



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

July 21, 2011

Thomas R. Frieden, M.D., M.P.H.
Director
Centers for Disease Control and Prevention
1600 Clifton Road, MS D-14
Atlanta, GA 30333

Dear Dr. Frieden:

This letter is in response to your May 5, 2011, submission¹ requesting that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for the emergency use of oral formulations of doxycycline products for the post-exposure prophylaxis (PEP)² of inhalational anthrax during a public health emergency involving aerosolized *Bacillus anthracis* (*B. anthracis*), pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3).

In 2004, the Secretary of the Department of Homeland Security (DHS) issued a Material Threat Determination indicating that *B. anthracis*, the biological agent that causes anthrax disease, presents a material threat against the population of the United States sufficient to affect national security. On September 23, 2008, pursuant to section 564(b)(1)(A) of the Act (21 U.S.C. § 360bbb-3(b)(1)(A)), the Secretary of DHS determined that there is a significant potential for a domestic emergency involving a heightened risk of attack with a specified biological, chemical, radiological, or nuclear agent or agents—in this case, *B. anthracis*.³ On October 1, 2008, pursuant to section 564(b) of the Act (21 U.S.C. § 360bbb-3(b)), and on the basis of such determination, the Secretary of Health and Human Services (HHS) then declared an emergency justifying the authorization of the emergency use of doxycycline hyclate tablets for PEP accompanied by emergency use information subject to the terms of any authorization issued under section 564(a) of the Act (21 U.S.C. § 360bbb-3(a)), and on October 1, 2009, and on October 1, 2010, renewed that declaration.⁴ On July 20, 2011, the Secretary of HHS renewed and amended that declaration so that it applies to all doxycycline products covered by this authorization.

¹ In submitting this request, the Centers for Disease Control and Prevention (CDC)/Department of Health and Human Services (DHHS) stated that it was acting in coordination with the Department of Homeland Security (DHS) and the Department of Defense. CDC/DHHS will be responsible for requesting any amendments to the EUA.

² The Act uses the terms “diagnosing, treating, or preventing” in section 564(c)(2)(A). Post-exposure prophylaxis is encompassed by these statutory terms.

³ Memorandum from Michael Chertoff to Michael O. Leavitt, Determination Pursuant to § 564 of the Federal Food, Drug, and Cosmetic Act (Sept. 23, 2008).

⁴ Declaration of Emergency Pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 360bbb-3(b) (Oct. 1, 2008); renewed October 1, 2009 (74 Fed. Reg. 51,279) (Oct. 6, 2009); renewed October 1, 2010 (75 Fed. Reg. 61,489) (Oct. 5, 2010).

The Centers for Disease Control and Prevention (CDC) requested this EUA because oral formulations of doxycycline products will be distributed and stored by stakeholders for preparedness purposes in advance of an actual anthrax event, with the intent that they may be dispensed post-event as part of a mass distribution strategy. As used in this letter, the term “stakeholder(s)” means the public agency or its delegate that has legal responsibility and authority for responding to an incident, based on political or geographical, e.g., city, county, tribal, State, or Federal boundary lines, or functional, e.g., law enforcement or public health range or sphere of authority to prescribe, administer, deliver, distribute, or dispense doxycycline in an emergency situation. An EUA is needed to facilitate stakeholder pre-event planning and preparedness activities, which may include elements that would otherwise violate provisions of the Act under FDA’s legal interpretations,⁵ to enable rapid initiation of antimicrobial therapy through various distribution and dispensing modalities during an actual emergency event involving *B. anthracis*.

Having consulted with the CDC and the National Institutes of Health (NIH), and having concluded that the criteria for issuance of this authorization under section 564(c) of the Act (21 U.S.C. § 360bbb-3(c)) are met, I am authorizing the emergency use of doxycycline products,^{6,7,8} where not contraindicated, for the post-exposure prophylaxis⁹ of inhalational anthrax in the event of a public health emergency involving *B. anthracis*, subject to the terms of this authorization. This EUA will apply in all circumstances in which stakeholders reasonably believe that there is a need to mass dispense authorized doxycycline products because of their constituent recipients’ suspected or likely imminent exposure to *B. anthracis* spores.

The remainder of this letter is organized into five sections: (I) Criteria for Issuance of Authorization; (II) Scope of Authorization; (III) Current Good Manufacturing Practice (CGMP); (IV) Conditions of Authorization; and (V) Duration of Authorization.

⁵ Such elements include but are not limited to: distribution and use of emergency use information sheets, e.g., fact sheet for health care professionals, fact sheet for recipients, and fact sheet for recipients with home preparation instructions for children or adults who cannot swallow pills; dispensing doxycycline without a prescription and without all of the required information on the prescription label per section 503(b)(2) (U.S.C. § 353(b)(2)); dispensing a partial supply of the full 60-day dosage regimen, i.e., initial start-up 10-day supply; pre-event storage or distribution of doxycycline packaged or repackaged for emergency distribution; and waiver of current good manufacturing practice requirements during an event, under certain circumstances.

⁶ FDA is authorizing the emergency use of oral formulations of doxycycline products for the post-exposure prophylaxis of inhalational anthrax as described in the scope section of this letter (see Section II. Scope of Authorization).

⁷ For the purpose of this letter, “emergency use of authorized doxycycline product(s)” includes stakeholders’ pre-event preparedness activities for, and post-event implementation of, post-exposure prophylaxis for inhalational anthrax with authorized doxycycline products for individuals who have been exposed, or who may have been exposed, to aerosolized *B. anthracis* spores.

⁸ For ease of reference, this letter of authorization will use the terms “authorized doxycycline product(s)” or “doxycycline product(s).”

⁹ Prophylaxis is generally considered to apply in situations in which the person receiving the drug has not exhibited symptoms. Because, in many cases in which doxycycline may be used pursuant to this authorization, it will not be practical to distinguish between persons who have exhibited symptoms and those who have not, this authorization permits the administration of doxycycline to persons who may have been exposed to *B. anthracis* during a public health emergency whether or not they have begun to exhibit symptoms. We would expect that responsible authorities would direct any persons who have begun to exhibit symptoms to appropriate medical care as expeditiously as possible.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of authorized doxycycline products, where not contraindicated, for the post-exposure prophylaxis of inhalational anthrax during an emergency involving *B. anthracis* meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

- (1) *B. anthracis* can cause inhalational anthrax, a serious or life-threatening disease or condition;
- (2) based on the totality of scientific evidence available to FDA, it is reasonable to believe that authorized doxycycline products may be effective for the post-exposure prophylaxis of inhalational anthrax, and that the known and potential benefits of authorized doxycycline products, when used for the post-exposure prophylaxis of inhalational anthrax in the specified population, outweigh the known and potential risks of such products; and
- (3) there is no adequate, approved, and available alternative to the emergency use of authorized doxycycline products for the post-exposure prophylaxis of inhalational anthrax.¹⁰

Therefore, I have concluded that the emergency use of authorized doxycycline products for the post-exposure prophylaxis of inhalational anthrax meets the above statutory criteria for issuance of an authorization.

II. Scope of Authorization

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited to the emergency use of authorized doxycycline products for purposes of stakeholder pre-event planning and preparedness activities, and, in a post-event scenario, implementation of post-exposure prophylaxis for inhalational anthrax for individuals who have been exposed, or who may have been exposed, to aerosolized *B. anthracis* spores. The emergency use of authorized doxycycline products under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below.

The authorized doxycycline products are as follows:

FDA-approved oral formulations of doxycycline, including capsule, tablet, and liquid formulations,¹¹ such as:

- Doxycycline hyclate 100 mg oral tablets, supplied in a unit-of-use (UoU) bottle containing 120 tablets for a 60-day treatment or containing 20 tablets for an initial 10-day supply;

¹⁰ No other criteria for issuance have been prescribed by regulation under section 564(c)(4) of the Act.

¹¹ FDA-approved drugs can be identified at the *Drugs at FDA* website at <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/>.

- Doxycycline monohydrate 100 mg oral capsules, supplied in a UoU bottle containing 120 capsules for a 60-day treatment or containing 20 capsules for an initial 10-day supply;
- Doxycycline 25 mg/5 mL suspension, supplied as dry powder in a 60 mL bottle;
- Doxycycline (Vibramycin) 50 mg/5 mL syrup in a 473 mL bottle; and
- Any other formulation of doxycycline that has been approved by the FDA for post-exposure prophylaxis to reduce the incidence or progression of disease, including inhalational anthrax, following exposure to aerosolized *B. anthracis*.

The examples provided are for purposes of illustration. During an emergency, this authorization would permit dispensing of FDA-approved drugs that are not supplied in a UoU container if necessary.

Doxycycline is a semisynthetic tetracycline antimicrobial product approved as a prescription drug by FDA for treatment and post-exposure prophylaxis of anthrax due to *B. anthracis*, including inhalational anthrax, to reduce the incidence or progression of disease following exposure to aerosolized *B. anthracis*.¹² The post-exposure prophylaxis indication generally means that drug administration is expected to start after a known or suspected exposure to aerosolized *B. anthracis* spores, but before clinical symptoms of the disease develop. The indication includes presumed exposure, since it is often difficult to know whether and when exposure has actually occurred. The indication also encompasses instances where *B. anthracis* exposure via inhalation is expected and likely imminent. In such cases, the first few doses of prophylaxis may be taken pre-exposure, but the remainder of the course would be taken post-exposure. The indication is commonly referred to as “post-exposure prophylaxis of inhalational anthrax,” and this term will be used throughout this document. Generally, once symptoms develop, the approved indication for “treatment” would apply. Although it is expected that stakeholder emergency use plans will, to the extent possible, direct symptomatic individuals to health care professionals for appropriate treatment, FDA recognizes that circumstances may necessitate dispensing doxycycline product to individuals seeking post-exposure prophylaxis who may be symptomatic; therefore, FDA is authorizing dispensing to symptomatic individuals without a prescription consistent with the conditions set out in this letter.

1. The above doxycycline products are authorized for pre-event storage and distribution, and for post-event storage, distribution, and dispensing, when packaged in their original manufacturers’ packaging or repackaged for emergency distribution with labels containing directions for use, National Drug Code, and lot number (pursuant to the requirements under Section III. CGMP of this document), despite the fact that they may not contain all of the required information on the prescription label under section 503(b)(2) of the Act (21 U.S.C. § 353(b)(2)), e.g., name and address of dispenser; serial

¹² The full course of doxycycline tablets for adults for the post-exposure prophylaxis of inhalational anthrax is 100 mg twice daily for 60 days. Children weighing 40 kg or more (89 pounds or more) should receive the adult dose. Children weighing less than 40 kg should receive 2.2 mg/kg of body weight per dose, by mouth, twice daily (maximum 100 mg per dose).

number; date of prescription or of its filling; name of prescriber; name of patient, if stated on prescription; directions for use and cautionary statements, if contained in the prescription. During an emergency, this authorization would permit dispensing of FDA-approved drugs that are not supplied in a UoU container if necessary.

2. The doxycycline products previously referenced are authorized to be dispensed without a prescription¹³ and to be accompanied by authorized emergency use information, to be made available to health care professionals and to recipients respectively, to facilitate understanding of anthrax disease and the risks and benefits of doxycycline therapy and to improve medication compliance. Representative examples of such information are as follows:

- Doxycycline EUA Fact Sheet for Health Care Professionals (Exhibit 1)
- Doxycycline EUA Fact Sheet for Recipients (Exhibit 2)

In addition, a short version and a long version of instructions for home preparation of doxycycline for those who cannot swallow pills are authorized as follows:

- Doxycycline EUA Fact Sheet for Recipients—Home Preparation Instructions for Children or Adults Who Cannot Swallow Pills (Exhibit 3—short version) (or as updated by FDA)¹⁴
- In an Emergency: How to Prepare Doxycycline for Children and Adults Who Cannot Swallow Pills (Exhibit 4—long version) (or as updated by FDA).¹⁵

3. The doxycycline products previously referenced are authorized to be stored, distributed, and dispensed as a partial supply,¹⁶ e.g., 10-day supply, of a full 60-day dosage regimen

¹³ It is expected that stakeholder emergency use plans will, to the extent possible under the circumstances, involve guidance from health care professionals in the dispensing of product under this EUA beyond the fact sheets contemplated by this request. In this request, however, FDA is being asked to recognize that, in some circumstances, such guidance may not be possible and thus to authorize dispensing without a prescription, including dispensing by non-health care professionals. Depending on the state or local health jurisdictions' preparedness plan for a mass distribution strategy, individuals responsible for dispensing doxycycline may include licensed health care professionals, pharmacists, emergency responders, volunteers, or others. This is not intended to be an exhaustive list. It is possible that public health officials or other volunteers might dispense authorized doxycycline products to recipients, if permitted, in accordance with applicable state and local law and/or in accordance with the public health and medical emergency response of the stakeholder to prescribe, administer, deliver, distribute, or dispense the covered countermeasures, and of their officials, agents, employees, contractors, or volunteers, following a declaration of an emergency.

¹⁴ Any such updates will be available at: <http://www.fda.gov/doxyprepare>.

¹⁵ The Exhibit 4 fact sheet is also available at: <http://www.fda.gov/doxyprepare>.

¹⁶ The required and FDA-approved duration of doxycycline therapy for PEP against inhalational anthrax is 60 days. An initial, partial supply of doxycycline may be utilized to facilitate a rapid initiation of antimicrobial therapy, i.e., to provide start-up doses through various distribution modalities. Thus, the partial dispensing of the required quantity of doxycycline to complete therapy duration will also be allowed under this EUA. Once the antimicrobial susceptibility of the associated *B. anthracis* strain involved in the exposure has been determined per its minimum inhibitory concentration, and potential exposure to *B. anthracis* has been confirmed, an additional supply of doxycycline must be dispensed to patients to allow the full 60-day antimicrobial PEP regimen. For example, an

when stored, distributed, and dispensed as part of a stakeholder mass distribution strategy.

4. The doxycycline products previously referenced may include pre-event storage, distribution, and potential use of doxycycline products that are distributed from certain stakeholders' stockpiles and are authorized to have their expiration date extended under the federal government's Shelf-Life Extension Program (SLEP).

CDC and stakeholders are also authorized to make available additional information relating to the emergency use of authorized doxycycline products that is consistent with the terms of this letter of authorization. (See Section IV. Conditions of Authorization.)

I have concluded, pursuant to section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of authorized doxycycline products, when used for the post-exposure prophylaxis of inhalational anthrax, outweigh the known and potential risks of such products.

I have concluded, pursuant to sections 564(c)(2)(A) and 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that the authorized doxycycline products may be effective for the post-exposure prophylaxis of inhalational anthrax. FDA has reviewed the scientific information available, including the information supporting the conclusions described in Section I above, and concludes that the authorized doxycycline products, when used for the post-exposure prophylaxis of inhalational anthrax in the specified population in accordance with the conditions set out in this letter, meet the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

Subject to the terms of this EUA and consistent with the Secretary of DHS's determination under section 564(b)(1)(A) of the Act and the Secretary of HHS's corresponding declaration under 564(b)(1) of the Act described above, the doxycycline products described above are authorized for the post-exposure prophylaxis of inhalational anthrax for individuals who have been exposed, or who may have been exposed, to aerosolized *B. anthracis* spores.

This EUA will cease to be effective when the declaration of emergency is terminated under section 564(b)(2) of the Act or when the EUA is revoked under section 564(g) of the Act. When this EUA ceases to be effective, the doxycycline products described herein will no longer be authorized for emergency use under this EUA.¹⁷

individual may only receive a 10-day supply as an initial start-up dose. The individual will receive further instructions on whether the additional 50-day supply is necessary based on the results of the antimicrobial susceptibility and on where to obtain the 50-day supply of doxycycline.

¹⁷ Pursuant to Section 564(f)(2) of the Act, 21 U.S.C. 360bbb-3(f)(2), continued use of a product authorized by this letter may continue after the expiration of this authorization to the extent found necessary by the patient's health care professional.

III. Current Good Manufacturing Practice

This authorization only covers doxycycline products that have been manufactured, (re)packaged, and (re)labeled under CGMP requirements and were stored in compliance with the manufacturers' labeled storage conditions for the products, except that, in the event of a release of *B. anthracis* and a decision on the part of the responsible stakeholder to mass dispense doxycycline under the terms and conditions of this EUA, doxycycline products may require transportation for rapid dispensing without the capacity to maintain labeled storage conditions in the midst of the response. The products, i.e., doxycycline tablets, doxycycline delayed release tablets, doxycycline capsules, doxycycline powder for oral suspension, and doxycycline oral suspension, may be stored with temperature excursions up to 40°C for a total period of up to 7 days.

IV. Conditions of Authorization

Pursuant to section 564 of the Act, I am establishing the following conditions on this authorization:

A. Information must be provided to health care professionals administering the product and to recipients that includes the following minimum elements:

(1) For Health Care Professionals:

- Statement that the product is authorized for emergency use, e.g., “The Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) for the distribution of doxycycline to people who may have been exposed to *Bacillus anthracis* (*B. anthracis*), the causative pathogen of anthrax.”;
- The significant known and potential benefits, e.g., “The expected benefits are prevention of disease, including death, associated with anthrax exposure.”;
- The significant known and potential risks of using this drug, including:
 - Serious allergic/hypersensitivity reactions (anaphylactic);
 - Dental problems in children associated with women taking doxycycline during the last half of pregnancy or when nursing, and associated with children under the age of 8 years taking doxycycline;
 - Slowed bone growth in children;
 - Antibiotic-associated diarrhea and pseudomembranous colitis;
 - Liver failure;
 - Esophageal ulcers;
 - Photosensitivity;
 - Unusual bleeding or bruising;
 - Severe headaches, dizziness, or double vision; and
 - Decreased effectiveness of oral contraceptives;
- The extent to which such benefits and risks are unknown, e.g., “It is unknown how recipients will respond to the emergency instructions, how many recipients will receive the full, 60-day course of PEP, or what the impact of dispensing without an individual prescription will be. The benefit of mass dispensing to

provide recipients with access to an initial supply of doxycycline is expected to outweigh the risks.”;

- If alternatives to the product are available to the recipients, an explanation of their benefits and risks, e.g., “In this emergency situation, you will be informed of any alternative products that are available. The risks and benefits of those products are explained separately with those products.”;¹⁸
- Authorized information on home preparation instructions for children or adults who cannot swallow pills, i.e., Exhibit 3 or Exhibit 4; these instructions are appropriate for tablet formulations;
- Dosing information, including for children weighing less than 14 kg (30 lbs) dosed by weight (see table below); and

Weight in Pounds (lbs)	Weight in kilograms (kg)	Dose in milliliters (mL) (based on 5mg/mL concentration) - Give one dose in the morning and one dose in the evening	Number of 60 mL bottles provided to each patient to cover first 10 days of treatment
0-5 lbs	0-2 kg	1 mL	ONE (1) Bottle
6-10 lbs	3-4 kg	2 mL	
11-15 lbs	5-7 kg	3 mL	
16-20 lbs	8-9 kg	4 mL	TWO (2) Bottles
21-25 lbs	10-11 kg	5 mL	
26-30 lbs	12-14 kg	6 mL	

- A statement on adverse event and medication error reporting, e.g., “You should report adverse events or medication errors to MedWatch at www.fda.gov/medwatch, by submitting a MedWatch Form 3500 (available at http://www.fda.gov/medwatch/safety/FDA-3500_fillable.pdf) or by calling 1-800-FDA-1088.” or similar information.

(2) For Recipients:¹⁹

- Statement that the product is authorized for emergency use, e.g., “Doxycycline is a prescription drug approved by the Food and Drug Administration (FDA) to prevent anthrax. Federal authorities have specially authorized certain uses of doxycycline, including use without a prescription, for this emergency situation.”;
- The significant known and potential benefits, e.g., “Taking doxycycline to treat anthrax will reduce your risk of getting sick and dying.”;

¹⁸ This authorization is intended to apply to the use of doxycycline in a wide range of different circumstances, and it is recognized that the availability of alternatives to the product will vary in different circumstances. If alternatives are available, this requirement may be satisfied by assuring that the health care professional has available any approved labeling for the alternative product or, if that product is covered by an EUA, the authorized health care professional information under that EUA.

¹⁹ To the extent feasible, stakeholders are encouraged to ensure that recipient fact sheets provide information in such a way as to adequately inform individuals with low literacy.

- The significant known and potential risks of using this drug, including:
 - Allergic reaction, such as swelling of the tongue, hands, or feet;
 - Tooth problems in children when women take doxycycline during the last half of pregnancy or when nursing, and associated with children under the age of 8 years taking doxycycline;
 - Slowed bone growth in children;
 - Diarrhea and stomach cramps;
 - Serious liver problems, including liver failure;
 - Pain when swallowing;
 - Sensitivity to the sun;
 - Unusual bleeding or bruising;
 - Severe headaches, dizziness, or double vision; and
 - Birth control pills might stop working;
- The extent to which such benefits and risks are unknown, e.g., “The benefit of providing you with emergency access to an initial supply of doxycycline is expected to outweigh the risks. However, it is unknown how well these emergency instructions will be used, how many individuals will receive the full, 60-day course of (PEP), or what the impact of dispensing without an individual prescription will be.”;
- Statement that the recipient is not required to use this drug and the consequences, if any, of refusing administration, e.g., “You do not have to take this drug, but taking doxycycline to treat anthrax will reduce your risk of getting sick and dying.”;
- If alternatives to the product are available to recipients, an explanation of their benefits and risks. But in circumstances in which alternatives are not available, an explanation that there are other drugs that may be used as alternatives to doxycycline, but those drugs may not be readily available to the recipient, accompanied by a statement that, if the recipient has access to a medical professional, the recipient may wish to discuss the benefits and risks of any available alternative therapies with that medical professional;
- Dosing information;
- Authorized information on home preparation instructions for children or adults who cannot swallow pills, i.e., Exhibit 3 or Exhibit 4; and
- A statement addressing the reporting of side effects or errors including advising recipients to contact their physician regarding side effects and providing MedWatch contact information for reporting (www.fda.gov/medwatch or 1-800-FDA-1088), e.g., “Tell your doctor right away and report side effects or medication errors to MedWatch at www.fda.gov/medwatch (1-800-FDA-1088).”.

B. For planning purposes, Exhibit 1, accompanied by either Exhibit 3 or Exhibit 4 (or any updated home preparation instructions that may be provided by FDA on the FDA website), meets the minimum requirements set forth above for the Doxycycline EUA Fact Sheet for Health Care Professionals. Exhibit 2, accompanied by either Exhibit 3 or Exhibit 4 (or any updated home preparation instructions that may be provided by FDA on the FDA website), meets the minimum requirements set forth above for the Doxycycline EUA Fact Sheet for Recipients.

CDC

- C. CDC will ensure that the terms and conditions of this EUA are made available through appropriate means.
- D. CDC will make available to stakeholders through appropriate means the following as representative examples of fact sheets pertaining to the emergency use authorized to be made available to health care professionals and to recipients:
 - (1) Exhibit 1: Doxycycline EUA Fact Sheet for Health Care Professionals. Exhibit 1 is an example fact sheet of the minimum information necessary to provide to health care professionals.
 - (2) Exhibit 2: Doxycycline EUA Fact Sheet for Recipients. Exhibit 2 is an example fact sheet of the minimum information necessary to provide to recipients.

CDC will make available to stakeholders through appropriate means the following authorized instructions of the home preparation instructions for children or adults who cannot swallow pills:

- (3) Exhibit 3: Doxycycline EUA Fact Sheet for Recipients—Home Preparation Instructions for Children or Adults Who Cannot Swallow Pills (short version) (or as updated by FDA); or
- (4) Exhibit 4: In an Emergency; How to Prepare Doxycycline for Children and Adults Who Cannot Swallow Pills (long version) (or as updated by FDA).

CDC will also make available to stakeholders through appropriate means at least one representative FDA-approved package insert that covers the dosage forms and strengths of authorized doxycycline products for each type of doxycycline product stockpiled or dispensed.

- E. CDC is authorized to issue additional recommendations and instructions related to the emergency use of authorized doxycycline products as described in this letter of authorization, to the extent that additional recommendations and instructions are necessary to meet public health needs during a declared public health emergency involving *B. anthracis* and are reasonably consistent with the authorized emergency use of the products.

Stakeholders (including CDC)

- F. Stakeholders will be responsible for authorizing public and/or private entities acting as part of the public health response to dispense authorized doxycycline products in accordance with the terms and conditions of this EUA, including instructing public

and/or private entities acting as part of the public health response about the terms and conditions of the EUA with regard to pre-event storage and distribution and post-event storage, distribution, and dispensing of doxycycline products, and for instructing their constituent recipients about the means through which their constituent recipients are to obtain authorized doxycycline products.

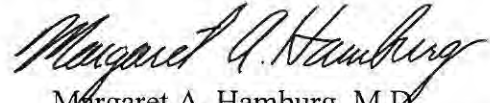
- G. Stakeholders must make available through appropriate means information provided to health care professionals and to recipients, respectively, that include the minimum elements set forth above in A. and B. of this section, as exemplified in Exhibit 1 and Exhibit 2, and as authorized in Exhibit 3 and Exhibit 4: Doxycycline EUA Fact Sheet for Health Care Professionals (Exhibit 1), Doxycycline EUA Fact Sheet for Recipients (Exhibit 2), Doxycycline EUA Fact Sheet for Recipients—Home Preparation Instructions for Children or Adults Who Cannot Swallow Pills (short version) (Exhibit 3) (or as updated by FDA), and In an Emergency: How to Prepare Doxycycline for Children and Adults Who Cannot Swallow Pills (long version) (Exhibit 4) (or as updated by FDA). Stakeholders may use Exhibit 1 as the fact sheet for health care professionals and Exhibit 2 as the fact sheet for recipients, or they may develop alternative fact sheets for health care professionals and for recipients, so long as any such information made available to health care professionals and to recipients includes the minimum elements set forth under this EUA in Section IV. Conditions of Authorization. Alternative fact sheets for home preparation instructions for children and adults who cannot swallow pills may not be developed by stakeholders for Exhibit 3 or Exhibit 4.
- H. Stakeholders must maintain an inventory record of doxycycline distribution (including lot number, quantity, receiving site, and distribution date) under this EUA, including distribution of doxycycline product prior to, during, or after an anthrax emergency. This requirement does not require record-keeping related to dispensing of doxycycline products to recipients during an emergency in those circumstances in which such record-keeping would not be consistent with an efficient program for the dispensing of the drug to recipients.²⁰ Stakeholders acting under this EUA will be aware of and ensure that anyone storing and distributing doxycycline for preparedness purposes and storing, distributing, and dispensing doxycycline for response purposes under this EUA are informed of and instructed on the actions necessary to enable stakeholders to comply with the terms and conditions of this EUA, such as data collection, recordkeeping, and records access. Stakeholders acting under this EUA will provide FDA access to such records when requested.
- I. Stakeholders are also authorized to make available additional information relating to the emergency use of authorized doxycycline products that is consistent with, and does not exceed, the terms of this letter of authorization.

The emergency use of authorized doxycycline products as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

²⁰ While such record-keeping is not a requirement of this EUA, it is expected that stakeholders will, to the extent possible, keep such records for purposes of their own follow-up of recipients, including for the purpose of assuring that any individual who has been provided less than a full course of doxycycline receives, if necessary, a full course.

V. Duration of Authorization

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.


Margaret A. Hamburg, M.D.
Commissioner of Food and Drugs

Enclosures