

Key Message Points for New EUAs

Background: The ability for public health officials to dispense medical countermeasures from the Strategic National Stockpile (SNS) to their populations during an anthrax emergency within 48 hours continues to be a major national priority and a critical planning objective for health authorities at all levels across the nation. The federal government has implemented many measures to assist health authorities with successfully achieving this goal.

Congress has also enacted several laws over the past few years to maximize the nation's ability to rapidly respond to such emergencies. Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3), as amended by the Project BioShield Act of 2004 (Public Law 108-276), allows FDA to authorize the use of an unapproved medical product or the unapproved use of an approved medical product during certain types of emergencies involving biological, chemical, radiological, or nuclear agents.

Section 319F-3 of the Public Health Service Act (42 U.S.C. 247d-6d), as enacted by the Public Readiness and Emergency Preparedness Act ("PREP Act") (Pub. L. No. 109-148), provides liability protection for activities causally related to, among other things, developing, manufacturing, distributing, prescribing, dispensing, administering and using "covered countermeasures," provided that the Secretary of HHS issues a declaration determining that a disease or other health condition or threat constitutes a public health emergency or that there is a credible risk that such health or threat may in the future constitute such an emergency. The PREP Act only applies to "covered countermeasures," which include "security countermeasures." "Security countermeasures" include medical products that are approved, cleared, or licensed, could qualify for approval or licensing within 8 years, or are authorized under an emergency use authorization.

As part of emergency preparedness and planning efforts, the Secretary of the Department of Health and Human Services (DHHS) issued a declaration pursuant to the PREP Act to provide targeted liability protections for anthrax countermeasures based on a credible risk that the threat of exposure to *Bacillus anthracis* and the resulting disease constitutes a public health emergency. (See 73 Fed. Reg. 58239 (October 6, 2008)).

Issue: During an anthrax emergency it is likely that doxycycline and ciprofloxacin would be distributed from the SNS and dispensed to the affected populations. Doxycycline and ciprofloxacin are approved for post-exposure prophylaxis against inhalational anthrax. It is anticipated, however, that when these drugs are dispensed in an anthrax emergency they would be accompanied by unapproved emergency use instructions and they would otherwise be dispensed for certain unapproved uses. For example, drugs might be accompanied by tablet crushing instructions, relabeled using the Shelf Life Extension Program-extended expiry, or repackaged outside the scope of the approved drug application. Under the law, these changes from the approved labeling and uses would render them unapproved and misbranded drugs. To help assure that these instruction/fact

sheets are consistent with FDA's current knowledge about the drugs, that any emergency use is accomplished as safely as possible, that PREP Act protections would apply in the event of an emergency, and that anthrax countermeasures would be legally distributed and dispensed, HHS/CDC is now planning for emergency distribution and dispensing of these countermeasures under an emergency use authorization (EUA). **Thus there are several changes involving anthrax response planning that should occur.**

Working with all pertinent federal partners, the CDC has developed and submitted pre-EUA documents to facilitate the issuance of an EUA should it be needed in the future.

The end goal is to ensure that medical countermeasures from the SNS are distributed and used legally in an anthrax emergency, that dispensers and recipients (patients) have the information they need about use of these drugs in an emergency, and that PREP Act liability protections with respect to these countermeasures are in place.

The following main issues are being addressed by the pre-EUA submissions:

1. Fact Sheets –

- a. **Issue:** The fact sheets accompanying ciprofloxacin and doxycycline that would be provided to patients or health care providers during an emergency are not part of the approved new drug applications or abbreviated new drug applications for those drugs. Therefore, distributing or dispensing of doxycycline or ciprofloxacin accompanied by these unapproved fact sheets would render those drugs unapproved and misbranded in violation of the law.
- b. **Action:** The CDC's pre-EUA submission includes standardized fact sheets that are *proposed* for dissemination during an anthrax emergency. CDC has been working with its federal partners to prepare proposed fact sheets for recipients (patients) and for health-care providers, to be distributed in conjunction with countermeasures in an anthrax emergency.

2. Required Prescription Drug Label Information–

- a. **Issue:** Under section 503(b)(2) of the Act (21 U.S.C. 353(b)(2)), the label of dispensed prescription drugs must include the following:
 - name and address of dispenser
 - serial 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

FDA has approved a Medication Guide for ciprofloxacin. Under 21 CFR 208.24(d) the label of each container or package, where the container is too small, of drug product for which a Medication Guide is required must instruct the authorized dispenser to provide a Medication Guide to each patient to

whom the drug product is dispensed and must state how the Medication Guide is provided.

It is anticipated that the SNS unit of use bottles of doxycycline or ciprofloxacin tablets might not include all of the required information for prescription product dispensing under section 503(b)(2) of the Act. In addition, it is anticipated that for ciprofloxacin the required Medication Guide label statements might not appear on the label. Inclusion of such required information during a declared emergency cannot be guaranteed and may even delay the necessary rapid dispensing of these countermeasures.

- b. **Action:** CDC's pre-EUA submission proposes distributing and dispensing of SNS unit-of-use bottles that may lack the required label information for doxycycline and ciprofloxacin in an anthrax emergency. CDC's pre-EUA submission proposes that certain information (e.g., dose in number of milliliters) be written on the label of each dispensed bottle of oral suspension. CDC is not proposing that additional patient information be added to the label of unit of use bottles of tablets.
3. **Information Regarding Post Exposure Prophylaxis Course –**
- a. **Issue:** The course of post-exposure prophylaxis for anthrax is 60 days of either ciprofloxacin or doxycycline, as described in the approved labeling of the respective drugs. Most states plan on dispensing an initial 10- day supply of drug, followed by the remaining 50 day supply, if needed. The Fact Sheets (See #1 above) include information regarding the 10-day supply of drug and describe the potential need to obtain the remaining 50-day course. This information is not part of the approved new drug applications or abbreviated new drug applications for doxycycline or ciprofloxacin.
 - b. **Action:** CDC's pre-EUA submission proposes that information be distributed regarding a partial course of post-exposure prophylaxis in an anthrax emergency.
4. **Shelf Life Extension Program (SLEP) –**
- a. **Issue:** Doxycycline and ciprofloxacin in the SNS may have undergone testing as part of the Shelf-Life Extension Program (SLEP). Under this program, FDA conducts tests of specified lots of doxycycline and ciprofloxacin to determine whether data support shelf life extension beyond the expiration dates originally printed on the label by the manufacturer. If the data support the extension, those products are generally relabeled with the extended expiration dates that are outside the scope of the approved drug applications.
 - b. **Action:** CDC's pre-EUA submission proposes in an anthrax emergency to use doxycycline and ciprofloxacin that have been part of the Shelf-Life Extension Program.
5. **Crushing Instructions –**
- a. **Issue:** Since oral suspension is in short supply, doxycycline tablet crushing guidelines have been developed. These instructions are not part of the

approved new drug applications or abbreviated new drug applications for doxycycline.

- b. **Action:** CDC's pre-EUA submission proposes that certain crushing instructions (http://www.fda.gov/cder/drug/infopage/penG_doxy/home_prep.htm) accompany doxycycline during an emergency, and does not propose that crushing instructions accompany ciprofloxacin during an emergency.

It is possible that FDA may identify other issues or conditions that need to be addressed. CDC's pre-EUA submission does not provide an independent legal basis for distributing or dispensing unapproved products or approved products for unapproved uses. The purpose of the pre-EUA submission is to allow FDA review to begin because, during exigent circumstances, the time available for the submission and review of an EUA request may be severely limited. An EUA would need to be issued in accordance with statutory criteria before unapproved products or approved products for unapproved uses could lawfully be distributed and dispensed under, and in accordance with, the EUA. This step is important to ensure that PREP Act protections apply.

DHHS/CDC/SNS acknowledges that the need for an EUA could have a significant impact and could cause changes in some Project Area planning efforts. CDC is working with other components of DHHS, including FDA, in order to address and resolve these matters. A Questions and Answers document is being developed to further expand on this topic and will be made available.

Thank you for your continued support and efforts to assure public health preparedness.