on a case-by-case basis.

The FDA recommends that requests for consideration for E.U.As include any available relevant scientific evidence regarding the following:

a) the mechanism(s) of the product's action to diagnose, treat, or prevent the disease or condition underlying the request
b) preclinical testing data, such as in vitro evidence of effect of the product in preventing or reducing the toxicity of the specified agent
c) 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)

d) evidence of effectiveness in humans (e.g., in published case reports, uncontrolled trials, controlled trials, if available, and any other relevant human use experience)

e) data to support the proposed dosage (including pharmacokinetics and pharmacodynamics data, and for vaccines or antibody therapies, immunogenicity and/or achievement of protective levels of relevant parameters of immunity) for the intended use

4.0 OTHER DATA CONSIDERATIONS

4.1 In general:

FDA 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:

I. 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

II. Any relevant statistical analyses; and

III. Source data for clinical studies, nonclinical laboratory studies, and any animal studies demonstrating activity or effectiveness 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 translations of source materials in a language other than English.

4.2 Data Quality:

The FDA recommends that requests for consideration for E.U.As 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.

4.3 Data Updates:

The FDA recommends that any data from any ongoing testing (e.g., longer term stability data) or other data or information that may change the FDA'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) be submitted to the Agency when such data become available.

4.4 Discussion of risks and benefits:

FDA recommends that a request for consideration for an E.U.A include a discussion of the drug’s known and potential risks and benefits, which includes a synthesis of the data and information requested above, including:

i. Measures taken to mitigate risk or optimize benefit
ii. Limitations, uncertainty, and data gaps
iii. A description of circumstances, if any, under which the product should not be used (e.g., contraindications).

4.5 Format of submissions:

Submissions shall be made in an electronic format: two (2) copies, either saved on a USB flash drive or on a CDs, together with an application letter addressed to the Chief Executive Officer (CEO) of the Food and Drugs Authority (FDA).

The FDA 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 FDA in a registration and/or marketing authorization application.

The FDA expects material to be provided in a reviewable form and sufficiently complete to permit substantive evaluation. Nevertheless, the FDA recognizes

that, in rapidly developing or unexpected emergency circumstances, or when previously unanticipated or unavailable medical 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 FDA 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. However, a request for consideration that is missing data or that is otherwise incomplete or poorly documented will make determination of whether the product's benefits outweigh its risks more difficult and may, for that reason, be more likely to result in a request for additional information, the need for a longer time period for evaluation, or a decision not to authorize emergency use of the drug.

The address for submission of a request for consideration for an E.U.A. is:

THE CHIEF EXECUTIVE OFFICER
FOOD AND DRUG AUTHORITY
P. O. BOX CT 2783
CANTONMENTS
ACCRA

4.6 Processing of an Emergency Use Authorization (E.U.A)

This section discusses FDA's role in pre-emergency activities for E.U.A drug, as well as the procedures the Authority will follow in processing a request for consideration for an E.U.A once the Minister has issued a declaration of public health emergency.

4.6.1 Prioritization of Pre-Emergency Activities:

The Authority intends to establish priorities for the activities it undertakes, prior to a determination of actual or potential emergency. Such prioritization may be based on the circumstances, such as:

a. the seriousness of the clinical condition;
b. the incidence of the clinical condition;
c. the effect use of the product may have in ensuring national security;

d. whether the product is included in government stockpiles or whether there is a significant likelihood that the product will be included in government stockpiles if an E.U.A is granted;
e. whether the product could be used by a large population or is limited to subpopulation(s);
f. request of another government agency;
g. 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);
h. the availability and, where known, safety and effectiveness of other countermeasures;
i. the urgency of the treatment need (i.e., the window of opportunity for treatment can vary between different medical conditions)
j. the available information concerning the likelihood that the product may be safe and effective in treating the condition
k. the adequacy of the supporting nonclinical and clinical information; and
l. the quantity of product available

The FDA intends to establish priorities for its pre-emergency activities at the Division level or higher and, as appropriate and feasible, will consult with the Ministry and may consult other agencies on its priority setting.

4.7 Pre-emergency submission:

To allow the FDA evaluation process to begin before a determination of actual or potential emergency, the FDA 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 submission will be determined on a case-by-case basis and will depend on the nature of the emergency.

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

4.8 Prioritization of requests for consideration for an E.U.A during a declared public health emergency:

Once the Minister has declared an emergency justifying the authorization to use an unregistered product or an unapproved use of an approved product, the FDA intends to prioritize its evaluation of requests for consideration for an E.U.A based on factors such as:

a. the seriousness of the clinical condition;
b. the incidence of the clinical condition;
c. the likelihood that the product may be effective in treating the condition;
d. the effect use of the product may have in ensuring national security;
e. whether the product is included in government strategic stockpiles;
f. 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);
g. request of another government agency;
h. 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);
i. the availability and, where known, safety and effectiveness of other countermeasures;
j. the urgency of the treatment need (i.e., the window of opportunity for treatment can vary between different medical conditions);
k. The adequacy of the supporting nonclinical and clinical information; and
l. The quantity of product available**.**

4.9 Consideration for an E.U.A request:

The FDA will be responsible for the overall disposition of the request and will interact directly with the entity submitting the request for consideration. The FDA 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 FDA 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.

FDA 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 FDA 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 evaluation of the information and data included in the request for consideration and make recommendations to the CEO. The letter of authorization or otherwise will be issued by the CEO of the FDA. The letter authorizing emergency use of a product will include a description of the intended use, as well as the indications and contraindications of the product.

4.10 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 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 F recognizes that it is likely that, in an emergency situation that is occurring or believed imminent, a request for consideration for an E.U.A will be acted upon within a matter of days.

4.11 Conditions of Authorization

4.11.1 Conditions of Authorization for Emergency Use of an unregistered or unapproved use of a registered drug:

4.11.1 Information for Health Care Providers or Authorized Dispensers:

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

4.11.2 Information for Recipients: Although informed consent is not required for administration of an E.U.A drug, the information dissemination requirements are mandatory only to the extent conditions establishing such requirements are practicable. FDA 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 FDA's CEO has authorized emergency use of the drug, and has evaluated the potential benefits and risks of the drug. 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.

FDA recommend 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 Authority 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 Authority recommends that the written information for recipients be tested (e.g., by focus groups) for clarity, particularly regarding messages on uncertainty and relative risks. FDA acknowledges, however, that exigent circumstances may dictate the use of other,

more appropriate, dissemination methods. Therefore, FDA 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.

4.11.3 Monitoring and Reporting of Adverse Events: FDA 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 drug. FDA 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, labeling, 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.

4.11.4 Records: FDA requires that records of unregistered product or unapproved use should be maintained and access be granted by the manufacturers to the Authority given the circumstances of the emergency. The FDA may impose comparable record requirements on any person other than a manufacturer who carries out any activity for an unapproved product. The Authority 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 FDA also may impose conditions regarding other matters that the Authority determines are appropriate and practicable given the circumstances of the emergency.

4.11.5 Additional Conditions for Unapproved Products: To the extent feasible given the circumstances of the emergency, the FDA may establish additional conditions for unapproved products, such as the following:

a. Restricted distribution under the E.U.A --conditions may be placed on which entities
b. may distribute the product and how distribution is to be performed.
c. 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.
d. Information -- conditions may be placed on the collection and analysis of information on the safety and effectiveness of the E.U.A product.

The FDA will establish these conditions on a case-by-case basis.

Additional conditions for an unapproved use of an approved product:

With respect to an E.U.A that authorizes a change in labeling of an approved product, but for which the manufacturer chooses not to make such labeling change, the E.U.A may not authorize a product distributor or any other person to alter or obscure the manufacturer's labeling. However, under such conditions, the FDA 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 labeling, with respect to the product.

The FDA 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 Authority for the distribution and administration of the product for an approved use. Any such additional conditions will be established by the FDA 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.

Compliance with GMPs or Alternative Approaches:

The FDA expects that an 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.

Advertising: The FDA may establish conditions on advertisements and other promotional descriptive printed matter relating to the use of E.U.A product.

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 FDA 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 FDA may establish other conditions on an authorization that may be necessary or appropriate to protect the public health.

CONDITION OF AUTHORIZATION	**UNREGISTERED PRODUCT**	**UNAPPROVED USE OF A REGISTERD PRODUCT**
Information for Health Care Providers and Authorized Dispensers	Mandatory for manufacturers and others	Mandatory for manufacturers
Information for	Mandatory for	Mandatory for

Recipients	manufacturers and others	Manufacturers
Adverse Event Monitoring/Reporting	Mandatory for manufacturers and others	Mandatory for manufacturers
Recordkeeping/Access	Mandatroy for manufacturers and others	Mandatory for manufacturers
Compliance with GMPs	Mandatory for manufacturers and others	Discretionary for manufacturers others
Advertising	Discretionary for manufacturers and others	Discretionary for manufacturers and others
Restricted Distribution	Discretionary for manufacturers and others	Discretionary for manufacturers and others
Restricted Administration	Discretionary for manufacturers and others	Discretionary for manufacturers and others
Data Collection/Analysis	Discretionary for manufacturers and others	

* Others may include relevant agencies

4.12 Revocation or Termination of an E.U.A

An E.U.A. will be in effect for the duration of the declaration under which it was "Declaration of a Public Health Emergency," above), unless the E.U.A is revoked because the criteria of issuance "Eligibility for an Emergency Use Authorization," above) are no longer met or revocation is appropriate to protect public health or safety.

Revocation: The FDA 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 Authority's conclusion that the product "may be effective" against a particular agent); and availability of a preferred product.

Termination: Upon termination of the declaration, unapproved product or labeling and product information for an unapproved use must be disposed of pursuant to section 110 of the Public Health Act, 2012 (Act 851). A manufacturer may choose to have unapproved product returned after termination for registration under section 118 of the Public Health Act, 2012 (Act 851). 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).

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.

APPENDIX 1

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 FDA has authorized the emergency use of [PRODUCT] for a use [IDENTIFY THE INTENDED USE] that has not yet obtained FDA approval or registration by usual FDA 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].

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.

FDA also recommends that E.U.A applicants include the following additional information in the Fact Sheet for Health Care Providers or Authorized Dispensers or Pharmacist if it is available.

APPENDIX 2

1.7 INSTRUCTIONS FOR USE

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;

If it is an in vitro diagnostic (IVD): what type of specimens should be collected for testing with the product, how to store the specimens, how the laboratory should use the product, how to interpret the results; and instructions for use in special populations (i.e. pregnant women, infants and children, and immunocompromised individuals), including special dosing instructions (e.g., weight-based dosing), special precautions.

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

Known efficacy information or performance characteristics (for IVDs)

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 FDA.

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:

a) 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.
b) 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 Fact Sheet 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.

APPENDIX 3

RECIPIENT 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 FDA has authorized the emergency use of [PRODUCT] for [IDENTIFY THE INTENDEDUSE]. 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 Fact Sheet 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].

FOOTNOTES

FDA may issue subsequent guidance providing greater detail on these recommendations and procedures.

The FDA may issue one or more E.U.As on the basis of a single declaration of emergency provided that the E.U.As are intended for use in the same emergency involving the same biological agents.

For purposes of this document, an "unapproved" product refers to a product that is not approved, licensed, or registered for commercial distribution under sections 118 of the Public Health Act 2012.

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

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

FDA anticipates that distribution of E.U.A products will be performed according to existing response plans, as practicable and appropriate.