
Emergency Use Authorization of Medical Products and Related Authorities

Guidance for Industry and Other Stakeholders

**U.S. Department of Health and Human Services
Food and Drug Administration
Office of the Commissioner
Office of the Chief Scientist
Office of Counterterrorism and Emerging Threats**

January 2017

**Procedural
OMB Control No. 0910-0595
Expiration Date 08/31/2019**

See additional PRA statement in section IX of this guidance.

Emergency Use Authorization of Medical Products and Related Authorities

Guidance for Industry and Other Stakeholders

Additional copies are available from:

*Office of Counterterrorism and Emerging Threats
Office of the Chief Scientist, Office of the Commissioner
Food and Drug Administration
10903 New Hampshire Ave., Silver Spring, MD 20993
Tel: 301-796-8510; Fax: 301-847-8615; Email: AskMCMi@fda.hhs.gov
<http://www.fda.gov/medicalcountermeasures>*

**U.S. Department of Health and Human Services
Food and Drug Administration
Office of the Commissioner
Office of the Chief Scientist
Office of Counterterrorism and Emerging Threats**

Procedural

TABLE OF CONTENTS

I.	INTRODUCTION.....	1
II.	SCOPE OF GUIDANCE.....	2
III.	EMERGENCY USE AUTHORIZATIONS	4
A.	EUA DECLARATION JUSTIFYING EMERGENCY USE.....	5
1.	Determinations to Support an EUA Declaration	5
2.	Termination of an EUA Declaration.....	6
B.	EUA MEDICAL PRODUCTS	7
1.	Criteria for Issuance.....	7
2.	Categories of Products	9
C.	PRE-EUA ACTIVITIES AND SUBMISSIONS.....	9
D.	REQUEST FOR AN EUA.....	11
1.	Preparedness and Response	11
2.	Information Recommendations.....	11
3.	Format of Submissions	16
4.	FDA Processing of an EUA Request.....	18
E.	CONDITIONS OF AUTHORIZATION	22
1.	Information Relating to the EUA Product	22
2.	Monitoring and Reporting of Adverse Events.....	25
3.	Records	26
4.	Additional Conditions of Authorization	26
5.	Waivers or Limitations of Compliance With Other Requirements	27
F.	CATEGORIZATION OF LABORATORY TESTS UNDER AN EUA	28
G.	DURATION AND REVISION OF AN EUA	28
1.	Revision and Revocation	29
2.	Product Disposition and Continued Use.....	29
H.	PUBLICATION.....	29
I.	OPTION TO CARRY OUT AUTHORIZED ACTIVITIES.....	30
IV.	EMERGENCY USE OF ELIGIBLE FDA-APPROVED MCMs WITHOUT AN EUA	30
A.	ELIGIBLE PRODUCTS.....	31

B.	EXPIRATION DATE EXTENSIONS WITHOUT AN EUA.....	31
	1. In General.....	33
	2. Procedures for Request and Issuance.....	33
D.	EMERGENCY DISPENSING WITHOUT AN EUA.....	34
	1. Procedures for Issuing Emergency Dispensing Orders	35
	2. Scope and Conditions of Emergency Dispensing Orders	37
	3. Duration of an Emergency Dispensing Order.....	37
E.	EMERGENCY USE INSTRUCTIONS WITHOUT AN EUA.....	38
V.	GOVERNMENTAL PRE-POSITIONING OF MCMs	38
VI.	PREEMPTION	39
VII.	LIABILITY PROTECTION	41
VIII.	IMPORTING AND EXPORTING MEDICAL PRODUCTS UNDER AN EUA.....	42
IX.	PAPERWORK REDUCTION ACT OF 1995	43
	List of Acronyms	44
	Appendix A. EUA Conditions of Authorization: Required vs. Discretionary	45

Emergency Use Authorization of Medical Products and Related Authorities¹

Guidance for Industry and Other Stakeholders

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance explains FDA's general recommendations and procedures applicable to the authorization of the emergency use of certain medical products under sections 564, 564A, and 564B of the Federal Food, Drug, and Cosmetic Act (FD&C Act)² as amended or added by the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA)³. The provisions in PAHPRA, described in section II of this guidance, include key legal authorities to sustain and strengthen national preparedness for public health, military, and domestic emergencies involving chemical, biological, radiological, and nuclear (CBRN) agents, including emerging infectious disease threats such as pandemic influenza. PAHPRA clarifies and enhances FDA's authority to support emergency preparedness and response and foster the

¹ This guidance was prepared by the Office of Counterterrorism and Emerging Threats (OCET) in cooperation with the Center for Biologics Evaluation and Research (CBER), Center for Devices and Radiological Health (CDRH), and Center for Drug Evaluation and Research (CDER).

² 21 U.S.C. 360bbb-3, 360bbb-3a, and 360bbb-3b. Section 564 was first added to the FD&C Act by the Project BioShield Act of 2004 (Public Law 108-276). Hereafter in this document, statutory references (e.g., "section ___") are to the FD&C Act, except where otherwise indicated.

³ Public Law 113-5. Section 3088 of the 21st Century Cures Act, signed into law by the President on December 13, 2016, amends sections 564, 564A, and 564B of the FD&C Act to add new authorities to: (1) authorize emergency use of unapproved animal drugs, (2) make applicable other emergency use authorities (e.g., to issue emergency dispensing orders, waive compliance with current good manufacturing practices (CGMPs), make available Centers for Disease Control and Prevention (CDC) emergency use instructions, and extend expiration dates) to approved animal drugs, and (3) allow unapproved animal drugs to be held for emergency use. While much of what is described in this guidance will apply to these new authorities, this guidance does not by its terms reference them; FDA asks anyone interested in utilizing these authorities to contact FDA directly to discuss how to proceed. FDA plans to review these new authorities and address any new procedural issues raised as we develop more experience with these new authorities.

Contains Nonbinding Recommendations

development and availability of medical products for use in these emergencies. These medical products, also referred to as “medical countermeasures” or “MCMs,” include drugs⁴ (e.g., antivirals and antidotes), biological products (e.g., vaccines, blood products, and biological therapeutics), and devices (e.g., *in vitro* diagnostics and personal protective equipment). This guidance finalizes the draft guidance, *Emergency Use Authorization of Medical Products and Related Authorities (April 2016)* and replaces the following two guidance documents, *Emergency Use Authorization of Medical Products (July 2007)* and *Emergency Use Authorization Questions and Answers (April 2009)*.

In general, 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 guidance means that something is suggested or recommended, but not required.

II. SCOPE OF GUIDANCE

This document is intended to inform all stakeholders⁵ involved in emergency response activities and FDA staff of FDA's general recommendations and procedures for:

- (1) Issuance of Emergency Use Authorizations (EUAs) under section 564;
- (2) Implementation of the emergency use authorities set forth in section 564A; and
- (3) Reliance on the governmental pre-positioning authority set forth in section 564B."

⁴ Throughout this guidance references to “drugs” and “drug products” include both drugs approved under the FD&C Act and biological products licensed under the Public Health Service (PHS) Act, but not biological products that also meet the definition of a device in section 201(h) of the FD&C Act (21 U.S.C. 321(h)).

⁵ For purposes of this guidance, “stakeholders” include industry and government sponsors and other government stakeholders/entities involved in emergency response activities (including Federal, State, local, tribal, or territorial government stakeholders/entities). The term “government stakeholders” refers to the public health and/or emergency response agencies or their agents/delegates that have legal responsibility and authority for responding to an incident, based on political or geographical boundaries (e.g., city, county, tribal, territorial, State, or Federal), or functional range or sphere of authority (e.g., law enforcement, public health, military health) to prescribe, administer, deliver, distribute, hold, or dispense a medical product during an emergency situation.

Contains Nonbinding Recommendations

Section 564, as amended by PAHPRA, permits the Commissioner⁶ to authorize the emergency use of an unapproved medical product or an unapproved use of an approved⁷ medical product for certain emergency circumstances (discussed in section III.A of this guidance) after the HHS Secretary has made a declaration of emergency or threat justifying authorization of emergency use. The Commissioner may issue an EUA to allow an MCM to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by a CBRN agent when there are no adequate, approved, and available alternatives. Section III of this guidance addresses EUAs.

Section 564A, as added by PAHPRA, establishes streamlined mechanisms to facilitate preparedness and response activities involving certain FDA-approved MCMs *without* FDA issuing an EUA, which can be a resource-intensive process. These authorities, and the definition of eligible products to which they apply, are discussed in section IV of this guidance. These authorities, which apply only to eligible FDA-approved medical products intended for use during a CBRN emergency, include provisions that:

- Empower FDA to extend the expiration date of an eligible FDA-approved MCM stockpiled for use in a CBRN emergency and to establish appropriate conditions relating to such extensions, such as appropriate storage, sampling, and labeling;
- Permit FDA to waive otherwise-applicable current good manufacturing practice (CGMP) requirements⁸ (e.g., storage or handling) to accommodate emergency response needs;
- Allow emergency dispensing of MCMs during an actual CBRN emergency event without requiring an individual prescription for each recipient⁹ of the MCM or all of the information otherwise required or by responders who may not otherwise be

⁶ As provided in section 1003 and existing delegations of authority (found in the FDA Staff Manual Guide 1410.10), the Secretary of Health and Human Services (HHS Secretary or Secretary of HHS) has delegated most of the authorities under sections 564, 564A, and 564B to the Commissioner of FDA (Commissioner). Thus, this guidance refers to either FDA or the Commissioner rather than the HHS Secretary, except where the HHS Secretary has traditionally exercised the authority or has delegated it to another official (e.g., the authority to issue emergency use instructions pursuant to section 564A(e) was delegated to the Director of the CDC).

⁷ Unless otherwise specified, the terms “approved product” and “FDA-approved product” refer to a product that is approved, licensed, or cleared under section 505, 510(k), or 515 of the FD&C Act or section 351 of the PHS Act, as applicable. For purposes of this document, an “unapproved” product refers to a product that is not approved, licensed, or cleared for commercial distribution under section 505, 510(k), or 515 of the FD&C Act or section 351 of the PHS Act; an “unapproved use of an approved product” refers to a product that is approved, licensed, or cleared under such a provision but for which the specific use is not an approved, licensed, or cleared use of the product. See section 564(a)(2).

⁸ As applied to medical devices, these are referred to as “Quality System Regulation” requirements. See 21 CFR 820.

⁹ For purposes of this guidance, the term “recipient(s)” refers to individual(s) to whom an MCM product is administered or on whom the product is used.

Contains Nonbinding Recommendations

licensed to dispense, if permitted by state law in the state where such dispensing occurs or if in accordance with an order issued by FDA; and

- Permit the Centers for Disease Control and Prevention (CDC) to create and issue “emergency use instructions” (EUI) concerning the FDA-approved conditions of use for eligible products.¹⁰

In addition, PAHPRA amended section 505-1(k) to authorize FDA to waive Risk Evaluation and Mitigation Strategy (REMS) requirements for CBRN emergencies.

Finally, section 564B, also added by PAHPRA, permits government stakeholders to pre-position (e.g., stockpile, forward-deploy) MCMs in anticipation of FDA approval or clearance, authorization of an investigational use, or the issuance of an EUA, to enable these stakeholders to prepare for potential rapid deployment during an actual CBRN emergency. This authority is discussed in section V of this guidance.

III. EMERGENCY USE AUTHORIZATIONS

The EUA authority under section 564 allows FDA to facilitate availability and unapproved uses of MCMs needed to prepare for and respond to CBRN emergencies. The EUA authority is separate and distinct from use of a medical product under an investigational application (i.e., Investigational New Drug Application (IND) or Investigational Device Exemption (IDE)), section 561 expanded access authorities,¹¹ and section 564A emergency use authorities discussed in section IV of this guidance.

¹⁰ U.S. Department of Health and Human Services, Delegation of Authority of section 564A(e) of the Federal Food, Drug, and Cosmetic Act, December 16, 2013, see <http://www.fda.gov/downloads/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/UCM510446.pdf>.

¹¹ For general information on expanded access mechanisms, see <http://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm>.

Contains Nonbinding Recommendations

A. EUA DECLARATION JUSTIFYING EMERGENCY USE

1. Determinations to Support an EUA Declaration

Before FDA may issue an EUA, the HHS Secretary must declare that circumstances exist justifying the authorization (section 564(b)(1)). This declaration (referred to in this guidance as an “EUA declaration”),¹² must be based on one of the following actions:

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 CBRN agent(s);¹³
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 CBRN agent(s);¹⁴
3. A determination by the Secretary of HHS that there is a public health emergency, or a significant potential for a public health emergency, that affects, or has a significant potential to affect, national security or the health and security of United States citizens living abroad, and that involves a CBRN agent or agents, or a disease or condition that may be attributable to such agent(s);¹⁵ or

¹² The HHS declaration of emergency or threat of emergency is issued only for purposes of empowering the FDA Commissioner to issue an EUA. It is distinct from, and is not dependent on, an HHS public health emergency declaration under section 319 of the PHS Act, a Public Readiness and Emergency Preparedness (PREP) Act declaration (discussed in section VII of this document), or any other type of emergency declaration.

¹³ Section 564(b)(1)(A).

¹⁴ Section 564(b)(1)(B).

¹⁵ Section 564(b)(1)(C). Prior to the PAHPRA amendments, the Secretary would have made the determination that there is a public health emergency under section 319 of the PHS Act. Under amended section 564(b)(1)(C), the Secretary can make the emergency or threat of emergency determination that includes any and all of the elements required by statute (e.g., that the emergency affects national security, U.S. citizens living abroad, etc.) when making the declaration justifying the EUA under section 564(b)(1)(C). If there is an applicable section 319 public health emergency determination in place, the Secretary may conclude that any additional elements required by the statute (e.g., that the emergency affects national security, citizens living abroad, etc.) are met when issuing a declaration under section 564(b)(1).

Contains Nonbinding Recommendations

4. The identification of a material threat, by the Secretary of Homeland Security pursuant to section 319F-2 of the Public Health Service (PHS) Act, that is sufficient to affect national security or the health and security of United States citizens living abroad.¹⁶

After the Secretary of HHS issues an EUA declaration based on one of these four determinations, and after consulting (to the extent feasible and appropriate given the applicable circumstances) with the Assistant Secretary for Preparedness and Response (ASPR), the Director of the National Institutes of Health (NIH), and the Director of CDC,¹⁷ the Commissioner may authorize the emergency use of an unapproved product or an unapproved use of an approved product, provided that other statutory criteria are met.

In appropriate circumstances, an HHS EUA declaration may support issuance of more than one EUA. For example, based on an HHS EUA declaration that circumstances exist to justify the authorization of emergency use of diagnostics for a specified biological agent, FDA may authorize emergency use for multiple diagnostic tests to meet the need, provided that each EUA meets the statutory criteria for issuance.

2. Termination of an EUA Declaration

When an EUA declaration is terminated, then any EUA(s) issued based on that declaration will no longer remain in effect.¹⁸ The HHS Secretary's EUA declaration will terminate on the earlier of: (1) a determination by the HHS Secretary that the circumstances that precipitated the declaration have ceased (after consultation as appropriate with the Secretary of Homeland Security or the Secretary of Defense), or (2) a change in the approval status of the product such that the authorized use(s) of the product are no longer unapproved (section 564(b)(2)). For example, an EUA issued to allow an unapproved use of an approved product may no longer be needed if that product is later approved by FDA for the use permitted by the EUA.

¹⁶ Section 564(b)(1)(D). We note that, while section 564(b)(1)(D) specifically refers to the identification of a material threat "sufficient to affect national security or the health and security of United States citizens living abroad," section 319F-2 of the PHS Act, 42 USC 274d-6b, refers only to a "material threat against the United States population sufficient to affect national security," without specific reference to "the health and security of United States citizens living abroad." Because Congress chose not to amend the latter provision when it added the "material threat" provision to section 564, FDA concludes that a material threat determination necessarily encompasses the health and security of U.S. citizens living abroad. And as such, it would be an appropriate basis for a declaration. Thus, an EUA could be justified by a threat to the health and security of U.S. citizens living abroad whether or not a particular material threat determination issued pursuant to section 319F-2 expressly refers to the health and security of U.S. citizens living abroad.

¹⁷ Section 564(c).

¹⁸ As discussed in section III.G of this guidance, an EUA may also be revoked under certain conditions.

Contains Nonbinding Recommendations

Before an EUA declaration terminates, the Secretary of HHS must provide advance notice that is sufficient to allow for the disposition of an unapproved product, and of any labeling or other information provided related to an unapproved use of an approved product (section 564(b)(3)).¹⁹

B. EUA MEDICAL PRODUCTS

1. Criteria for Issuance

During the effective period of the HHS Secretary's EUA declaration, FDA may authorize the introduction of a medical product into interstate commerce when the product is intended for use during an actual or potential emergency. EUA candidate products include medical 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.

After the requisite determination and declaration have been issued, and after feasible and appropriate consultations, FDA may issue an EUA only if FDA concludes that the following four statutory criteria for issuance have been met. If the product does not meet the statutory criteria for issuance or is not otherwise an appropriate candidate, an alternative regulatory mechanism (i.e., access under an IND or IDE, which can include expanded access protocols²⁰) may be an appropriate means to provide patients access to an unapproved use of a product in a CBRN emergency.

a. Serious or Life-Threatening Disease or Condition

For FDA to issue an EUA, the CBRN agent(s) referred to in the HHS Secretary's EUA declaration must be capable of causing a serious or life-threatening disease or condition.

b. Evidence of Effectiveness

Medical products that may be considered for an EUA are those that "may be effective" to prevent, diagnose, or treat serious or life-threatening diseases or conditions that can be caused by a CBRN agent(s) identified in the HHS Secretary's declaration of emergency or threat of emergency under section 564(b). Potential EUA products also include those that may be effective to mitigate a disease or condition caused by an FDA-regulated product (including a product authorized for emergency use under section 564 or an approved product) used to diagnose, treat, or prevent a disease or condition caused by a CBRN agent.

¹⁹ The Secretary of HHS publishes in the Federal Register notice of each EUA declaration justifying issuance of an EUA, with an explanation of the basis of the declaration under section 564(b)(1), as well as any advance notice of termination of such a declaration.

²⁰ For general information on expanded access mechanisms, see <http://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm>.

Contains Nonbinding Recommendations

The "may be effective" standard for EUAs provides for a lower level of evidence than the "effectiveness" standard that FDA uses for product approvals.²¹ FDA intends to assess the potential effectiveness of a possible EUA product on a case-by-case basis using a risk-benefit analysis, as explained below. If, based on the totality of the scientific evidence available, it is reasonable to believe that the product may be effective for the specified use, FDA may authorize its emergency use, provided that other statutory criteria for issuing an EUA also are met.

c. Risk-Benefit Analysis

A product may be considered for an EUA if the Commissioner 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 making this assessment, FDA must take into consideration the material threat posed by the CBRN agent(s) identified in the HHS Secretary's declaration of emergency or threat of emergency if applicable (section 564(c)).

In determining whether the known and potential benefits of the product outweigh the known and potential risks, FDA intends to look at the totality of the scientific evidence to make an overall risk-benefit determination. Such evidence, which could arise from a variety of sources, may include (but is not limited to): results of domestic and foreign clinical trials, *in vivo* efficacy data from animal models, and *in vitro* data, available for FDA consideration. FDA will also assess the quality and quantity of the available evidence, given the current state of scientific knowledge. The types of evidence that FDA may consider and that should be submitted to support a request for an EUA are discussed more fully in section III.D.2 of this guidance.

d. No Alternatives

For FDA to issue an EUA, there must be no adequate, approved, and available alternative to the candidate product for diagnosing, preventing, or treating the disease or condition. A potential alternative product may be considered "unavailable" if there are insufficient supplies of the approved alternative to fully meet the emergency need. A potential alternative product may be considered "inadequate" if, for example, there are contraindicating data for special circumstances or populations (e.g., children, immunocompromised individuals, or individuals with a drug allergy), if a dosage form of an approved product is inappropriate for use in a special population (e.g., a tablet for individuals who cannot swallow pills), or if the agent is or may be resistant to approved and available alternative products.

²¹ Regulations regarding treatment INDs and IDEs also use the terminology "may be effective." A request for a treatment IND for a drug or biologic intended to treat an immediately life-threatening disease may be granted when, among other things, there is evidence that the drug may be effective for its intended use in its intended population (21 CFR 312.320(a)(3)(ii)). For devices, a treatment IDE may be withdrawn if FDA determines that the available scientific evidence fails to provide a reasonable basis for concluding that the device "may be effective for its intended population" (21 CFR 812.36(d)(2)(iv)(A)). It should be noted that FDA's decisions on requests for EUAs and treatment INDs and IDEs involve product-specific and circumstance-dependent determinations of risks and benefits. FDA also notes that the amount, type, and quality of evidence available to support an EUA may not always be the same as that required for expanded access, IDEs, or humanitarian device exemptions under the FD&C Act and FDA regulations.

Contains Nonbinding Recommendations

2. Categories of Products

MCMs that may be considered for an EUA include unapproved products as well as approved products intended for unapproved uses.²² Examples of "unapproved uses of approved products" include:

- Use of an approved antibiotic as prophylaxis based on exposure to, or treatment of, a disease caused by a bacterium (or class of bacteria) that is not included in the indications and usage section of the approved labeling for the antibiotic;
- Substitution of a critical reagent of a cleared *in vitro* diagnostic (IVD) with another reagent that has not been cleared for use with the device.

Submission of an IND or IDE is not required for potential EUA products, although FDA anticipates that many unapproved products for which an EUA is requested will already be under evaluation through such mechanisms. In fact, human data derived in the course of studies conducted under an IND or IDE may help to support an FDA conclusion that the available evidence is adequate to support an EUA consistent with the statutory criteria for issuance.

C. PRE-EUA ACTIVITIES AND SUBMISSIONS

Early engagement between an industry or government sponsor²³ and FDA about potential EUA products will facilitate more complete EUA requests and enhance FDA's ability to review and ultimately grant the EUA as appropriate. FDA also recognizes that circumstances can change rapidly, and planning for a potential emergency may unexpectedly transition to a response effort. Therefore, FDA strongly encourages the sponsor of a product that might be considered for an EUA, particularly one at an advanced stage of development, to contact the appropriate FDA Center before submitting a formal request for an EUA. For purposes of this guidance, these submissions and related interactions are referred to as "pre-EUA" activities.

FDA's review of a pre-EUA submission is not an indication of FDA's views on the product's potential to be used under an EUA, or that the sponsor has obtained or submitted all the information necessary for FDA to review a formal request for consideration of an EUA. Pre-EUA activities are not a substitute for sponsor efforts to develop the product toward approval, including submission and, when appropriate, implementation of proposals for clinical trials

²² EUAs may be requested and issued to authorize prescribing for unapproved uses of approved products, often referred to as "off-label" uses because, under emergency circumstances, licensed prescribers may not be able to make the case-by-case individual patient prescribing decisions that occur within the practice of medicine. CDC, for example, may act as the nation's doctor in recommending an unapproved use of an approved product. In such cases, CDC may request that FDA issue an EUA to authorize such unapproved use, often with the intended purpose of preserving liability protections afforded under the Public Readiness and Emergency Preparedness (PREP) Act, described in section VI of this guidance.

²³ For purposes of this guidance, the term "sponsor" is used when referring to the applicant, submitter, or person requesting an EUA. If specifically referring to a government or industry sponsor only, then "government" or "industry" is used as an adjective to describe the specific type of sponsor, e.g. government sponsor or industry sponsor.

Contains Nonbinding Recommendations

designed to determine whether the product is safe and effective for its intended use. In addition to design and implementation of clinical trials for development efforts in non-emergency settings, for some MCMs and for some emergency response plans, FDA encourages sponsors to design and propose appropriately controlled clinical trials that could be conducted during the emergency response either to run in parallel with an EUA or instead of an EUA.

Pre-EUA activities may include discussions with FDA about a potential EUA product. Such discussions may occur prior to the submission of a formal request for consideration of an EUA or issuance by the HHS Secretary of an EUA declaration. They may also include discussions about the appropriate vehicle to use (e.g., IND or IDE, Master File, pre-EUA submission) for submitting data on the product prior to submission of a formal request for consideration of an EUA.

Generally, FDA recommends that a sponsor submitting data as part of "pre-EUA" activities follow recommendations for submitting pre-IND, IND, and device pre-submissions to the relevant medical product Center.²⁴ A "pre-EUA" submission is typically separate from other developmental submissions on file with FDA; its existence does not imply that any specific set of qualifications has been met but represents the initiation of a series of preliminary interactions to discuss potential suitability for EUA consideration. In addition, FDA requests that the sponsor follow the recommendations for the content of the submission outlined in section III.D.2 of this guidance and for the format of the submission contained in section III.D.3 of this guidance.

As with requests for issuance of EUAs, FDA prioritizes its pre-EUA activities based on a variety of factors. Many of these are discussed more fully in section III.D.4.a of this guidance. Examples of additional factors FDA may take into account in prioritizing pre-EUA activities may include: progress on product development targets or milestones; competing FDA obligations or exigent circumstances (e.g., user fee deadlines, other Agency priorities); and whether there is a significant likelihood that the product would be retained in or added to government stockpiles if the product is authorized for use in an emergency. The extent of, and timelines for, review of such submissions 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), the circumstances of the emergency, and the workload of the review staff.

²⁴ For detailed information on meetings about product development with CDER and CBER, see FDA's guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants* (Revision 1). In the *Federal Register* of March 11, 2015 (80 FR 12822), FDA published a notice announcing the availability of a draft guidance *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products* (Revision 2). The revised draft guidance updates the guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants* (Revision 1) and, when finalized, will represent the Agency's current thinking on the topic. For detailed information on meetings about product development for a device, including those that are regulated by CBER, see *Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff* (February 2014) at <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf>.

Contains Nonbinding Recommendations

D. REQUEST FOR AN EUA

1. Preparedness and Response

FDA can issue an EUA not only during an emergency to support a rapid public health response, but also for significant potential of an emergency (e.g., in advance of an emergency) based on the requisite EUA declaration by the HHS Secretary, to support preparedness planning. The circumstances of a CBRN emergency may afford FDA or other stakeholders little time to consider the statutory criteria and appropriate conditions to ensure safe and effective use of an MCM when an event occurs. For instance, some CBRN events may require dispensing of MCMs within just a few hours of identification or notification of an exposure. It may be necessary to use other MCMs, such as IVDs, to identify the presence of a CBRN agent in an individual. An EUA issued before an emergency could permit use of an MCM during an emergency without the need for further authorization by FDA, assuming no new information about the product or emergency requires amendment and/or reissuance of the EUA. Section 564 thus reflects the fact that some scenarios may support issuance of an EUA before an emergency (including if the emergency is occurring in another country but not yet in the U.S.) to better enable federal, state, local, tribal, and territorial governments to plan for such use during an emergency.

Based on experience, FDA expects that many requests for an EUA will be submitted by government sponsors (e.g., HHS or the Department of Defense (DoD)), although industry sponsors may also submit such a request.

2. Information Recommendations

a. Summary of Recommended Information and/or Data

FDA recommends that a request for an EUA include a well-organized summary of the available scientific evidence regarding the product's safety and effectiveness, risks (including an adverse event profile) and benefits, and any available, approved alternatives to the product. The exact type and amount of data needed to support an EUA may vary depending on the nature of the declared emergency or threat of emergency and the nature of the candidate product. 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.²⁵

FDA recommends that the following information be submitted in any request for an EUA:

- 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; where, when, and how the product is anticipated to be used; and/or the population(s) for which the product may be used);

²⁵ FDA recognizes that data and information available in support of a request for an EUA for preparedness purposes and a request for an EUA during an emergency response may differ.

Contains Nonbinding Recommendations

- A description of the product's FDA approval status (e.g., whether the product is unapproved or whether it is approved but the EUA is for an unapproved use); whether the product or intended use is under an investigational application (e.g., if an IND/IDE is in effect or has been submitted; whether the product is approved in a foreign country for either the proposed use or another use; information on the use of the medical product by either a foreign country or an international organization (e.g., the World Health Organization (WHO));
- The need for the product, including identification of any approved alternative product(s) and their availability and adequacy for the proposed use, and the unmet need(s) the EUA would address;
- Available safety and effectiveness information for the product (discussed in more detail below);
- A discussion of risks and benefits, including available information concerning the threats posed by the CBRN agent(s) involved (discussed in more detail below within this section);
- Information on chemistry (as applicable), manufacturing, and controls; a list of each site where the product, if authorized, is or would be manufactured, and the current CGMP status of the manufacturing site(s);
- Information about the quantity of finished product on hand and the surge capabilities of the manufacturing site(s);
- Information comparable to an FDA-approved package insert or instructions for use; drafts of the “Fact Sheets” to be furnished to health care professionals or authorized dispensers²⁶ and recipients of the product, which typically are part of pre-EUA discussions (see section III.E.1 of this guidance); and a discussion of the feasibility of providing such information in an emergency;

²⁶ It may be appropriate in certain emergency scenarios for responders (e.g., government personnel, volunteers) to administer or dispense an MCM authorized for use under an EUA. These responders could include individuals who are not licensed health care professionals or who are licensed health care professionals yet would be acting outside of their State’s professional scope of practice by administering or dispensing the MCM. Such responders are referred to in this guidance as “authorized dispensers.”

Contains Nonbinding Recommendations

- If seeking an extension of a product's labeled expiration date, any available information in support of such an extension²⁷ (e.g., information on product stability such as test results; prior and anticipated storage and handling conditions; the lots, batches, or other units affected; any prior expiration date extensions; and for medical devices, an explanation of labeled expiration date, such as whether the inclusion of such information was based on a premarket requirement, requirements of another regulatory body, or a business decision); and
- Any right of reference²⁸, as applicable.

b. Recommended Safety Information

(i) *In General*

The amount and type(s) of safety information that FDA recommends be submitted as part of a request 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 anticipates that, for some products, data from controlled clinical trials will be available. For others, FDA expects to consider clinical experience from other than a controlled trial if the circumstances warrant. In addition, for some devices (e.g., IVDs), if clinical data are not available, FDA may consider accepting data solely from bench testing, if the circumstances warrant. FDA expects to interpret safety information in light of the seriousness of the clinical condition, alternative diagnostics, prophylaxis, or alternative therapies (if any), and the specific circumstances of the emergency or threat of emergency. FDA encourages any sponsor of a candidate product to have early discussions with FDA (even before a determination of actual or potential emergency) about the nature and type of safety data that might be appropriate to submit to FDA.

(ii) *Unapproved Uses of Approved Products*

If the new indication uses a similar dose, duration, route of administration, or mechanism of action (as appropriate given the nature of the product), and the intended patient population is

²⁷ Although FDA generally intends to address extensions of product expiration dates pursuant to section 564A(b) separately (see section IV.B of this guidance), there may be instances when an EUA candidate product may be beyond or nearing its labeled expiration date during an emergency. For example, if FDA issues an EUA for an approved product (i.e., to address unapproved use of that product), then the EUA may include expiration date extension as part of the authorization (section 564(e)(2)(B)(i)). Thus, FDA recommends that a request for an EUA for use, or anticipated use, of an approved product that is approaching or beyond its labeled expiration date include any available information that may support an extension of the product's expiration date (e.g., storage conditions, name of manufacturer, lot number(s), labeled expiration date, etc.).

²⁸ For purposes of this guidance, a "right of reference" means the authority to rely upon, and otherwise use, data submitted from reports of an investigation or data previously submitted to FDA in support of an application, including the ability to make available the underlying raw data for FDA audit, if necessary. Sponsors who are not the owner of the submitted document(s)/data may need to seek written permission demonstrating their right of reference.

Contains Nonbinding Recommendations

similar, to that for which the product is approved, FDA recommends that the request for an EUA reference the approved application, including right of reference as applicable. If the new use poses a different risk to the patient population (e.g., suggesting the possibility of increased toxicity), FDA 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.

(iii) Unapproved Products

The range of available data for unapproved 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. FDA also encourages that human safety information from clinical trials and individual patient experience be provided, if available. Data submitted in the request should attempt to link the likely exposure to the MCM to any relevant, existing preclinical data. Similarly, when animal data are used, sufficient information should be provided to link the results of these data to expected exposures to the MCMs related to the proposed use in humans. Any information on safety associated with use in humans of this or related compounds or devices of a similar design should also be submitted.

c. Recommended Effectiveness Information

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 also depend on the circumstances of the CBRN 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 include²⁹ any available relevant scientific evidence regarding the following:

- Product's mechanism(s) of action to diagnose, treat, or prevent the disease or condition underlying the request;
- For drugs, preclinical testing data, such as *in vitro* evidence of the effect of the product in preventing or reducing the toxicity of the specified agent;
- Data on activity or effectiveness in animals that would contribute to understanding potential effects in humans, including but not limited to any animal efficacy studies available for products being developed under the Animal Rule;³⁰

²⁹ For products under an IND or IDE, or for which there is a Drug or Device Master File, sponsors may refer to the appropriate document on file containing such information, with appropriate right of reference as applicable.

³⁰ See 21 CFR 314.600 (drugs) or 21 CFR 601.90 (biological products); see also *Product Development Under the Animal Rule – Guidance for Industry* (October 27, 2015), available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM399217.pdf>.

Contains Nonbinding Recommendations

- Evidence from human experience relevant to assessing activity, effectiveness, and dosing (e.g., in published case reports, uncontrolled trials, controlled trials, and any other relevant human use experience);
- For drugs, data to support the proposed dosage for the intended use (including pharmacokinetics and pharmacodynamics data, and for vaccines or antibody therapies, immunogenicity and/or achievement of protective levels of relevant parameters of immunity); and
- For IVDs, device performance data to support the intended use such as analytical sensitivity and analytical specificity, and data from testing fresh, contrived, banked or archived specimens.

d. Other Data Considerations

FDA recommends that a request for an EUA include the following types of data, as appropriate and to the extent feasible:

- Well-organized study reports that provide a complete assessment and analysis, including any statistical analyses, 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; and
- Source data for clinical studies, nonclinical laboratory studies, and any animal studies that contribute to assessing 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 that are in a language other than English.

FDA recommends that requests for EUAs include statements on whether the nonclinical laboratory studies were conducted in compliance with applicable Good Laboratory Practice for Nonclinical Laboratory Studies regulations (GLP)³¹ and whether the clinical studies were conducted in compliance with applicable Good Clinical Practice standards³². FDA also recommends specifying the methods and quality systems used to ensure the quality and integrity of data from any animal studies submitted in support of an EUA request but not performed under GLP.

Data from any ongoing testing (e.g., longer term stability data) or other data or information that may change FDA's evaluation of the product's safety or effectiveness and that become available

³¹ See 21 CFR Part 58.

³²Information available at <http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm>.

Contains Nonbinding Recommendations

during the period of review or the term of the EUA. Such data should be submitted to FDA when such data become available, including any appropriately controlled clinical trials conducted in parallel with the EUA during the emergency response. Data that are required to be submitted under the condition(s) established as part of the authorization of an EUA should be submitted as specified in the EUA.

e. Discussion of Risks and Benefits

FDA recommends that a request for an EUA include a discussion of the candidate product's known and potential risks and benefits, which includes a synthesis of the data and information requested above, including:

- Measures taken to mitigate risk or optimize benefit;
- Limitations, uncertainty, and data gaps;
- A description of circumstances, if any, under which the product should not be used (e.g., contraindications); and
- To the extent known, information concerning the threats posed by the CBRN agent(s) (actually or potentially) involved, and anticipated response and operational considerations that may be relevant to an assessment of risks and benefits.

3. Format of Submissions

FDA recommends that each submission begin with a section that describes the contents and organization of the included materials. The sponsor of an investigational or marketing application for the product or anyone with a right of reference may refer to data or other information previously submitted to the FDA in a marketing application, investigational application, or Master File.³³

FDA expects material to be provided in a reviewable form and sufficiently complete to permit substantive review. Nevertheless, FDA recognizes that, in rapidly developing or unexpected emergency circumstances, or when previously unanticipated or unavailable MCMs are being considered, it may not be possible for a sponsor to provide all of the requested data or to provide it in the format suggested in a timely manner. In such circumstances, FDA will accept and evaluate the request for an EUA based on data in the form the sponsor is able to submit. However, a request that is missing data, poorly documented, or otherwise incomplete will make FDA's determination of whether the product's benefits outweigh its risks more difficult and could 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.

Prior to submitting any materials to FDA, FDA recommends contacting the relevant medical product Center (e-mails provided below) for any specific directions unique to the

³³ FDA requests that references to previously submitted data or information specify where the data or information can be found (e.g., identify file by submission date, name, reference number, volume, and page number).

Contains Nonbinding Recommendations

submission. Submissions, including a cover letter, may be provided in electronic or paper format. General information, as well as links to Center-specific submission preparation guidelines, is included in the Center contact information below. When a request is submitted in paper, FDA recommends that a minimum of three copies be provided to the relevant medical product Center address below.

In addition, FDA recommends that an email alert, highlighting the urgency if related to an imminent or ongoing emergency and including the cover letter to the submission, be sent to the following email addresses:

- The identified Center email address below;
- EUA.OCET@fda.hhs.gov; and
- Any other previously established contacts within the Center familiar with the submission.

For the Center for Biologics Evaluation and Research:

Emails for EUAs related to biological products regulated by CBER: CBEREUA@fda.hhs.gov

Paper submissions:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

Electronic submissions:

CBER is prepared to receive electronic EUA submissions in standardized electronic Common Technical Document (eCTD). Contact ESUBPREP@fda.hhs.gov for information or visit <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm>

Contains Nonbinding Recommendations

For the Center for Devices and Radiological Health:

Email for EUAs related to IVD medical devices: device@fda.hhs.gov

Email for EUAs related to non-IVD medical devices: cdnhemcm@fda.hhs.gov

Paper submissions for both:
Food and Drug Administration
Center for Devices and Radiological Health
Document Control Center
Food and Drug Administration
10903 New Hampshire Avenue
WO66-G609
Silver Spring, MD 20993-0002
ATTN: EUA

For the Center for Drug Evaluation and Research:

Emails for drug and biological products regulated by CDER: CDEREUA@fda.hhs.gov

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

Electronic submissions:
CDER is prepared to receive electronic EUA submissions in standardized electronic Common Technical Document (eCTD) format as well as non-eCTD format. Contact ESUB@fda.hhs.gov for information or visit <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm>.

4. FDA Processing of an EUA Request

a. Prioritization of Requests

(i) In General

FDA intends to establish priorities for its review of requests to issue an EUA based on a variety of factors. These include:

- The seriousness and incidence of the clinical disease or condition (e.g., based on federal requirements, federal partner prioritization requests);

Contains Nonbinding Recommendations

- The public health need for the product and, when known, the safety and effectiveness of other potential MCMs;
- The urgency of the treatment need (i.e., the window of opportunity for treatment can vary for different medical conditions);
- Availability and adequacy of the information concerning the likelihood that the product may be safe and effective in preventing, treating, or diagnosing the condition;
- The potential role that use of the product may have in ensuring national security;
- Whether the product is included in government stakeholder stockpiles;
- The extent to which the product would serve a significant unmet medical need, including in:
 - A subpopulation (e.g., pregnant women, infants, and children, and immunocompromised persons)
 - The stage of the emergency response (e.g., evolving understanding of the disease or condition and/or MCMs in the context of an ongoing public health response, availability of previously authorized MCMs);
- Whether the request is from (or supported by) a government stakeholder (e.g., the proposed emergency use will be appropriately coordinated with, augment, and not interfere with official government stakeholder response efforts³⁴);
- The availability of the product, (e.g., the quantity and manufacturing capacity); and
- Whether other mechanisms, such as developing a clinical study protocol under an IND or IDE for investigational use, typically in coordination with government stakeholders, or granting access to an investigational product under an IND or IDE expanded access authority, might be more appropriate for allowing emergency access to products under development (e.g., when there are little or no safety or efficacy data available).

(ii) Additional Considerations for Prioritizing Requests for an EUA in Advance of an Emergency

The statutory criteria for issuing an EUA are the same whether the EUA is issued before or during a CBRN emergency. Therefore, in deciding whether to issue an EUA in advance of an emergency for preparedness purposes, FDA will make a case-by-case assessment of product risks and benefits based on the totality of available safety and efficacy data consistent with the

³⁴ For example, FDA often encourages EUA submissions from commercial developers of diagnostic tests to expand laboratory testing capacity during emergencies, consistent with U.S. government response plans.

Contains Nonbinding Recommendations

criteria for issuance of an EUA in section 564(c), just as it would in considering a request for an EUA to be issued during an emergency response.

It will not be appropriate to issue an EUA for every potential MCM or in anticipation of each emergency scenario. For example, FDA anticipates that, in all but the most catastrophic scenarios, only comparatively mature products (e.g., those with demonstrated safety data and in advanced stages of efficacy testing) are likely to meet the minimum risk-benefit criteria for an EUA for preparedness purposes. In addition, the extent to which the proposed use of an MCM is supported by operational planning, whether the MCM is already held in a government stockpile, and whether timely and comprehensive pre-EUA submissions have been available for FDA review will be relevant to the prioritization of a request for an EUA for preparedness purposes.

Nevertheless, the extent to which the sponsor is actively pursuing FDA approval for the MCM is relevant to FDA's prioritization of requests to issue an EUA in advance of an emergency for preparedness purposes³⁵, and the duration of such an EUA if issued. An EUA is not a long-term alternative to obtaining FDA approval, licensure, or clearance for MCMs; the issuance of an EUA in advance of an emergency (or during an emergency) is not an appropriate endpoint for new product development.

Section 564 expressly states that FDA's authority to allow emergency use of an unapproved product, or unapproved use of an approved product, does not authorize a delay in FDA's review or other consideration of any pending application. If an EUA remains in effect for more than one year, FDA must provide the sponsor written explanation of obstacles to approval and specific actions to be taken by FDA and the sponsor to overcome them.³⁶ Moreover, FDA is required to review the circumstances and appropriateness of an EUA periodically, including progress made with respect to the approval of the product.³⁷ FDA generally does not anticipate allowing an EUA issued in advance of an emergency for preparedness purposes to remain in effect indefinitely. If the sponsor is not actively working to advance the MCM's development for an approval, FDA may reconsider the EUA's status and/or consider terminating the EUA.

b. Review of Requests to Issue an EUA

A formal request to issue an EUA generally should not be submitted until the Secretary of HHS has issued an EUA declaration under section 564(b)(1). In particular, although section 564 allows FDA to issue an EUA for preparedness purposes, in such cases the HHS Secretary must first declare that circumstances exist justifying such an authorization in advance of an actual emergency based on a formal determination of a significant potential for emergency or a material

³⁵ As stated in section III.C with regard to pre-EUA activities, an EUA is not a substitute for sponsor efforts to develop the product toward approval, including conducting clinical trials designed to determine whether the product is safe and effective for its intended use. When appropriate, FDA encourages sponsors to design and propose appropriately controlled clinical trials that could be conducted during the emergency response either to run in parallel with an EUA or instead of an EUA.

³⁶ Section 564(b)(5).

³⁷ Section 564(g)(1).

Contains Nonbinding Recommendations

threat determination. FDA typically coordinates closely with HHS and other relevant government sponsors throughout the EUA process, from pre-EUA submissions to final disposition, including the need for issuance of the EUA declaration and any consultations on EUAs with federal partners.³⁸ Moreover, a formal request for issuance of an EUA typically will have the benefit of FDA feedback based on pre-EUA submission activities.

A sponsor seeking an EUA should submit its formal request in the form of an EUA submission, including reference to relevant pre-EUA submissions previously reviewed by FDA, and request to issue the EUA through the same process outlined in section III.D.3 of this guidance. Typically the data and other information in EUA submissions have already been reviewed by FDA and have had the benefit of FDA Center feedback based on pre-EUA submissions and interactions with FDA prior to submission of the request to issue an EUA.

c. Disposition of Requests

FDA is prepared to issue EUAs expeditiously (e.g., within hours or days) when circumstances warrant and adequate information has been made available for prior review through pre-EUA interactions. Generally, the timelines for FDA review and action on a request to issue an EUA will be determined on a case-by-case basis and will depend on factors such as:

- The product profile;
- The existence, if any, of pending applications for the product;
- The nature of the emergency, potential emergency, or threat of emergency;
- The organization and completeness of the request submission; and
- The workload of the reviewing Center's personnel.

A letter to the sponsor authorizing the emergency use(s) of an MCM will be signed by the Commissioner (or his/her designee) and will include a description of the authorized product and its use(s), any contraindications for the product, the criteria for issuance of the authorization, the scope of the authorization, waiver of certain requirements (if applicable), and any conditions on the authorized use. An authorized EUA will consist of (1) the signed letter of authorization and (2) any accompanying authorized materials (e.g., Fact Sheet for health care professionals, Fact Sheet for recipients, instructions for use, etc.).³⁹

FDA may decline to review or issue an EUA based on any number of factors. For example, the candidate product may fail to meet the necessary criteria identified in section 564 and discussed in section III.B.1 of this guidance, or it may fail to meet any one of the factors given the

³⁸ Section 564(c).

³⁹ The EUA letter of authorization and accompanying authorized materials will be posted on FDA's website at:
<http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm182568.htm#current>.

Contains Nonbinding Recommendations

circumstances of the emergency or threat of emergency (see section III.D.4.a of this guidance for a discussion of factors FDA will consider in reviewing requests for prioritization of EUA requests). Under such circumstances, the relevant product Center will notify the sponsor that the EUA review cannot be prioritized or FDA declines to issue an EUA for the candidate product.

E. CONDITIONS OF AUTHORIZATION

FDA may establish conditions on an EUA necessary or appropriate to protect the public health. Section 564(e)(1) establishes conditions applicable to unapproved products; section 564(e)(2) sets forth conditions applicable to unapproved use of approved products, which are similar, but not identical, to those applicable to unapproved products. Within these sections, some conditions are required (to the extent practicable given the applicable circumstances of the emergency or threat of emergency), whereas others may be imposed entirely at the discretion of FDA.⁴⁰

1. Information Relating to the EUA Product

a. Information for Health Care Professionals or Authorized Dispensers

For an unapproved product (section 564(e)(1)(A)(i)) and for an unapproved use of an approved product (section 564(e)(2)(A)), FDA must (to the extent practicable given the circumstances of the emergency) establish conditions to ensure that health care professionals who administer the EUA product are informed:

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

Therefore, FDA recommends that a request for an EUA include a “Fact Sheet” for health care professionals or authorized dispensers that includes essential information about the product. In addition to the required information, Fact Sheets should include:

- A description of the disease/condition;
- Any contraindications or warnings;

⁴⁰ See Appendix A for a table of required and discretionary conditions. Note that the statute states that FDA shall “establish such conditions on an authorization under this section as [FDA] finds necessary or appropriate to protect the public health” with respect to unapproved products and then provides examples of such conditions by use of the term “including” (section 564(e)(1)(A)). FDA interprets this language as giving FDA the authority and the responsibility to impose other conditions, not specified as examples in the statutory language, that may be necessary or appropriate in the circumstances of a particular emergency.

Contains Nonbinding Recommendations

- Dosing information (if applicable), including any specific instructions for special populations; and
- Contact information for reporting adverse events and additional information about the product.

Health care professionals or authorized dispensers will likely have very limited time to review Fact Sheets during an emergency and, therefore, FDA anticipates that Fact Sheets typically will be brief (i.e., a few pages). FDA makes available on its website Fact Sheets for products for which an EUA is issued.⁴¹

FDA further recommends that Fact Sheets target the health care professional or authorized dispenser who has the most basic level of training, recognizing that individuals responding to an emergency may have different levels of training, could come from a variety of backgrounds, and may have different types of experience or speak different languages. FDA recommends that Fact Sheets accompany the EUA product in an accessible form (e.g., printable as a hard copy) when the product is distributed to the health care professional or authorized dispenser if practicable. To the extent consistent with other conditions of authorization, information on the EUA product also may be disseminated to health care professionals or authorized dispensers through mass media (including print, broadcast, radio, satellite, Internet, or other electronic means of dissemination), videos/DVDs, or direct communication from public health agencies.

For unapproved drug products, which do not have FDA-approved labeling for any indication, FDA recommends that, in addition to the brief summary information found in a Fact Sheet, the sponsor also develop more detailed information similar to what health care professionals are accustomed to finding in FDA-approved package inserts. For medical devices regulated, such as *in vitro* diagnostics, in addition to the brief summary information found in a Fact Sheet, FDA recommends the sponsor also develop separate Instructions for Use.⁴²

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 (section 564(e)(2)(B)).⁴³ In such a situation, however, FDA must, to the extent practicable given the applicable circumstances, authorize a person acting pursuant to such EUA to provide, in

⁴¹For examples of Health Care Professional Fact Sheets, see FDA's website at: <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm182568.htm#current>.

⁴²For examples of Instructions for Use, see FDA's website at: <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm182568.htm#current>.

⁴³We note that this prohibition does not apply to changes in expiration dating permitted pursuant to section 564A(b). See section IV.B of this guidance.

Contains Nonbinding Recommendations

addition to the manufacturer's labeling, appropriate information with respect to the product, such as that provided in the brief Fact Sheet described above.⁴⁴

b. Information for Recipients

Although informed consent as generally required under FDA regulations⁴⁵ is not required for administration or use of an EUA product, section 564 does provide EUA conditions to ensure that recipients are informed about the MCM they receive under an EUA. For an unapproved product (section 564(e)(1)(A)(ii)) and for an unapproved use of an approved product (section 564(e)(2)(A)), the statute requires that FDA ensure that recipients are informed to the extent practicable given the applicable circumstances:

- That FDA has authorized emergency use of the product;
- Of the significant known and potential benefits and risks associated with the emergency use of the product, and of the extent to which such benefits and risks are unknown;
- That they have the option to accept or refuse the EUA product and of any consequences of refusing administration of the product;⁴⁶ and
- Of any available alternatives to the product and of the risks and benefits of available alternatives.

Therefore, FDA recommends that a request for an EUA include a "Fact Sheet" for recipients that includes essential information about the product. In addition to the above information, the Agency recommends that the content of the Fact Sheets for recipients include the following information:

- Product name and explanation of the intended use of the product;
- A description of the disease/condition;

⁴⁴ Additional information provided 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.

⁴⁵ See 21 CFR part 50.

⁴⁶ The President may under certain circumstances waive the option for members of the armed forces to accept or refuse administration of an EUA product (10 U.S.C. 1107a). In addition, the option to accept or refuse may not be practicable with regard to certain diagnostics because, for example, when a sample is taken from an individual it may be unknown, even to the health care professional, which diagnostic test will be used to test the sample. For this reason, Fact Sheets for both health care professionals and recipients may not accompany an EUA diagnostic product, but instead be publicly posted for reference when receiving test results.

Contains Nonbinding Recommendations

- A description of items to discuss with a health care provider and adverse event information, including contact information for how to get more information and for reporting adverse reactions; and
- Dosing information (if applicable), including specific instructions for home use or preparation (if applicable).

FDA recommends that recipients be given as much appropriate information as possible given the nature of the emergency and the conditions of the authorization.⁴⁷ Ordinarily, FDA expects that some written form of information will be given to recipients with the MCM, similar to the Fact Sheet for health care professionals or authorized dispensers. FDA recognizes that these Fact Sheets, like those for health care professionals or authorized dispensers, will generally be brief. To ensure that individuals of varying educational levels comprehend the information provided, FDA recommends that all written information be stated in the simplest language possible using techniques to improve health literacy.⁴⁸ In addition, translations to other languages may be appropriate if practicable.⁴⁹ FDA recognizes that some flexibility may be needed for health care providers or authorized dispensers to make minor, nonsubstantive changes to the fact sheets for recipients such as adding local contact information, using specific letterhead or minor format changes.

FDA acknowledges that exigent circumstances may dictate the use of other appropriate dissemination methods. Therefore, FDA expects that information would be disseminated in the most effective and expeditious way possible to reach the recipient before administration or use of an EUA product.⁵⁰ If, however, taking the time needed to provide such information would diminish or negate the effectiveness of the product for the recipient, FDA may include as a condition of authorization that the information be provided to the recipient as soon as practicable after dispensing. Other methods of dissemination may include internet posting, mass media, videos/DVDs, or direct communication from health care professionals and public health agencies.

2. Monitoring and Reporting of Adverse Events

For an unapproved product (section 564(e)(1)(A)(iii)), EUA conditions for monitoring and reporting of adverse events are required to the extent practicable given the circumstances of the emergency; such conditions may be established for an EUA for an unapproved use of an approved product (section 564(e)(2)(A)), at the discretion of FDA.

⁴⁷ For examples of Patient/Recipient Fact Sheets, see FDA's website at: <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm182568.htm#current>.

⁴⁸ See, e.g., <http://www.health.gov/communication/literacy/quickguide/healthinfo.htm>.

⁴⁹ When the translation of a fact sheet to a foreign language is determined to be appropriate and necessary, the party producing the translation is responsible for the accuracy and completeness of the translation; FDA does not intend to review translations to ensure their accuracy.

⁵⁰ As noted above, however, this may not be practicable or appropriate for certain diagnostic tests.

Contains Nonbinding Recommendations

Conditions may be placed to enable the collection and analysis of information on the safety and effectiveness of the EUA product during the period when the authorization is in effect and for a reasonable time following such period. FDA expects that the primary focus of adverse event-related conditions will be capturing serious adverse events and applying appropriate mechanism(s) for the collection of follow-up clinical information. Some reporting may be directed to predefined mechanisms to capture adverse event data (e.g., FDA's Safety Information and Adverse Event Reporting System (MedWatch) or Vaccine Adverse Event Reporting System (VAERS)). FDA will work with product sponsors in some circumstances to develop proposals for more active data collection and follow-up mechanisms to capture adverse event information under the EUA. FDA encourages EUA sponsors to provide proposals for data collection and follow-up during pre-EUA interactions.

3. Records

To the extent practicable given the circumstances of the emergency, FDA must establish conditions for a manufacturer of an unapproved product to maintain records and to grant FDA access to records concerning the EUA product.⁵¹ FDA anticipates that such conditions may relate to, for example, the number of doses, devices, or other unit(s) (including lot identification) that have been shipped or sold under an EUA; or the name and addresses of the facilities to and from which the EUA product was shipped. FDA may also impose comparable recordkeeping requirements on any person (e.g., an authorized distributor or dispenser) other than a manufacturer who carries out any activity for an unapproved EUA product (section 564(e)(1)(B)(iv)).

FDA may also impose recordkeeping and records access requirements on any person (including a manufacturer) engaged in an activity for which an EUA is issued for an unapproved use of an approved product (section 564(e)(2)(A)). In addition to the examples noted above for unapproved EUA products, examples may include conditions relating to actual use of the product and disposition of any unused product, and monitoring of patients who have been administered the product under an EUA.

4. Additional Conditions of Authorization

FDA, on a case-by-case basis and to the extent feasible given the circumstances of the emergency, may establish additional conditions that FDA finds to be necessary or appropriate to protect the public health (section 564(e))⁵², such as the following:

- *Distribution and administration*— conditions may be placed on which entities may distribute and who may administer the product, and how distribution and administration are to be performed. In addition, conditions may be placed on the

⁵¹ Section 564(e)(1)(A)(iv).

⁵² Section 564(e)(1)(B) (for unapproved products) and 564(e)(2)(A) (for unapproved uses of approved products).

Contains Nonbinding Recommendations

categories of individuals to whom, and the circumstances under which, the product may be administered. FDA anticipates that distribution and administration of EUA products will be performed according to existing official government response plans, as practicable and appropriate. In some cases, administration of an MCM may go hand-in-hand with dispensing the MCM. In establishing conditions with respect to the distribution and administration of an approved product for an unapproved use, FDA may not impose conditions that would restrict distribution or administration of the product when distributed or administered for the approved use.⁵³

- *Advertising*⁵⁴— conditions (e.g., limitations) may be placed on advertisements and other promotional descriptive printed matter (e.g., press releases issued by the EUA sponsor) relating to the use of an EUA product, such as requirements applicable to prescription drugs under section 502(n) and requirements applicable to restricted devices under section 502(r).

5. Waivers or Limitations of Compliance With Other Requirements

a. CGMPs

FDA generally expects that EUA products will be produced, stored, and distributed in compliance with CGMPs; however, limits or waivers may be granted in an EUA on a case-by-case basis, after consideration of the circumstances and of any alternative proposed approach (section 564(e)(3)).⁵⁵

b. Prescription Requirements

FDA may waive otherwise applicable prescription requirements, to the extent appropriate given the circumstances of an emergency (section 564(e)(3)). For example, operational considerations for a large-scale emergency response may demand that large numbers of individuals receive a medical product at centralized locations or locations that are not traditional health care settings, typically called “points of dispensing” (PODs). In such situations, the goal is to dispense medical product as quickly as possible to protect the public health, so it may not be practicable for each person to interact with a licensed practitioner before receiving a product authorized under an EUA (e.g., authorized dispensers may be responsible for dispensing or administering some or all MCMs). FDA also expects to include such waivers in EUAs on a case-by-case basis,

⁵³ Section 564(e)(2)(C).

⁵⁴ Section 564(e)(4).

⁵⁵ Section 564A(c) separately empowers FDA to authorize deviations from otherwise applicable CGMP requirements for the manufacture, processing, packing, or holding of eligible, FDA-approved products without issuing an EUA. This independent authority is discussed in section IV.C of this guidance.

Contains Nonbinding Recommendations

after consideration of the anticipated or actual circumstances of an emergency and the operational plans for a response.⁵⁶

c. REMS

FDA may waive otherwise applicable REMS requirements based on all CBRN emergencies that would trigger an EUA (section 505-1(k)). If it is determined that a waiver is needed, the waiver may apply to all REMS elements.⁵⁷

F. CATEGORIZATION OF LABORATORY TESTS UNDER AN EUA

Section 564(m) allows FDA, if issuing an EUA for a diagnostic device, to indicate whether the test can be performed at a point-of-care setting or only in a laboratory able to handle more complex tests. FDA may determine that a laboratory examination or procedure associated with such a device shall be deemed, for purposes of section 353 of the PHS Act, to be in a particular category of examinations and procedures, including the category described by subsection (d)(3) of such section (commonly termed “waived” devices) if, based on the totality of scientific evidence available:

- The categorization would be beneficial to protecting the public health; and
- The known and potential benefits of such categorization under the circumstances of the authorization outweigh the known and potential risks of the categorization.

FDA may also establish appropriate conditions on the performance of the test. The complexity categorization made under this authority is effective for the same period as the EUA and is independent of that made under Clinical Laboratory Improvement Amendments (CLIA) regulations.

G. DURATION AND REVISION OF AN EUA

FDA will specify the effective date of an EUA issued under section 564. In general, an EUA will remain in effect for the duration of the EUA declaration under which it was issued (see section III.A.2 of this guidance, which describes termination of an EUA declaration and its impact on existing EUAs), unless the EUA is revoked because the criteria for issuance as described in section III.B of this guidance are no longer met or revocation is appropriate to protect public health or safety (section 564(f),(g)).

⁵⁶ Section 564A(d) separately empowers FDA to issue an order authorizing emergency dispensing of eligible, FDA-approved products without issuing an EUA. This independent authority is discussed in section IV.D of this guidance.

⁵⁷ For further information on REMS, see FDA's draft *Guidance for Industry Format and Content of Proposed Risk Evaluation and Mitigation Strategies (REMS), REMS Assessments, and Proposed REMS Modifications* (October 2009) at <http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm184128.pdf>.

Contains Nonbinding Recommendations

1. Revision and Revocation

FDA will periodically review the circumstances and appropriateness of an EUA, including circumstances that might warrant revocation of the EUA. The review will include regular assessment based on additional information provided by the sponsor of the progress made with respect to the approval, licensure, or clearance of the unapproved product, or of the unapproved use of an approved product, for which an EUA was issued.

FDA may revise or revoke an EUA if the circumstances justifying its issuance (under section 564(b)(1)) no longer exist, the criteria for its issuance are no longer met, or other circumstances make a revision or revocation appropriate to protect the public health or safety.⁵⁸ Such circumstances may include significant adverse inspectional findings (e.g., when an inspection of the manufacturing site and processes has raised significant questions regarding the purity, potency, or safety of the EUA product that materially affect the risk/benefit assessment upon which the EUA was based); reports of adverse events (number or severity) linked to, or suspected of being caused by, the EUA product; product failure; product ineffectiveness (such as newly emerging data that may contribute to revision of the FDA's initial conclusion that the product "may be effective" against a particular CBRN agent); a request from the sponsor to revoke the EUA; a material change in the risk/benefit assessment based on evolving understanding of the disease or condition and/or availability of authorized MCMs; or as provided in section 564(b)(2), a change in the approval status of the product may make an EUA unnecessary.

2. Product Disposition and Continued Use

Upon revocation of an EUA or its termination as a result of the termination of the HHS EUA declaration supporting it, an unapproved product or its labeling, and product information for an unapproved use of an approved product, must be disposed of pursuant to section 564(b)(2)(B) and (b)(3).⁵⁹ Notwithstanding any such revocation or termination, under section 564(f)(2) an authorization shall continue to be effective to provide for continued use in any patient who began treatment before revocation or termination (to the extent found necessary by the patient's attending physician). Any study or future use of an EUA product beyond the term of a declaration is subject to investigational product regulations (e.g., IND regulations).

H. PUBLICATION

FDA will promptly publish in the Federal Register a notice of each EUA, including an explanation of the reasons for issuance, a description of the intended use, and any contraindications of the EUA product. The Agency also will promptly publish in the Federal Register each termination or revocation of an EUA and an explanation of the reasons for the decision. Although FDA is not required to publish notice of an EUA revision(s) in the Federal

⁵⁸ Section 564(g)(2).

⁵⁹ Section 564(b)(2)(B) provides that FDA shall consult with the manufacturer of the product with respect to the appropriate disposition.

Contains Nonbinding Recommendations

Register, FDA plans to post any revisions to EUAs on FDA's website at <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm182568.htm>.⁶⁰

I. OPTION TO CARRY OUT AUTHORIZED ACTIVITIES

If a manufacturer is the sole source of an unapproved product authorized for emergency use, that manufacturer must inform FDA, within a reasonable time after the authorization, if the manufacturer does not intend to make its product available for use under the EUA (section 564(l)). 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), however, does not limit FDA's authority to impose conditions on persons who carry out any activity for which an EUA is issued.

IV. EMERGENCY USE OF ELIGIBLE FDA-APPROVED MCMs WITHOUT AN EUA

Section 564A allows FDA to facilitate certain emergency activities involving FDA-approved MCMs without an EUA. This authority is independent of the EUA authority under section 564. In the past, to address concerns about potential FD&C Act violations related to the activities discussed in this section involving MCMs, FDA has either: (1) exercised its enforcement discretion with respect to the activity; or (2) issued an EUA to ensure that use of such MCMs remains covered under any otherwise applicable protections under the PREP Act⁶¹ (discussed in section VII of this guidance). MCMs used under this authority qualify for applicable PREP Act protection.⁶²

In some cases, FDA and CDC may coordinate activities under section 564A authorities including the issuance of an emergency dispensing order, waiver of cGMPs, waiver of REMS, extension of expiration dating, and/or issuance of EUI for specific MCMs.⁶³

⁶⁰ In publicly releasing information on an EUA, FDA will take necessary steps to protect nonpublic information and information otherwise protected by law, as appropriate.

⁶¹ See 42 U.S.C. 247d-6d.

⁶² See 42 U.S.C. 247d-6d(i)(1)(C), (i)(7)(B)(iii).

⁶³ See, e.g., Emergency Dispensing Information tables for doxycycline and ciprofloxacin at: <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm495126.htm#doxy>
<http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm495126.htm#cipro>.

Contains Nonbinding Recommendations

A. ELIGIBLE PRODUCTS

The emergency authorities in section 564A apply only to those medical products that are “eligible” (as defined in section 564A(a)) (referred to in this document as “eligible MCMs”). Eligible MCMs must be:

- Approved by FDA;
- Intended for their approved use to prevent, diagnose, or treat a disease or condition involving a CBRN agent(s), or a serious or life-threatening disease or condition caused by a product used for such a purpose; and
- Intended for use during circumstances in which there has been either:
 - A determination of an emergency or a significant potential for an emergency made by the Secretary of Homeland Security, the Secretary of Defense, or the Secretary of HHS (as described in subparagraph (A), (B), or (C) , respectively, of section 564(b)(1)) (i.e., one of the three EUA determinations that may support issuance of an EUA declaration, as described in section III.A of this guidance); or
 - A material threat (described in subparagraph (D) of section 564(b)(1)) identified by the Secretary of Homeland Security pursuant to section 319F–2 of the PHS Act that is sufficient to affect national security or the health and security of U.S. citizens living abroad (i.e., a Department of Homeland Security (DHS) material threat determination, which may also support issuance of an EUA declaration, as described in section III.A of this guidance).⁶⁴

B. EXPIRATION DATE EXTENSIONS WITHOUT AN EUA

FDA may extend the expiration date of an eligible, FDA-approved MCM stockpiled for use in a CBRN emergency if the extension is supported by an appropriate scientific evaluation that is conducted or accepted by FDA. An "expiration date" is defined as “the date established through appropriate stability testing...to ensure that the product meets applicable standards of identity, strength, quality, and purity at the time of use” (section 564A(b)(4)).

For each expiration date extension granted, FDA must identify the “specific lot, batch, or other unit of the product”⁶⁵ and the duration of the extension.⁶⁶ In addition, FDA must

⁶⁴ As noted previously with respect to EUAs, FDA has construed a material threat identification pursuant to section 319F-2 to apply to the health and security of U.S. citizens living abroad, even though that provision does not specifically focus on citizens outside the United States. Thus, a material threat determination may, in appropriate circumstances, serve as a basis for exercise of emergency authorities under section 564A(b),(c), and (d) and 505-1 as necessary for the protection of U.S. citizens living abroad.

⁶⁵ Section 564A(b)(2)(A).

Contains Nonbinding Recommendations

identify any other requirements or conditions related to each expiration date extension that the Agency deems appropriate for the protection of the public health, which may include requirements for, or conditions on:

- Product sampling,
- Storage,
- Packaging or repackaging,
- Transport,
- Labeling,
- Notice to product recipients,
- Recordkeeping,
- Periodic testing or retesting, or
- Product disposition.⁶⁷

The expiration date extension authority in section 564A applies to any eligible MCM, including eligible MCMs tested through the federal Shelf-Life Extension Program (SLEP). Since the mid-1980s FDA has engaged with federal partners in SLEP; DoD administers the program, while FDA tests the stability of certain federally stockpiled drug products to assess and extend, as appropriate, the useful shelf-life of such products. The explicit expiration date extension authority added by PAHPRA does not displace the longstanding federal SLEP, but eliminates any uncertainty about the legal status of eligible products for which FDA authorizes an extended expiration date, whether or not FDA also issues an EUA.

At this time FDA is not proposing or recommending any changes to SLEP or procedures for expiration date extensions for products tested through SLEP. For drugs tested within the SLEP program, federal participants should continue to submit requests to extend the expiration date of eligible MCMs using established processes. FDA is considering approaches for expiration extension for eligible products that are not tested within the SLEP program. Government stakeholders should consult with FDA via email or letter to the relevant Center and OCET points of contact identified in section III.D.3 of this guidance.⁶⁸

⁶⁶ Section 564A(b)(2)(B).

⁶⁷ Section 564A(b)(2)(C).

⁶⁸ For additional information about expiration dating extensions see <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm411446.htm>.

Contains Nonbinding Recommendations

Although FDA may rely on section 564A to authorize an expiration date extension without issuing an EUA, if an EUA is requested for a product that is nearing or beyond its labeled expiration date, FDA may consider extending that expiration date and imposing conditions in connection with an EUA request as discussed in section III.D.2.a of this guidance.

1. In General

FDA may authorize deviations from otherwise applicable CGMP requirements for the manufacture, processing, packing, or holding of eligible, FDA-approved products without issuing an EUA (section 564A(c)). Products that receive a waiver from applicable CGMPs will not be considered adulterated or misbranded under the FD&C Act. This includes requirements under section 501 or 520(f)(1) or applicable conditions prescribed with respect to the eligible product by an order under section 520(f)(2).

Although FDA may rely on section 564A to waive CGMP requirements without issuing an EUA, if an EUA is requested for a product for which a CGMP waiver is also requested, FDA may consider waiving CGMP requirements and imposing conditions in connection with the EUA as discussed in section III.E.5 of this guidance.

2. Procedures for Request and Issuance

FDA may issue waivers on its own initiative, but expects that any such action will be uncommon. Since the need for a waiver will be driven by the exigencies and other demands of responding to a CBRN emergency, FDA expects that in most cases a waiver will be based on a request from a government stakeholder or other interested party. For example, government stakeholders or manufacturers of products intended for use in a CBRN emergency may submit a request for a CGMP waiver for eligible products based on actual or anticipated emergency response activities that necessitate the waiver. FDA recommends, however, that requests be submitted only after consultation with and among relevant government stakeholders (e.g., CDC, and government officials in adjacent jurisdictions) that are or eventually may be part of a coordinated or related response effort involving the CBRN agent(s) or MCM. For example, absent compelling justification and to maintain response consistency, FDA does not expect to grant multiple CGMP waivers for the same MCM or CBRN use. FDA generally will not issue a waiver based on a request from an individual state if FDA has already issued the same type of waiver for the same MCM on a nationwide basis. Similarly, if FDA receives CGMP waiver requests for a particular MCM from multiple states or federal partners at the same time, FDA generally anticipates it will issue a single waiver (if a waiver is appropriate). Advance consideration and coordination are critical to ensure appropriate consistency and avoid unnecessary duplication.

FDA intends to evaluate requests for CGMP waivers pursuant to section 564A(c) on a case-by-case basis. A waiver may be issued when, based on the information available, the Agency concludes it is reasonable to issue a waiver to facilitate a CBRN emergency response or preparedness efforts. Requests for waivers should include the following information:

Contains Nonbinding Recommendations

- The identity and quantity of the medical product involved (e.g., product name(s); dosage form(s) and strength(s); number of doses, units, lots, or other unit(s); and unit/lot identifiers, as appropriate);
- The manufacturer's name, address, and contact information;
- The FDA application file number for the product, if known (e.g., NDA, BLA, IND, IDE);
- The actual or potential CBRN emergency for which the product is intended to be used;
- The anticipated conditions (e.g., storage, handling, transport, packaging) that will or may deviate from CGMP requirements and for which a waiver is being requested, including why such deviation may be necessary and the anticipated duration; and
- Available information about the potential impact of the deviation on the safety or efficacy of the product (e.g., strength, purity, quality).

FDA may request additional information to assess the request and decide whether to grant a waiver. A waiver of CGMP requirements pursuant to section 564A(c) may either (1) be issued independent of any other FDA action or, when appropriate, (2) be included with an emergency dispensing order under section 564A(d) (see section IV.D of this guidance).

Submit a request for a CGMP waiver for an eligible MCM via e-mail or letter to the relevant Center and OCET points of contact identified in section III.D.3 of this guidance.

D. EMERGENCY DISPENSING WITHOUT AN EUA

Emergency dispensing of eligible, FDA-approved products is allowed under section 564A(d) without adhering to the requirements of section 503(b) or 520(e). This authority includes dispensing such products without an individual prescription for each recipient (often referred to as “mass dispensing”)⁶⁹ if: (1) permitted by state law where the product is dispensed (section 564A(d)(2)(A)) or (2) dispensed in accordance with an emergency dispensing order issued by FDA (section 564A(d)(2)(B)). This streamlined mechanism permits emergency response activities that involve an emergency dispensing strategy needed to meet immediate public health needs, but that otherwise may not comply with the FD&C Act’s prescription requirements.⁷⁰ Like other provisions in section 564A, FDA may issue an emergency dispensing order to allow emergency dispensing of eligible products without having to issue an EUA. Products that are

⁶⁹ The term “emergency dispensing” includes, but is not limited to, the public health response activity of “mass dispensing” of MCMs (e.g., through points of dispensing).

⁷⁰ This may include dispensing without an individual prescription, or dispensing with an incomplete prescription, e.g., without all of the information otherwise required by FDA, such as the name and address of the dispenser, name of the prescriber, serial number, etc. (see, e.g., section 503(b)(2) (21 U.S.C. § 353(b)(2)). This also may include dispensing by a non-health care professional.

Contains Nonbinding Recommendations

dispensed pursuant to section 564A(d) (i.e., under state law or under an FDA emergency dispensing order) will not be considered unapproved, adulterated, or misbranded under the FD&C Act.

Although FDA may rely on section 564A to allow emergency dispensing of FDA-approved products without issuing an EUA, if an EUA is requested for a product for which emergency dispensing is also requested, FDA may consider waiving prescription requirements and imposing conditions in connection with considering the EUA (as discussed in section III.E.5 of this guidance).

1. Procedures for Issuing Emergency Dispensing Orders

States may have in place provisions that facilitate emergency dispensing of eligible MCMs or may choose to take legal actions (e.g., pass laws, issue emergency orders) that facilitate emergency dispensing of eligible MCMs.⁷¹

Section 564A(d) provides a mechanism for FDA to fill any gaps in state law or to ensure adequate and consistent emergency response within and across state lines by issuing an order to allow emergency dispensing of eligible MCMs (i.e., an emergency dispensing order). FDA may issue such an order before or during an emergency. However, to receive the protections from potential violations of the FD&C Act under section 564A(d), eligible MCMs may only be dispensed during (not before) an emergency, as may be determined by relevant government stakeholders (see section IV.D.2 of this guidance).

FDA intends to issue orders to allow emergency dispensing when, based on available information about the MCM, emergency response plans, and operational needs, the Agency concludes that it is reasonable to permit emergency dispensing of eligible FDA-approved products. FDA anticipates that government stakeholders will submit a request for an emergency dispensing order. However, in the event that FDA deems it appropriate to issue an order without such a request, FDA will notify the relevant government stakeholders (e.g., ASPR, CDC, DHS, and/or DoD, regional authorities) as appropriate.

a. Federal requests

FDA expects that federal government stakeholders will initiate any requests relating to federally-maintained or federally-controlled MCMs, and to the extent possible, will consider emergency dispensing activities of the same MCMs at all jurisdictional levels including state, local, tribal, and territorial jurisdictions. For example, if both the CDC Strategic National Stockpile and state or local jurisdictions stockpile an antibiotic for use for post-exposure prophylaxis of inhalational

⁷¹ Whether or not a particular state legal provision or action is sufficient to permit the government stakeholder's anticipated emergency dispensing strategy within their state rests in large part on the interpretation of that state's law, which is a matter that should first be directed to the appropriate legal authority within the relevant jurisdiction (e.g., the state Attorney General). To ensure clarity, and perhaps increase the likelihood that state laws, regulations, orders, or other legal actions to permit emergency dispensing are deemed legally sufficient, it is recommended that such actions address the same eligibility, scope, duration, and other elements that FDA intends to address in its emergency dispensing orders.

Contains Nonbinding Recommendations

anthrax, FDA anticipates that a CDC request for an order to allow emergency dispensing for that antibiotic would address all other relevant government stakeholder stockpiles. FDA also expects that a federal stakeholder seeking an emergency dispensing order, or to which such an order is otherwise directed, will communicate with other government stakeholders as necessary to ensure a coordinated emergency response.

b. Non-federal requests

FDA also anticipates receiving requests relating to MCMs maintained or controlled solely by non-federal government stakeholders (e.g., public health officials at the state level or in major metropolitan areas that independently maintain MCM stockpiles) to address the possibility that such assets may be deployed independent of reliance on federal assets. FDA strongly recommends that such requests be submitted only after consultation with relevant federal government stakeholders (e.g., CDC), as well as other relevant government stakeholders (e.g., officials in adjacent jurisdictions) that are or may be part of a coordinated or related response effort involving the same CBRN agent(s) or MCM.

c. Content of requests

FDA anticipates that a request for an emergency dispensing order will include the following information:

- The CBRN agent(s) involved;
- The FDA-approved product(s) for which the order is requested (including the product name(s), manufacturer, quantity, dosage form(s), strength(s), dosing regimen(s), lot or batch number(s), expiration date(s), and any other identifying information);
- The intended use(s) of the product;
- The jurisdiction(s) to be covered (e.g., nationwide, state, region);
- How soon the order needs to be issued;
- The source of the product (e.g., Strategic National Stockpile (SNS), state or local MCM stockpile, multiple sources);
- The proposed duration of the order; and
- The relevant government stakeholders' roles in an anticipated response.

FDA may also request additional information to evaluate and make a decision on the request. Examples of additional information include: information about anticipated dispensing strategies, dispensing locations, dispensing personnel, recipient screening, or how health care professionals or authorized dispensers and recipients will be informed about product safety, efficacy, and use during an emergency (e.g., whether corresponding CDC-issued EUI will be needed to accompany the product).

Contains Nonbinding Recommendations

d. Processing of Requests

Submit a request for an emergency dispensing order for an eligible MCM via email or letter to the relevant Center and OCET points of contact identified in section III.D.3 of this guidance.

2. Scope and Conditions of Emergency Dispensing Orders

An emergency dispensing order issued by FDA would authorize emergency dispensing, but not direct or require emergency dispensing to occur; government stakeholders typically will be responsible for determining when to commence emergency dispensing consistent with the conditions specified in the order. The Agency expects that in most cases, an emergency dispensing order will allow dispensing in all circumstances in which government stakeholders reasonably believe that a need exists because of their constituent recipients' known, suspected, or likely imminent exposure to the CBRN agent(s) identified in the order. FDA also expects that any dispensing contemplated within government stakeholder emergency response plans will, to the extent possible, involve guidance from licensed health care professionals in the dispensing of product. Nevertheless, an emergency dispensing order issued under section 564A(d) may also state that, in some circumstances, direct or immediate involvement or guidance by licensed health care practitioners may not be possible, and the emergency dispensing order may authorize others, provided the product is otherwise dispensed as part of the official government emergency response plan during a CBRN event.

FDA may specify in the emergency dispensing order who is responsible for contacting additional government stakeholders who may become engaged in a response to a CBRN event covered by the order (1) to ensure that relevant government emergency response plans are coordinated or revised as appropriate, (2) to specify different or additional conditions as appropriate, including information provided in support of a request for issuance of an emergency dispensing order (e.g., to accommodate or address specific response strategies or operational considerations), and (3) when appropriate, to waive CGMP requirements under section 564A(c), as discussed more fully in section IV.C of this guidance.

In appropriate cases, FDA may also coordinate with CDC so that FDA issuance of an emergency dispensing order accompanies CDC issuance of emergency use instructions for the same MCM, as discussed in section IV.E of this guidance.

3. Duration of an Emergency Dispensing Order

In most cases, an emergency dispensing order issued by FDA for preparedness purposes in advance of a CBRN event will remain in effect until it is revised or revoked by a subsequent FDA order. FDA may specify a duration (e.g., 1 year) for an emergency dispensing order, but, if it does so, may extend the order as appropriate.

Contains Nonbinding Recommendations

E. EMERGENCY USE INSTRUCTIONS WITHOUT AN EUA

CDC may create, issue, and disseminate special emergency use instructions (EUI) concerning an eligible MCM's approved, licensed, or cleared conditions of use (section 564A(e)).⁷² EUI are intended to be similar to "Fact Sheets" that have been authorized in past EUAs, and may be directed to health care professionals and authorized dispensers or to recipients of an eligible MCM. EUI may be created and disseminated both before a CBRN event occurs and during a response.

During past public health emergencies, there were concerns that instructions for administering MCMs, even those MCMs that were FDA-approved for the disease or condition (e.g., doxycycline for post-exposure prophylaxis of inhalational anthrax), that deviate from FDA-approved product labeling would violate the FD&C Act and thus invalidate any liability protection otherwise provided under the PREP Act. When an EUI is issued pursuant to this provision, that issuance would not deprive the product of otherwise-applicable PREP Act protection. Therefore, the EUI provisions offer enhanced flexibility for CDC to prepare and disseminate EUI concerning a disease or condition for which an MCM is FDA-approved, licensed, or cleared without further limitation. FDA and CDC interpret this provision as permitting the creation of EUI that describe how the approved drug may be used, for the disease or condition for which it is approved, but in ways that may deviate from or extend beyond the FDA-approved labeling. EUI would not, on the other hand, be permitted to describe uses of an FDA-approved product for diseases or conditions for which the product has not been approved.

V. GOVERNMENTAL PRE-POSITIONING OF MCMs

A new provision added by PAHPRA permits pre-positioning of MCMs without FDA approval when the product(s) is intended to be held (and not used) for emergency use (section 564B), allowing stakeholders to prepare for rapid deployment of MCMs during an emergency. This authority allows government stakeholders, or a person acting on behalf of a government stakeholder, e.g., an agent of the government stakeholder, to introduce into interstate commerce (e.g., stockpile or transport) a medical product intended for emergency use without violating the FD&C Act regardless of a product's regulatory status (i.e., without an IND, IDE, or any other acknowledgement by FDA), but in anticipation that use will be permitted under an appropriate regulatory mechanism (i.e., FDA approval, authorization, or for investigational use).

The authority to pre-position MCMs applies to all categories of medical products intended for emergency use, including those that are approved, unapproved, investigational, or authorized for use under an EUA. However, a government stakeholder may only rely on this authority if the

⁷² Section 564A(e) allows a designated HHS official to create and issue EUI. Although EUI authority is part of the FD&C Act, on the joint recommendation of FDA, CDC, and the ASPR, the Secretary of HHS granted the authority to create EUI to the Director of CDC (or his/her designee). Allowing CDC to create and disseminate EUI is consistent with CDC's clinical expertise in providing event-driven treatment recommendations and facilitating emergency response with external stakeholders, as well as its front-line role in managing the SNS of medical products for which EUI may be most needed. See FDA and CDC's Memorandum of Understanding related to EUI coordination at FDA's website: <http://www.fda.gov/aboutfda/partnershipcollaborations/memorandaofunderstandingmous/domesticmous/cm487464.htm>.

Contains Nonbinding Recommendations

MCMs are in fact held and not used to diagnose, treat, or prevent the CBRN-related disease or condition until permitted under one of these mechanisms. This means, for example, that even though a government stakeholder may stockpile an unapproved MCM, additional action likely will be required to ensure that any pre-positioned MCM can be used when needed. FDA, therefore, recommends that government stakeholders also consider and, if appropriate, initiate steps to ensure an approval can be granted, or that an IND/IDE or EUA is in place or can be readily put in place if necessary.

Those relying on this provision will have to maintain documentation that shows the product qualifies to be held for emergency use, including records reflecting the government stakeholder's initial intent to hold and not use the MCM until such time as it may be used under an appropriate regulatory mechanism. At this time, FDA is not specifying any additional recordkeeping methods relating specifically to pre-positioned MCMs. The Agency recommends, however, that to the extent feasible government stakeholders maintain sufficient records or other information to be able to readily identify their pre-positioned MCMs (e.g., by product name, manufacturer's name, dosage form and strength, quantity held, lot number) as well as the distribution, storage, and ultimate disposition of those MCMs.⁷³ For unapproved products, this information likely will be an element of the records required to be maintained for use under an IND/IDE or EUA. In addition, this information will help minimize the risks of misidentification, theft or other loss, and product deterioration. As an example, an MCM that a government stakeholder cannot verify has been properly stored might not qualify for use under an EUA or for an otherwise applicable extension of the product's shelf life because of a lack of information about the condition of the product.

VI. PREEMPTION

FDA anticipates that conflicts between federal and state law⁷⁴ may arise when FDA acts under sections 564, 564A, and 564B if states have existing requirements governing the shipment, holding, dispensing, administration, or labeling of unapproved medical products or approved medical products for unapproved uses.⁷⁵ Courts have stated that the Supremacy Clause of the U.S. Constitution can operate to nullify both state legislative requirements and state common-law

⁷³ Absent a CGMP waiver (see section III.E.5 of this guidance), government stakeholders, or person(s) acting on their behalf, should continue to store and handle pre-positioned MCMs to support their use according to CGMP standards.

⁷⁴ While FDA believes that preemption applies here, it recognizes that this is a controversial area of the law. Because attorneys advising some state response programs may take a different view than that expressed here, FDA encourages state programs to consult with their legal counsel as to whether they believe that their states would need to take complementary legal action to assure that their state laws would not conflict with actions that the Federal government might take pursuant to section 564 and 564A or that might affect pre-positioning under section 564B. If such state action is considered to be necessary, it will be important that any required changes in state law, or any steps necessary to implement state laws to permit emergency preparedness actions pursuant to these sections, be determined as part of the state's emergency planning.

⁷⁵ Such issues may also arise when FDA issues a waiver of CGMP requirements pursuant to section 564A(c), or an order to permit emergency dispensing pursuant to section 564A(d).

Contains Nonbinding Recommendations

duties.⁷⁶ Under the legal principles of implied conflict preemption, courts have found state law preempted where it is impossible to comply with both federal and state law, or when the state law "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress."⁷⁷ 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."⁷⁸

FDA believes that the terms and conditions of an EUA issued under section 564 preempt state or local law, both legislative requirements and common-law duties, that impose different or additional requirements on the medical product for which the EUA was issued in the context of the emergency declared under section 564. Similarly, an order or waiver issued under section 564A and pre-positioning under section 564B preempt state or local law, both legislative requirements and common-law duties, that impose different or additional requirements related to the activity authorized under sections 564A or 564B.

To the extent state or local law may impose requirements different from or in addition to those imposed by the EUA for a particular medical product within the scope of the declared emergency or threat of emergency (e.g., requirements on prescribing, dispensing, administering, or labeling of the medical product), such law "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress," and "conflicts with the exercise of Federal authority under [§ 564]." The same rationale applies to an order or waiver issued under section 564A and pre-positioning of an MCM under section 564B.

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 prescribing or dispensing of medical products, such as laws limiting who may prescribe or dispense medical products and under what circumstances.

Moreover, the PREP Act, which expressly provides immunity from tort liability associated with certain MCM activities, preempts state laws that are different from, or in conflict with, any requirement applicable to a covered countermeasure under the PREP

⁷⁶ *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 same reasoning, state regulations and local ordinances would also be preempted.

⁷⁷ See *Arizona v. United States*, 132 S. Ct. 2492, 2501, 2505, 2507 (2012); *Crosby v. National Foreign Trade Council*, 530 U.S. 363, 373 (2000); *Geier v. American Honda Motor Company, Inc.*, 529 U.S. 861, 873 (2000); *Hines v. Davidowitz*, 312 U.S. 52, 67 (1941).

⁷⁸ Exec. Order No. 13132, 64 FR 43255 (August 4, 1999).

Contains Nonbinding Recommendations

Act and relating to, among other things, any matter applicable because of a requirement of the FD&C Act.⁷⁹ This includes actions taken to meet the terms of an EUA, an order or waiver issued under section 564A, pre-positioning of an MCM under section 564B, an IND or IDE, or any FDA approval of an MCM.

In an emergency, it is critical that the conditions that are part of the EUA or an order or waiver issued pursuant to section 564A—those that FDA 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 to also comply with requirements contained in preempted state law, FDA anticipates incorporating such requirements into the terms and conditions of the EUA.

Similarly, an extension of expiration dating under section 564A(b), a waiver of CGMP requirements under section 564A(c), and an FDA order permitting emergency dispensing pursuant to section 564A(d) are actions intended to protect the public health by enabling rapid public access to potentially life-saving medical products during an emergency. State laws that govern CGMP requirements or the dispensing of products covered by an FDA extension of expiration dating, CGMP waiver, or emergency dispensing order and that impose different or additional conditions that would limit the access to eligible products covered by FDA's action, would be an obstacle to achieving that goal. Therefore, FDA believes that state laws within the jurisdictional coverage of an FDA extension of expiration dating, CGMP waiver, or emergency dispensing order that impose more restrictive conditions or requirements on dispensing products covered by the FDA order, or pre-positioning of MCMs under section 564B will be preempted.

As noted above, however, state laws may permit emergency dispensing of eligible MCMs. Under section 564A(d), such laws may provide another basis on which government stakeholders may be able to provide for emergency dispensing without a prescription or adherence to other prescription requirements that might otherwise apply.⁸⁰ An FDA order issued under section 564A(d) is not intended to replace those frameworks as long as they are not more restrictive than the FDA's order in providing for access to the FDA-approved product(s) that the order covers.

VII. LIABILITY PROTECTION

Apart from any applicable preemption principles, sections 564, 564A, and 564B do not confer explicit liability protections for stakeholders who carry out any activity under these authorities.

⁷⁹ 42 U.S.C. § 247d-6d(b)(8).

⁸⁰ Whether or not a particular state legal provision or action is sufficient to permit the emergency dispensing strategy that state or local government stakeholders anticipate conducting within their state rests in large part on the interpretation of that state law, which is a matter that should first be directed to the appropriate legal authority within the relevant jurisdiction (e.g., the state Attorney General). To ensure clarity, and perhaps increase the likelihood that state laws, regulations, orders, or other legal actions to permit emergency dispensing are deemed sufficient, it is recommended that such actions address the same eligibility, scope, duration, and other elements FDA intends to address in its emergency dispensing orders, as described above.

Contains Nonbinding Recommendations

The PREP Act,⁸¹ however, may provide for immunity from tort liability related to activities authorized under such authorities. More specifically, the PREP Act authorizes the HHS Secretary to issue a declaration (called a PREP Act declaration) that provides immunity (except for willful misconduct) for claims related to administration or use of countermeasures against CBRN agents to entities and individuals involved in the development, manufacture, testing, distribution, administration, and use of such countermeasures.⁸² The PREP Act authority, including the authority to issue PREP Act declarations, resides with the Secretary of HHS and has not been delegated to FDA.

The PREP Act liability protections apply to “covered countermeasures” as defined by the statute.⁸³ Covered countermeasures include medical products that are approved, cleared, or licensed by FDA; authorized for investigational use under an IND or IDE by FDA; authorized for emergency use under section 564; or otherwise permitted to be held or used pursuant to sections 564A and 564B. As discussed in section IV of this guidance, in the past, EUAs have been issued in part to address concerns that certain activities related to MCMs potentially violated provisions of the FD&C Act, jeopardizing otherwise-applicable PREP Act protections. PAHPRA added sections 564A and 564B to the definitions of “covered countermeasure” in part to preserve these otherwise-applicable PREP Act protections.

VIII. IMPORTING AND EXPORTING MEDICAL PRODUCTS UNDER AN EUA

Although an EUA is not an FDA-approval, a medical product authorized for emergency use under an EUA may be introduced into interstate commerce during the effective period of the EUA declaration, and as such, contingent upon compliance with the terms and conditions of the authorization, may be legally imported and exported under section 801 of the FD&C Act (21 U.S.C. 381). The letter of authorization should serve as appropriate documentation or certification that the product may be legally imported or exported.

In the past, FDA has received EUA requests for which the primary emergency use of the investigational medical product would be in a foreign country (e.g. for use in West Africa during the Ebola crisis). The assessment of whether to issue an EUA in these cases is the same as for any other emergency use: FDA must determine whether the requisite EUA determination, declaration, and criteria (as described in section III.A and III.B of this guidance) are met and consider whether it is feasible or practicable in the foreign setting to comply with the necessary and appropriate conditions of use (as described in section III.E of this guidance).

⁸¹ 42 U.S.C. 247d-6d. For information on the PREP Act, see HHS’s website at <http://www.phe.gov/Preparedness/legal/prepact/Pages/default.aspx>.

⁸² 42 U.S.C. 247d-6d(b).

⁸³ 42 U.S.C.247d-6d(i)(1) and (7).

Contains Nonbinding Recommendations

IX. PAPERWORK REDUCTION ACT OF 1995

This guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520).

The time required to complete this information collection is estimated to average 85 hours per response, including the time to review instructions, search existing data sources, gather the data needed, and complete and review the information collection.

Send comments regarding this burden estimate or suggestions for reducing this burden to: Office of Counterterrorism and Emerging Threats, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993-0002.

This guidance refers to previously approved collections of information found in FDA regulations. The collections of information for: adverse experience reporting for biological products is approved under OMB control number 0910-0308; adverse drug experience reporting is approved under OMB control number 0910-0230; adverse device experience reporting is approved under OMB control number 0910-0471; investigational new drug application regulations are approved under OMB control number 0910-0014; and investigational device exemption reporting is approved under OMB control number 0910-0078.

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. The OMB control number for this information collection is 0910-0595 (expires 08/31/2019).

Contains Nonbinding Recommendations

List of Acronyms

Assistant Secretary for Preparedness and Response (ASPR)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Centers for Disease Control and Prevention (CDC)
Center for Drug Evaluation and Research (CDER)
Chemical, biological, radiological, and nuclear (CBRN)
Clinical Laboratory Improvement Amendments (CLIA)
Current Good Manufacturing Practice (CGMP)
Department of Health and Human Services (HHS)
Department of Homeland Security (DHS)
Department of Defense (DoD)
Emergency Use Authorizations (EUAs)
Emergency Use Instructions (EUI)
Federal Food, Drug, and Cosmetic Act (FD&C Act)
Federal Shelf-Life Extension Program (SLEP)
Food and Drug Administration (FDA)
Good Laboratory Practice for Nonclinical Laboratory Studies regulations (GLP)
Investigational Device Exemption (IDE)
Investigational New Drug Application (IND)
In Vitro Diagnostic (IVD)
Medical Countermeasure (MCM)
National Institutes of Health (NIH)
Office of Counterterrorism and Emerging Threats (OCET)
Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA)
Points of Dispensing (PODs)
Public Health Service (PHS) Act
Public Readiness and Emergency Preparedness (PREP) Act
Risk Evaluation and Mitigation Strategy (REMS)
Safety Information and Adverse Event Reporting System (MedWatch)
Secretary of Health and Human Services (HHS Secretary or Secretary of HHS)
Strategic National Stockpile (SNS)
Vaccine Adverse Event Reporting System (VAERS)
World Health Organization (WHO)

Contains Nonbinding Recommendations

Appendix A. EUA Conditions of Authorization: Required^a vs. Discretionary^b

Condition	Unapproved Product	Unapproved Use of an Approved Product	FD&C Act Section
Information (“fact sheets”) for healthcare providers administering the product (significant known/potential benefits/risks of product and extent to which benefits/ risks are unknown; FDA has authorized emergency use)	Required	Required	§ 564(e)(1)(A)(i) § 564(e)(2)(A)
Information (“fact sheets”) for product recipients (significant known/potential benefits/risks of product and extent to which benefits/ risks are unknown, option to accept or refuse product, consequences of refusing, available alternatives, FDA has authorized emergency use)	Required	Required	§ 564(e)(1)(A)(ii) § 564(e)(2)(A)
Adverse event monitoring and reporting	Required	Discretionary	§ 564(e)(1)(A)(iii) § 564(e)(2)(A)
Recordkeeping and reporting (by product manufacturers)	Required	Discretionary	§ 564(e)(1)(A)(iv) § 564(e)(2)(A)
Recordkeeping and reporting (by persons other than product manufacturers)	Discretionary	Discretionary	§ 564(e)(1)(B)(iv) § 564(e)(2)(A)
Product distribution (which entities may distribute product and how to perform distribution)	Discretionary	Discretionary ^c	§ 564(e)(1)(B)(i) § 564(e)(2)(A)
Product administration (who may administer product and categories of individuals to whom, and circumstances under which, product may be administered)	Discretionary	Discretionary ^c	§ 564(e)(1)(B)(ii) § 564(e)(2)(A)
Data collection and analysis (concerning product safety/effectiveness)	Discretionary	Discretionary	§ 564(e)(1)(B)(iii) § 564(e)(2)(A)
CGMP and prescription waiver or limit	Discretionary	Discretionary	§ 564(e)(3)
Advertising/other promotional material	Discretionary	Discretionary	§ 564(e)(4)
Other (any other condition FDA finds necessary or appropriate to protect the public health)	Discretionary	Discretionary	§ 564(e)(1)(B) § 564(e)(2)(A)

^a Under section 564(e)(1)(A) of the FD&C Act, “required conditions” must be imposed by FDA in an EUA to the extent practicable given the applicable circumstances described in the HHS Secretary’s EUA declaration under section 564(b)(1) of the FD&C Act. See also section 564(e)(2)(A) (same rule for unapproved uses of an approved drug).

^b Discretionary conditions may be included in an EUA at FDA’s discretion as deemed necessary to protect the public health. See section 564(e)(1)(B); section 564(e)(2)(A).

^c Such conditions for an unapproved use of an approved product may not restrict distribution or administration of the product when it is distributed or administered for the approved use. See section 564(e)(2)(C).