DRAFT GUIDANCE

Emergency Use Authorization of Medical Products

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U.S. Department of Health and Human Services
Food and Drug Administration
Office of the Commissioner
Office of Counterterrorism Policy and Planning

June 2005

Contains Nonbinding Recommendations

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U.S. Department of Health and Human Services
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DRAFT GUIDANCE[1]
Emergency Use Authorization of Medical Products

This draft guidance document represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You may use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, please contact the appropriate FDA staff.

I. INTRODUCTION

This draft guidance, when final, will explain FDA's policies for authorizing the emergency use of medical products under section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360bbb-3), which was amended by the Project BioShield Act of 2004 (Public Law 108-276).[2] Section 564 permits the FDA Commissioner to authorize the use of an unapproved medical product or an unapproved use of an approved medical product during a declared emergency involving a heightened risk of attack on the public or U.S. military forces.

The Emergency Use Authorization (EUA) authority recently granted by Congress allows the FDA Commissioner to strengthen the public health protections against biological, chemical,

[1] This draft guidance was prepared by the Emergency Use Authorization (EUA) Principals Group and the EUA Working Group. The EUA Working Group (WG) is composed of members with expertise in public health, medical, regulatory, legal, ethical, and risk communication areas. The WG, on an ongoing basis, examines issues related to issuance and implementation of an EUA. This group provides expert advice to both the Commissioner of the Food and Drug Administration (FDA Commissioner) and the Secretary of Health and Human Services (the Secretary).

[2] Section 903 of the FD&C Act and existing delegations of authority, found in the FDA Staff Manual Guide 1410.10, permit the authority of the Secretary to issue an EUA under section 564 of the FD&C Act to be delegated to the FDA Commissioner. The Secretary has delegated his authority to issue an EUA under section 564 to the FDA Commissioner. Thus, in this document the FDA Commissioner is identified rather than the Secretary except where the Secretary retains the authority.

radiological, and nuclear agents that may be used to attack the American people or the U.S. armed forces. Under section 564, the FDA Commissioner may allow medical countermeasures to be used in an emergency 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.

The document is intended to inform industry, government agencies, and FDA staff of the Agency's general recommendations and procedures for issuance of EUAs.[3] FDA expects that requests for consideration for an EUA would be submitted by government agencies (e.g., the Department of Health and Human Services or the Department of Defense (DoD)) or private entities. FDA may seek additional data and information on a case-by-case basis to ensure that the statutory criteria for issuance of an EUA are met.

Additionally, the Secretary of Health and Human Services (the Secretary) will establish a permanent Emergency Use Authorization Working Group (EUA WG), headed by the Assistant Secretary of Public Health Emergency Preparedness (ASPHEP), with representatives from FDA, the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), the Department of Defense (DoD), the Department of Homeland Security (DHS), the Department of Veterans Affairs and, as appropriate, participants from other Federal agencies, to identify and provide expert consultation on potential EUA candidates prior to and during declared emergencies.

[3] FDA Centers may issue subsequent guidance providing greater detail on these recommendations and procedures.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. DECLARATION OF EMERGENCY

Section 564(b)(1) of the FD&C Act provides that, before an EUA may be issued, the Secretary must declare an emergency based on one of the following grounds:

(1) a determination by the Secretary of Homeland Security that there is a domestic emergency, or a significant potential for a domestic emergency, involving a heightened risk of attack with a specified biological, chemical, radiological, or nuclear agent or agents;

(2) a determination by the Secretary of Defense that there is a military emergency, or a significant potential for a military emergency, involving a heightened risk to United States military forces of attack with a specified biological, chemical, radiological, or nuclear agent or agents; or

(3) a determination by the Secretary of a public health emergency under section 319 of the Public Health Service Act (PHS Act) that affects, or has the significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such agent or agents.

Once the Secretary has declared an emergency justifying an authorization under section 564 to use an unapproved medical product or an approved product for an unapproved use, the ASPHEP may convene the EUA Working Group to provide expert consultation to the FDA.[4] Based on his review of the information and data submitted to the Agency and input from the EUA WG (if convened) and after consulting with the Director of NIH and the Director of CDC (to the extent feasible and appropriate given the circumstances of the emergency), the FDA Commissioner may authorize the emergency use of a particular product, assuming other statutory criteria and conditions are met.[5]

Section 564(b)(2) states that a declaration of emergency will terminate one year after issuance or earlier if the Secretary determines, in consultation (as appropriate) with the Secretary of Homeland Security or the Secretary of Defense, that the circumstances that precipitated the declaration have ceased. Before a declaration terminates, the Secretary must provide, under section 564(b)(3), advance notice that is sufficient to allow for disposition of unapproved product or any labeling or other information provided related to an unapproved use of an approved product. Section 564(b)(2)(B) also authorizes the Secretary to renew a declaration.

Publication: The Secretary will promptly publish in the Federal Register notice of each determination of actual or potential emergency, the Secretary's declaration of emergency,

[4] The FDA Commissioner may issue one or more EUAs on the basis of a single declaration of emergency, under section 564(b)(1), provided that the EUAs are intended for use in the same emergency involving the same biological, chemical, radiological, or nuclear agent or agents.

[5] For purposes of this document, an "unapproved" product refers to a product that is not approved, licensed, or cleared for commercial distribution under sections 505, 510(k), or 515 of the FD&C Act or section 351 of the Public Health Service Act (PHS Act); an "unapproved use of an approved product" refers to a product that is approved, licensed, or cleared under such provisions but which use is not an approved, licensed, or cleared use of the product (21 U.S.C. 360bbb-3).

advance notice of termination, and renewal of a declaration issued under section 564(b).[6] The FDA Commissioner will promptly publish in the Federal Register a notice of each authorization, including an explanation of the reasons for issuance, a description of the intended use of the EUA product, and its indications and contraindications. The FDA Commissioner also will promptly publish in the Federal Register each termination or revocation of an authorization and an explanation of the reasons for the decision.[7] In addition, FDA plans to provide notice of an emergency use authorization on the Agency's website, at *www.fda.gov*, and through announcements disseminated to the media.[8]

III. ELIGIBILITY FOR AN EUA

Section 564 permits the FDA Commissioner to authorize the introduction into interstate commerce of a drug, device, or biological product intended for use in an actual or potential emergency during the effective period of a declaration. EUA candidates include products and uses that are not approved, cleared, or licensed under sections 505, 510(k), and 515 of the FD&C Act or section 351 of the PHS Act. The FDA Commissioner may issue an EUA only if, after consultation with the Director of NIH and the Director of CDC (to the extent feasible and appropriate given the circumstances of the emergency), the FDA Commissioner concludes—

1) that the agent specified in the declaration of emergency can cause a serious or life-threatening disease or condition;

[6] To the maximum extent feasible given the circumstances, Federal Register publication of the notice will occur prior to the action that is the subject of the notice.

[7] *See supra* note 6.

[8] In publicly releasing information on an EUA, FDA will take necessary steps to protect classified information and information otherwise protected by law, as appropriate.

2) 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 564, or approved, cleared, or licensed under the FD&C Act or PHS Act, 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;

3) 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

4) 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.

Categories of Products: The range of potential EUA products includes drugs, biological products (e.g., vaccine, blood products, and biological therapeutics), and devices (e.g., *in vitro* diagnostics). (Throughout this document, the term "drugs" includes biological products.) Candidate products include those products that have not been approved or cleared under the FD&C Act or the PHS Act ("unapproved products"), as well as unapproved uses of approved drugs and approved or cleared devices ("unapproved uses of approved products"). Examples of "unapproved uses of approved products" may include: 1) use of an approved antibiotic as prophylaxis for exposure to a bacterium that is not included on the approved labeling for the antibiotic; and 2) distribution of a prescription drug by a non-licensed provider (e.g., delivery of

oral antibiotics by U.S. postal carriers). Section 564 does not require that an investigational new drug application (IND) or investigational device exemption (IDE) be filed for EUA candidate products, although FDA anticipates that many of the unapproved products already will have been under evaluation through such mechanisms.

Effectiveness: Products and uses that are eligible for authorization are those that "may be effective" to prevent, diagnose, or treat in humans serious or life-threatening diseases or conditions that can be caused by the specified biological, chemical, radiological, or nuclear agent(s) that led to or caused the declared emergency. Eligible products and uses also include those that may be effective to mitigate a disease or condition caused by an FDA-regulated product (including an EUA product, or an approved, cleared, or licensed product) used to diagnose, treat, or prevent a disease or condition caused by such agent. The "may be effective" standard for EUAs provides for a lower level of evidence than the "effectiveness" standard that FDA uses for product approvals.[9]

FDA intends to assess the potential effectiveness of an EUA product on a case-by-case basis. The Agency has significant experience assessing effectiveness where clinical information is limited, including experience with treatment INDs and IDEs and humanitarian device exemptions. However, the amount, kind, and quality of evidence available to support an EUA may not always be the same as that required for treatment INDs, IDEs, and humanitarian device exemptions under the FD&C Act and Agency regulations. If, based on the totality of the

[9] The terminology "may be effective" also appears in 21 CFR 312.34(b)(3)(A), where it states that a request for a Treatment IND (tIND) for a drug intended to treat an immediately life-threatening disease may be denied due to a lack of evidence that the drug "may be effective for its intended use in its intended population." Nevertheless, the

scientific evidence available, including adequate and well-controlled clinical trials, if they are available, it is reasonable to believe that the product may be effective for the specified use, the FDA Commissioner may authorize its emergency use--provided that other statutory criteria (e.g., relating to the risk-benefit analysis and alternatives) also are met.

Risk-Benefit Analysis: Products are eligible for emergency use authorization 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 Agency 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 review and consider all evidence, including results of domestic and foreign clinical trials, animal data, and *in vitro* data, available for Agency consideration. FDA anticipates that, for some candidate products, data from controlled clinical trials will be available. For others, the Agency expects to consider clinical experience from other than a controlled trial if the circumstances warrant. The FDA Commissioner will consult with the Director of NIH and the Director of CDC (to the extent feasible and appropriate given the circumstances of the emergency) and will evaluate all the evidence in light of the specific

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Agency's decisions on requests for EUAs and tINDs involve product-specific and circumstance-dependent determinations of risks and benefits.

circumstances of the emergency, including potential risks of not receiving treatment with the candidate product, in determining whether to issue an EUA.[10]

Alternatives to the Product: The FDA Commissioner may issue an EUA if he determines that there is no adequate, approved, and available alternative to the candidate product. A potential alternative product may be considered "unavailable" if there are insufficient supplies to meet fully the emergency need. A potential alternative product may be considered "inadequate" if there are contraindicating data for special circumstances or populations (e.g., immunocompromised individuals or individuals with a drug allergy).

IV. REQUEST FOR CONSIDERATION FOR AN EUA

Although an EUA may not be issued until after an emergency has been declared by the Secretary, FDA recognizes that during such exigent circumstances, the time available for the submission and review of an EUA request may be severely limited. Therefore, the Agency strongly encourages an entity with a possible candidate product, particularly one at an advanced stage of development, to contact the FDA Center responsible for the candidate product even before a determination of actual or potential emergency. This draft 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 draft guidance sets out the types of

[10] Such evidence includes the possible consequences of not taking or using the candidate product (e.g., possible health effects and the need for quarantine).

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 EUA.

Pre-Emergency Activities: Such activities may include discussions with FDA about a prospective EUA product and the appropriate vehicle to use, such as an IND, IDE, or Master File, when submitting data on the product prior to a determination of actual or potential emergency.[11] The Agency 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 EUA, the Agency may share appropriate information on such product with the Secretary's EUA WG.

Emergency Activities: Once a determination of actual or potential emergency has been made under section 564(b)(1), the Secretary may declare an emergency justifying the authorization to use an unapproved medical product or an approved medical product for an unapproved use. The Secretary will consult with the EUA WG; other technical experts from FDA, NIH, and CDC; and other agencies and private entities, where appropriate, to identify products that may be eligible for an EUA in light of the circumstances of the emergency and to facilitate timely submission of the EUA request by an appropriate entity.

Submission of a Request for Consideration: Section 564(c) requires that the data to support authorization demonstrate that, based on the totality of scientific evidence available to

[11] FDA anticipates that the appropriate mechanism to use for submitting data on a candidate product during the pre-emergency period will vary depending on the circumstances.

the FDA Commissioner (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 EUA may vary depending on the nature of the declared emergency and the nature of the candidate product. To facilitate FDA review of such data, the Agency recommends that a request for consideration for an EUA 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 chart below summarizes the types of data that FDA recommends be submitted to support a request for consideration for an EUA.

Summary of Recommended Data to Support a Request for Consideration:

For FDA to evaluate a request for consideration for an EUA, the Agency recommends that the following information be submitted:

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. identification and an explanation of what unmet need(s) would be addressed by issuance of the EUA;

3. a description of the product's approval or clearance status, if any, under the FD&C Act or licensure status under the PHS Act, and whether the product is under an investigational application (e.g., whether the product is unapproved or whether it is approved but the EUA is for an unapproved use; whether an IND or IDE is in effect or has been submitted); whether the product is licensed for either the proposed or another use in a foreign country; information on the use of the medical product by either a foreign country or an international mutual defense organization such as NATO;

4. 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;

5. identification of any approved alternative products, including their availability and adequacy for the proposed use (if known);

6. available safety and effectiveness information for the product;

7. a discussion of risks and benefits;

8. 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;

9. information on chemistry, manufacturing, and controls;

10. instructions for use of the EUA product (e.g., if follow-up treatment is required); and

11. proposed labeling (if applicable).

We discuss these recommendations in more detail below.

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 EUA 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 expects to 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 a candidate product to discuss with the Agency 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.

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 EUA 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 Agency 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.

Products under development: The range of available data for such products will differ widely. FDA recommends that any request for consideration for an EUA include available

preclinical testing data, such as *in vitro* and animal toxicology data. The Agency 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.

Recommended Effectiveness Data

In general: FDA recognizes that comprehensive effectiveness data are unlikely to be available for every EUA candidate 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. 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.

FDA recommends that requests for consideration for EUAs include (or, for products that are developed under IND or IDE or have Drug or Device Master Files, refer to the appropriate document containing) any available relevant scientific evidence regarding the following:

(a) 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) for drugs, demonstration of 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);[12]

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

(e) for drugs, 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; and

(f) for devices, clinical testing data to support the proposed intended use, as necessary and appropriate.

Other Data Considerations

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:

[12] See, e.g., Food and Drugs; Applications for FDA Approval to Market a New Drug; Approval Based on Evidence of Effectiveness from Studies in Animals, 21 CFR 314.610(a)(2) and (3).

(a) 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;

(b) Any relevant statistical analyses; and

(c) 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.

Data quality: The Agency recommends that requests for consideration for EUAs include statements on whether the nonclinical laboratory studies were conducted in compliance with applicable Good Laboratory Practice requirements in 21 CFR part 58 and whether the clinical studies were conducted in compliance with applicable Good Clinical Practice standards.

Data updates: FDA recommends that any data from any ongoing testing (e.g., longer term stability data) or other data or information that may change the Agency's evaluation of the product's safety or effectiveness that become available during the period of review or the term of the EUA (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.

370

371 **Discussion of Risks and Benefits:** FDA recommends that a request for consideration for
372 an EUA include a discussion of the candidate product's known and potential risks and benefits,
373 which includes a synthesis of the data and information requested above, including:

374 (a) Measures taken to mitigate risk or optimize benefit;

375 (b) Limitations, uncertainty, and data gaps; and

376 (c) A description of circumstances, if any, under which the product should not be
377 used (e.g., contraindications).

378

379 **Format of Submissions:** Submissions may be provided in paper or electronic format.
380 Specific information for electronic format may be obtained by reviewing guidance from the
381 appropriate FDA Center (CBER--www.fda.gov/cber/esub/esubguid.htm; CDER--
382 www.fda.gov/cder/regulatory/ersr; and CDRH--www.fda.gov/cdrh/elecsub.html). Where a paper
383 submission is filed, FDA recommends that a minimum of three copies be provided.

384

385 The Agency recommends that each submission begin with a section that describes the
386 contents and organization of the included materials. The submitter of the original application or
387 anyone with a right of reference may refer to data or other information previously submitted to
388 the Agency in a marketing application, investigational application, or Master File.

389

390 FDA expects material to be provided in a reviewable form and sufficiently complete to
391 permit substantive review. Nevertheless, the Agency recognizes that, in rapidly developing or
392 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 Agency will accept and evaluate the request for consideration for an EUA 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 review, or a decision not to authorize emergency use of the candidate product.

The addresses for submission of a request for consideration for an EUA are as follows:

For the Center for Biologics Evaluation and Research:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center, HFM-99, Suite 200N
1401 Rockville Pike
Rockville, MD 20852-1448
ATTN: EUA

For the Center for Devices and Radiological Health:

Document Mail Center (HFZ-401)
Center for Device and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, MD 20850
ATTN: EUA

For the Center for Drug Evaluation and Research:

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266
ATTN: EUA

V. PROCESSING OF AN EUA

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This section discusses FDA's role in pre-emergency activities for candidate EUA products, as well as the procedures the Agency will follow in processing a request for consideration for an EUA once the Secretary has issued a declaration of emergency.

Prioritization of Pre-Emergency Activities: The Agency intends to establish priorities for the activities it undertakes, prior to a determination of actual or potential emergency, on candidate products. 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 U.S. government stockpiles or whether there is a significant likelihood that the product will be included in U.S. government stockpiles if an EUA 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);

(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.

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 Secretary's EUA WG and may consult other agencies on its priority setting.

Review of Pre-Emergency Submissions: To allow FDA review to begin before a determination of actual or potential emergency, the Agency recommends that a pre-emergency submission be filed using existing processes (e.g., IND or IDE), to the extent feasible and appropriate. The extent of, and timelines for, review of such submission will be determined on a case-by-case basis and will depend on the nature of the submission (e.g., whether an IND or IDE for the product already is on file) and the workload of the reviewing Center. Subject to those considerations and other exigent circumstances beyond Agency control, FDA anticipates that pre-emergency submissions for high priority activities may be reviewed in a matter of weeks.

469

470 **Prioritization of Requests for Consideration for an EUA During a Declared**
471 **Emergency:** Once the Secretary has declared an emergency justifying the authorization to use
472 an unapproved product or an unapproved use of an approved product, the Agency intends to
473 prioritize its review of requests for consideration for an EUA based on factors such as:

474 (a) the seriousness of the clinical condition;
475 (b) the incidence of the clinical condition;
476 (c) the likelihood that the product may be effective in treating the condition;
477 (d) the effect use of the product may have in ensuring national security;
478 (e) whether the product is included in U.S. government strategic stockpiles;
479 (f) whether the product could be used by a large population or is limited to
480 subpopulation(s) (unless such use may be critical in managing a public health
481 threat or in protecting a subpopulation with no other suitable measures available);
482 (g) request of another government agency;
483 (h) the extent to which the product would serve a significant unmet medical need
484 in a special population (e.g., pregnant women);
485 (i) the availability and, where known, safety and effectiveness of other
486 countermeasures;
487 (j) the urgency of the treatment need (i.e., the window of opportunity for
488 treatment can vary between different medical conditions);
489 (k) the adequacy of the supporting nonclinical and clinical information; and
490 (l) the quantity of product available.

491

FDA intends to establish priorities for its review of requests for consideration at the Division level or higher and, as appropriate and feasible, will consult with the EUA WG and may consult with other agencies on its priority setting.

Review Process for a Request for Consideration for an EUA: The relevant FDA Center will be responsible for the overall coordination of the Agency's disposition of the request and will interact directly with the entity submitting the request for consideration. The Office of the Commissioner will arrange for the consultations with the Director of NIH and the Director of CDC to occur, to the extent that such consultations are feasible and appropriate given the circumstances of the emergency. The Commissioner's Office also will work with the ASPHEP to coordinate interactions with the EUA Working Group, if convened, although technical input from the EUA WG will be communicated directly to the appropriate FDA review division. The review division also may consult with other countermeasures working groups and expert technical groups within the Agency and, depending on the complexity of the issues presented and the nature of the declared emergency, 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 EUA may vary depending on the nature of the declared emergency and the nature of the candidate product. The Agency intends to evaluate each request in light of the circumstances and the statutory criteria for issuance.

FDA expects that the responsible FDA Center, in coordination with internal and external technical experts (as appropriate and feasible), will perform its review of the information and data included in the request for consideration and make recommendations to the Commissioner. FDA anticipates that the letter authorizing, or not authorizing, a specific emergency use or uses of the candidate product will be issued by the Office of the Commissioner. 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. FDA anticipates that when an EUA is issued, the relevant Center will work with the Office of the Commissioner in drafting the Federal Register notice of the EUA for publication by the Office of the Commissioner. In addition, FDA plans to post information about the EUA on the Agency website (*www.fda.gov*).

Timelines for Review: The timelines for FDA review and action on a request for consideration for an EUA 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 FDA action will vary, the Agency recognizes that it is likely that, in an emergency situation that is occurring or believed imminent, a request for consideration for an EUA will be acted upon within a matter of hours or days.

VI. CONDITIONS OF AUTHORIZATION

Under section 564, the FDA Commissioner may establish conditions on an EUA. Section 564(e) requires the FDA Commissioner (to the extent practicable given the circumstances of the emergency) to establish certain conditions on an EUA authorization that the Commissioner finds

necessary or appropriate to protect the public health, and permits the Commissioner to establish other conditions that he finds necessary or appropriate to protect the public health. Conditions authorized by section 564(e) include, for example: requirements for information dissemination to health care providers or authorized dispensers and product recipients; adverse event monitoring and reporting; data collection and analysis; recordkeeping and records access; restrictions on product advertising, distribution, and administration; and limitations on GMP requirements. Some conditions, the statute specifies, are mandatory to the extent practicable for authorizations of unapproved products and discretionary for authorizations of unapproved uses of approved products. Moreover, some conditions may apply to manufacturers of an EUA product, while other conditions may apply to any person who carries out any activity for which the authorization is issued. Section 564 also gives the FDA Commissioner authority to establish other conditions on an authorization that he finds to be necessary or appropriate to protect the public health.

Conditions of Authorization for Emergency Use of an Unapproved Product: Section 564(e)(1) describes certain requirements with respect to the emergency use of an unapproved product. For example, requirements to disseminate certain information to health care providers or authorized dispensers and recipients and to perform adverse event monitoring and reporting are mandatory under section 564(e)(1)(A) on any person who carries out any activity for which an authorization for an unapproved product is issued, unless the FDA Commissioner determines that such conditions are not practicable given the circumstances of the emergency. Section 564(e)(1)(A) further provides that the FDA Commissioner shall establish appropriate conditions with respect to manufacturers' recordkeeping, reporting, and records access, to the extent that

such conditions are practicable. The FDA Commissioner also may, under section 564(e)(1)(B), impose comparable records conditions on any person (other than a manufacturer) who carries out any activity for which an authorization is issued. In addition, the Commissioner may impose, under section 564(e)(1)(B), the following requirements on any person (including a manufacturer) who carries out any activity for which the authorization of an unapproved product is issued: restrictions on distribution of the EUA product and on who may administer it, as well as requirements to collect and analyze safety and effectiveness data on the product. Additionally, section 564(e)(3) authorizes the FDA Commissioner to waive or limit (as appropriate) existing GMP requirements, and section 564(e)(4) permits the Commissioner to establish conditions for advertising and other promotional descriptive printed matter relating to the unapproved product. Each of the conditions described in section 564(e) is summarized below.

Conditions of Authorization for Emergency Use of an Approved Product for an Unapproved Use: Section 564(e)(2) describes certain requirements with respect to the emergency use of an unapproved use of an approved product. For example, the requirements of section 564(e)(1)(A)(i) and (ii) -- to impose conditions with respect to the dissemination of information to health care providers or authorized dispensers and recipients -- is mandatory under section 564(e)(2)(A), to the extent practicable given the circumstances of the emergency, if a manufacturer of an approved product authorized for an unapproved use carries out any activity for which an EUA is authorized. The FDA Commissioner also may, if he chooses under section 564(e)(2)(A), impose on such manufacturers requirements for adverse event monitoring and reporting as well as recordkeeping, reporting, and records access.

Under section 564(e)(2)(B), with respect to an EUA that authorizes a change in labeling of an approved product, but for which the manufacturer chooses not to make such labeling change, the EUA may not authorize the product's distributor or any other person to alter or obscure the manufacturer's labeling. However, under such conditions, the FDA Commissioner must authorize, to the extent practicable given the circumstances of the emergency, any person (other than the manufacturer) acting pursuant to such EUA to provide appropriate information, in addition to the manufacturer's labeling, with respect to the product.[13]

In addition, section 564(e)(2)(C) allows the FDA Commissioner to establish, with respect to the distribution and administration of the product, conditions that are no more restrictive than those established with respect to the distribution and administration of the product for the approved use.

Additional Conditions of Authorization: Section 564 also permits the FDA Commissioner to establish other conditions on an EUA. For example, section 564(e)(3) authorizes the FDA Commissioner to waive or limit, as appropriate, existing GMP requirements, and section 564(e)(4) permits the Commissioner to establish conditions for advertising and other promotional descriptive printed matter relating to the unapproved use. These and other conditions are described below.

Information for Health Care Providers or Authorized Dispensers: Under section 564(e)(1)(A)(i) (for an unapproved product) and section 564(e)(2)(A) (for a manufacturer

[13] Additional information required under section 564(e)(2)(B)(ii) as a condition of authorization is not considered "labeling" for purposes of section 502 of the FD&C Act while the EUA for the product is effective.

carrying out any activity concerning an unapproved use of an approved product), the FDA Commissioner must establish conditions on an authorization (to the extent practicable given the circumstances of the emergency) to ensure that health care providers or authorized dispensers who administer the EUA product are informed that the FDA Commissioner has authorized the emergency use of the product, of its significant known and potential benefits and risks and the extent to which such benefits and risks are unknown, as well as the available alternatives and their benefits and risks. FDA recommends that the request for consideration for an EUA include a "Fact Sheet" for the health care provider or authorized dispenser that would include essential information about the product. FDA plans to review submitted Fact Sheets for accuracy and completeness. A sample "Fact Sheet for the Health Care Provider or Authorized Dispenser" template is provided at the end of the guidance as Appendix A. FDA recommends that the Fact Sheet include, at a minimum, the information listed on the first page of the sample template. FDA further recommends that the Fact Sheet target the health care provider or authorized dispenser who has the most basic level of training, recognizing that such individuals may have different levels of training (nurse, doctor, other), could come from a variety of backgrounds (state, local, military, civilian), and may have different types of experience. FDA recommends that the Fact Sheet accompany the EUA product when the product is distributed, and be in a form that is readily accessible to the health care provider or authorized dispenser. To the extent consistent with other conditions of authorization, information on the EUA product also may be disseminated to providers through media, videos/DVDs, the Internet, and direct communication from public health agencies.

Information for Recipients: Although informed consent under part 50 of FDA regulations (21 CFR part 50) is not required for administration of an EUA product and the information dissemination requirements of section 564 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. Under section 564(e)(1)(A)(ii)(III) (for an unapproved product) and section 564(e)(2)(A) (for a manufacturer carrying out any activity concerning an unapproved use of an approved product), recipients must be informed that the FDA Commissioner has authorized emergency use of the product, of the significant known and potential benefits and risks of the EUA product, and of the extent to which such benefits and risks are unknown. Recipients must have an opportunity to accept or refuse the EUA product and must be informed of any consequences of refusing administration of the product.[14] Recipients also must be informed of available alternatives to the product and of their risks and benefits under section 564(e)(1)(A)(ii)(III) (for an unapproved product) and section 564(e)(2)(A) (for a manufacturer carrying out any activity concerning an approved product for an unapproved use).

Ordinarily, FDA expects that some form of written information will be given to recipients, similar to the Fact Sheet for health care providers or authorized dispensers. To assure that individuals of all educational levels comprehend the information provided, FDA recommends that it be written in the simplest language possible. The Agency 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

[14] However, Congress authorized the President to waive, under certain circumstances, the option for members of the armed forces to accept or refuse administration of an EUA product (10 U.S.C. 1107a).

instructions for home use (if necessary), and adverse event information, including contact information should adverse events occur. A sample "Fact Sheet for Recipients" template is provided at the end of the guidance as Appendix B. FDA recommends that the Fact Sheet include the information in the template and be submitted to the Agency as part of the request for consideration for an EUA. Furthermore, the Agency recommends that the Fact Sheet or other 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, videos/DVDs, the Internet, and direct communication from health care providers and public health agencies. Section 564(e)(1)(A)(ii) (for an unapproved product) and section 564(e)(2)(A) (for a manufacturer carrying out any activity concerning an unapproved use of an approved product) contemplates that the Fact Sheet or other recipient information will be provided to recipients before administration of an EUA product. If, however, taking the time needed to provide such information would diminish or negate the effectiveness of the product for the recipient, the FDA Commissioner may include as part of the condition that the information be provided to the recipient as soon as practicable afterward.

Monitoring and Reporting of Adverse Events: Section 564(e)(1)(A)(iii) (for an unapproved product) and section 564(e)(2)(A) (for a manufacturer carrying out any activity concerning an unapproved use of an approved product) provide for adverse event monitoring and reporting for EUA products. 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 (e.g., MEDWATCH and VAERS). 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 a Fact Sheet, as described above).

Records: Section 564(e)(1)(A)(iv) requires (to the extent practicable given the circumstances of the emergency) that manufacturers of an unapproved product be required to maintain records and to grant to the Agency access to records concerning the EUA product. The FDA Commissioner may impose comparable records requirements on any person other than a manufacturer who carries out any activity for an unapproved product under section 564(e)(1)(B)(iv) and on the manufacturer of an approved product for an unapproved use under section 564(e)(2)(A). The Agency anticipates that such records requirements may, for manufacturers, relate to the number of doses, devices, etc. (including lot number identification) that have been shipped or sold under an EUA; the name and addresses of the facilities where the EUA product was shipped; and may, for persons other than manufacturers, relate to the monitoring of patients who have been administered a product under an EUA. The FDA Commissioner also may impose conditions regarding other matters the Agency determines are appropriate and practicable given the circumstances of the emergency.

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

Restricted distribution under the EUA--conditions may be placed on which entities may distribute the product and how distribution is to be performed.[15]

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 EUA product.

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

Additional Conditions for an Unapproved Use of an Approved Product: Under section 564(e)(2)(B), with respect to an EUA that authorizes a change in labeling of an approved product, but for which the manufacturer chooses not to make such labeling change, the EUA may not authorize a product distributor or any other person to alter or obscure the manufacturer's labeling. However, under such conditions, the FDA Commissioner must authorize, to the extent practicable under the circumstances of the emergency, any person (other than the manufacturer) acting pursuant to such EUA to provide appropriate information, in addition to the manufacturer's labeling, with respect to the product.[16]

[15] FDA anticipates that distribution of EUA products will be performed according to existing response plans, as practicable and appropriate.

[16] *See supra* note 13.

The FDA Commissioner may, under section 564(e)(2)(C), establish conditions for distribution and administration of an approved product for an unapproved use that are no more restrictive than those established by the Agency for the distribution and administration of the product for an approved use. Any such additional conditions will be established by the Commissioner 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 Agency expects that EUA products will be produced in compliance with GMP; however, limits or waivers may be granted under section 564(e)(3), on a case-by-case basis, after consideration of the circumstances and of any alternative proposed approach.

Advertising: Section 564(e)(4) allows the FDA Commissioner to establish conditions on advertisements and other promotional descriptive printed matter relating to the use of an EUA product, such as, for drugs (including biologics), requirements applicable to prescription drugs under section 502(n) of the FD&C Act and, for devices, requirements applicable to restricted devices under section 502(r) of the FD&C Act.

Summary of Conditions Described in Section 564(e): The following chart sets out conditions described in section 564(e) that may be imposed on an EUA for unapproved products and for unapproved uses of approved products, respectively. A condition is identified as "mandatory" in the chart below if section 564(e) requires the FDA Commissioner, to the extent practicable given the circumstances of the emergency, to establish such condition when it is

738 necessary or appropriate to protect the public health. A condition identified as "discretionary" in
739 the chart below is one that the FDA Commissioner may, under section 564(e), impose as he finds
740 necessary or appropriate to protect the public health. In addition to the conditions described as
741 "mandatory" and "discretionary" in the chart below, section 564 allows the FDA Commissioner
742 to establish other conditions on an authorization that he finds to be necessary or appropriate to
743 protect the public health.

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CONDITION OF AUTHORIZATION	UNAPPROVED PRODUCT	UNAPPROVED USE OF AN APPROVED PRODUCT
Information for Health Care Providers and Authorized Dispensers	Mandatory for manufacturers and others*	Mandatory for manufacturers[17]
Information for Recipients	Mandatory for manufacturers and others*	Mandatory for manufacturers[18]
Adverse Event Monitoring/Reporting	Mandatory for manufacturers and others*	Discretionary for manufacturers
Recordkeeping/Access	Mandatory for manufacturers; discretionary for others*	Discretionary for manufacturers
Compliance with GMPs	Discretionary for manufacturers and others*	Discretionary for manufacturers and 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*	

745 * Others may include, for example, the U.S. government.

746

747 **Option To Carry Out Authorized Activities:** Section 564(l) requires the manufacturer

748 of a sole-source unapproved product authorized for emergency use to inform the FDA

[17] Under section 564(e)(2)(B), with respect to an EUA that authorizes a change in labeling of an approved product, but for which the manufacturer chooses not to make such labeling change, the EUA may not authorize a product distributor or any other person to alter or obscure the manufacturer's labeling. However, under such conditions, the FDA Commissioner must authorize, to the extent practicable under the circumstances of the emergency, any person (other than the manufacturer) acting pursuant to such EUA to provide appropriate information, in addition to the manufacturer's labeling, with respect to the product.

Commissioner, within a reasonable time after authorization, that the manufacturer does not intend to carry out any activity under the EUA. Although the Commissioner does not have the authority under section 564 to require a person to carry out any activity for which an EUA is issued, section 564(l) does not limit the Commissioner's authority to impose conditions on persons who choose to carry out any activity pursuant to an EUA.

Rules of Statutory Construction: Section 564(j) provides that nothing in section 564 impairs the authority of the President as Commander in Chief of the Armed Forces under the Constitution. In addition, section 564(j) indicates that nothing in section 564 impairs the authority of the Secretary of Defense with respect to the Department of Defense (including the armed forces), under other provisions of Federal law. Section 564(j) also provides that nothing in section 564, including any action by a manufacturer with respect to an unapproved use of an approved product, impairs the authority of the United States to use or manage quantities of a product that are owned or controlled by the United States (including products maintained in the stockpile managed under section 319F-2 of the PHS Act).

VII. REVIEW, REVOCATION, OR TERMINATION OF AN EUA

Section 564(f) provides that an EUA will be in effect for the duration of the declaration under which it was issued (see Section II, "Declaration of Emergency," above), unless the EUA is revoked because the criteria of issuance (see Section III, "Eligibility for an Emergency Use Authorization," above) are no longer met or revocation is appropriate to protect public health or safety.

[18] *See supra* note 17.

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773 **Revocation:** The FDA Commissioner will periodically to review the circumstances and
774 appropriateness of an EUA, including circumstances that might warrant revocation of the EUA.
775 Such circumstances may include significant adverse inspectional findings (e.g., where an
776 inspection of the manufacturing site and processes have raised significant questions regarding the
777 purity, potency, or safety of the EUA product that materially affect the risk/benefit assessment
778 upon which the EUA was based); reports of adverse events (number or severity) linked to, or
779 suspected of being caused by, the EUA product; product failure; product ineffectiveness (such as
780 newly emerging data that undermine the Agency's conclusion that the product "may be effective"
781 against a particular agent); and availability of a preferred product.

782

783 **Termination:** Upon termination of the declaration, unapproved product or labeling and
784 product information for an unapproved use must be disposed of pursuant to section 564(b)(2)(C)
785 and (b)(3). A manufacturer may choose to have unapproved product returned after termination.
786 Notwithstanding any such termination, under section 564(f)(2) an authorization shall continue to
787 be effective to provide for continued use in any patient who began treatment before termination
788 (to the extent found necessary by the patient's attending physician).

789

790 **Continued Use:** Any use of an EUA product beyond the term of a declaration is subject
791 to investigational product regulations (e.g., IND regulations), except for use by patients who
792 began treatment when the declaration was in effect, to the extent found necessary by such
793 patient's attending physician.

794

VIII. PREEMPTION

FDA anticipates that preemption issues may arise when an EUA is issued to the extent that states have existing requirements governing the dispensing and administration of unapproved medical products or approved medical products for unapproved uses. The Supremacy Clause can operate to nullify both state legislative requirements and state common-law duties. *Medtronic v. Lohr*, 518 U.S. 470, 503 (1996) (Breyer, J., concurring in part and concurring in the judgment); *id.* at 510 (O'Connor, J., joined by Rehnquist, C.J., Scalia, J., and Thomas, J., concurring in part and dissenting in part); *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 521 (1992) (plurality opinion); *id.* at 548-49 (Scalia, J., joined by Thomas, J., concurring in judgment in part and dissenting in part). Under the principles of implied conflict preemption, courts have found state law preempted where it is impossible to comply with both federal and state law or where the state law "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *See English v. General Electric Co.*, 496 U.S. 72, 79 (1990); *Florida Lime & Avocado Growers, Inc.*, 373 U.S. 132, 142-43 (1963); *Hines v. Davidowitz*, 312 U.S. 52, 67 (1941). Consistent with this case law, section 4(a) of Executive Order 13132 states that "[a]gencies shall construe . . . a Federal statute to preempt State law only where the statute contains an express preemption provision or there is some other clear evidence that the Congress intended preemption of State law, or where the exercise of State authority conflicts with the exercise of Federal authority under the Federal statute."

FDA believes that the terms and conditions of an EUA issued under section 564 preempt state law--legislative requirements and common-law duties--imposing different or additional

requirements on the dispensing or administration of the medical product for which the EUA was issued in the context of the emergency declared under section 564. To the extent state law may impose requirements different from or in addition to those imposed by the EUA for a particular medical product within the scope of a declared emergency, such state law "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress," *See Hines*, 312 U.S. at 67, and "conflicts with the exercise of Federal authority under [§ 564]." Executive Order 13132. Affected state laws may include, but are not limited to, laws governing the administration of investigational medical products, such as informed consent laws and laws requiring Institutional Review Board approval, and laws governing the dispensing of medical products, such as laws limiting who may dispense medical products and under what circumstances. FDA anticipates consulting state officials when the terms and conditions of an EUA may preempt state law.

In an emergency, it is critical that the conditions that are part of the EUA--those that the Commissioner has determined to be necessary or appropriate to protect the public health--be strictly followed, and that no additional conditions be imposed. To the extent there may be circumstances in which FDA would like people carrying out activities under an EUA also to comply with requirements contained in preempted state law, FDA anticipates that the Commissioner will incorporate such requirements into the terms and conditions of the EUA.

IX. LIABILITY PROTECTION UNDER OTHER STATUTES

Section 564 of the FD&C Act does not offer liability protection to manufacturers or others who carry out any activity for which an EUA is issued, and liability protection is beyond the mission and authority of the FDA. However, certain persons or certain products may be eligible for liability protection under other statutes and programs, such as the Federal Employee Compensation Act (5 U.S.C. 8101 *et seq.*); the Federal Tort Claims Act (28 U.S.C. 1346(b)); the Smallpox Vaccine Injury Compensation Program and the liability protections of section 304 of the Homeland Security Act, as amended by Smallpox Emergency Personnel Protection Act of 2003 (42 U.S.C. 233(p)); and the National Vaccine Injury Compensation Program (42 U.S.C. 300aa-10 *et seq.*).

The Final Guidance on the Emergency Use of Medical Products will contain a list of contacts for the liability statutes and programs listed above.

APPENDIX A

FACT SHEET for the Health Care Provider or Authorized Dispenser

[PRODUCT for INTENDED USE]

1. An emergency has been declared by the Secretary of Health and Human Services.

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

3. The FDA Commissioner has authorized the emergency use of [PRODUCT] for a use [IDENTIFY THE INTENDED USE] that has not yet obtained FDA approval 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.

4. 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].

5. 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].

6. 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 EUA product may face.]

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

As the health care provider or authorized dispenser 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 "Fact Sheet for Recipients" 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.

If you follow these instructions when administering or using [PRODUCT], you do not need to comply with state laws--legislative requirements and common-law duties--imposing different or additional requirements on the dispensing or administration of the product in this emergency situation.

FDA also recommends that EUA applicants include the following additional information in the Fact Sheet for Health Care Providers or Authorized Dispensers, if it is available:

- **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 (procedure), how to interpret the results; and
  - Instructions for use for special populations (e.g., pregnant women 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 also may report adverse events to MEDWATCH at www.fda.gov/medwatch/report/hcp.htm or 1-800-FDA-1088, or to VAERS (for vaccines) at www.vaers.org or 1-800-822-7967.

- **Alternatives.** If other agents (approved/licensed/cleared products or EUA 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, 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 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 B

FACT SHEET for the Recipient

[PRODUCT for INTENDED USE]

1. An emergency has been declared by the Secretary of Health and Human Services.

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

3. The FDA Commissioner has authorized the emergency use of [PRODUCT] for [IDENTIFY THE INTENDED USE]. This authorization will terminate on [DATE 1 YEAR FROM THE DATE OF DECLARATION], or when the emergency has ceased to exist, whichever is earlier.

4. 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].

5. 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].

6. 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 EUA product may face.]

7. [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].