

Q and A's

Emergency Use Authorization

1. What is an emergency use authorization?

An Emergency Use Authorization (EUA) may be issued by the Food and Drug Administration (FDA) to allow either the use of an unapproved medical product or an unapproved use of an approved medical product during certain types of emergencies with specified agents. Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act), amended by the Project BioShield Act of 2004, permits authorization of such products for use in diagnosing, treating, or preventing serious or life-threatening diseases or conditions caused by biological, chemical, radiological, or nuclear agents, if certain statutory criteria are met.

2. What is required before FDA may issue an EUA?

The Act requires that, before an emergency use may be authorized, the Secretary of Health and Human Services (the HHS Secretary) must declare an emergency justifying the emergency use, based on one of the following grounds:

- (1) The Secretary of Homeland Security determines that there is a domestic emergency, or a significant potential for a domestic emergency, involving a heightened risk of attack with a specified biological, chemical, radiological, or nuclear agent or agents; or
- (2) The Secretary of Defense determines that there is a military emergency, or a significant potential for a military emergency, involving a heightened risk to United States military forces of attack with a specified biological, chemical, radiological, or nuclear agent or agents; or
- (3) The HHS Secretary determines that there is a public health emergency under the Public Health Service Act (PHS Act) that affects, or has a significant potential to affect, national security, and involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such agent or agents.

The HHS Secretary's declaration of emergency justifying the emergency use will terminate one year after issuance, unless terminated earlier or renewed. Notice of each declaration, determination, advance notice of termination, and renewal will be published in the Federal Register.

3. On what basis may FDA issue an EUA?

Once the Secretary has declared an emergency justifying the emergency use, the FDA Commissioner may authorize an emergency use only if, after consultation

with the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC) (to the extent feasible and appropriate given the circumstances of the emergency), he determines that certain statutory criteria have been met. Specifically, the Commissioner must conclude, as follows:

- (1) That the agent specified in the declaration of emergency can cause a serious or life-threatening disease or condition;
- (2) That, based on the totality of scientific evidence available, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing—
 - (a) The serious or life threatening disease or condition, or
 - (b) A serious or life-threatening disease or condition caused by a product authorized under section 564, or approved, cleared, or licensed under the Act or PHS Act, for diagnosing, treating, or preventing the disease or condition referred to in paragraph (1) and caused by the agent specified in the declaration of emergency;
- (3) That the known and potential benefits of the product outweigh the known and potential risks of the product when used to diagnose, prevent, or treat the serious or life threatening disease or condition that is the subject of the declaration; and
- (4) That there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating such serious or life threatening disease or condition.

An EUA may remain in effect for the duration of the declaration justifying the emergency use unless revoked. The law requires FDA to publish notice of each EUA in the Federal Register, each termination or revocation of an authorization, and an explanation of the reasons for the action.

4. Are there any limits on the use of an EUA product?

The law requires the FDA Commissioner (to the extent practicable given the circumstances of the emergency) to establish certain conditions on an EUA authorization that the Commissioner finds necessary or appropriate to protect the public health, and permits the Commissioner to establish other conditions that he finds necessary or appropriate to protect the public health. Such conditions may include a requirement to disseminate information to health care providers or authorized dispensers and prospective patients and other consumers regarding the authorization, the product's significant known and potential benefits and risks and the extent to which such benefits and risks are unknown; available alternatives and their benefits and risks; and, for prospective patients and consumers, the

option to accept or refuse the product and any consequences of refusal. Other conditions may include adverse event reporting and monitoring, data collection and analysis, and recordkeeping and records access.

Use of a product under an authorization must be consistent with any conditions imposed on the EUA.

5. What happens if the unapproved drugs or approved drugs for unapproved uses are distributed outside the scope of, or inconsistent with, the conditions of the EUA once it has been issued?

If FDA issues an EUA to allow for the lawful distribution or dispensing of anthrax countermeasures for emergency use under certain circumstances and states do not distribute or dispense anthrax countermeasures in accordance with the scope and conditions of the EUA, liability protections afforded by the Public Readiness and Emergency Preparedness (PREP) Act may be lost.

6. What is a pre-EUA submission?

A 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 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 under, and in accordance with, the EUA.

CDC/SNS Assets

7. Has CDC submitted a pre-EUA submission?

Yes.

8. Will the CDC pre-EUA submission cover anthrax countermeasures not supplied by SNS?

No. At this time, CDC's pre-EUA submission covers doxycycline and ciprofloxacin anthrax countermeasures supplied by the SNS, accompanied by written emergency use information, and distributed or dispensed to affected populations under certain circumstances. Countermeasures that are not deployed from the SNS are outside the scope of CDC's pre-EUA submission.

9. Can SNS ciprofloxacin or doxycycline accompanied by written emergency use information, ciprofloxacin or doxycycline labeled with SLEP-extended expiration dates, or ciprofloxacin or doxycycline for other unapproved uses (maintained

under federal control) be legally distributed or dispensed before an EUA is issued?

No. An EUA would need to be issued before such products could be legally distributed or dispensed under the EUA. An EUA is a legal mechanism that would allow for such products to be legally distributed provided the EUA authorizes the unapproved uses and the requisite statutory criteria have been met.

Fact Sheets

10. Will the recipient and health care provider fact sheets and doxycycline home preparation instructions be available in multiple language translations?

CDC's pre-EUA submission does not include translated versions of fact sheets or doxycycline home preparation instructions. Nonetheless, it is possible that any EUA that might be issued by FDA could include conditions relating to distribution of translated fact sheets, doxycycline home preparation instructions, or other materials under certain circumstances. If FDA issues an EUA with such conditions, then such translated materials could be distributed along with anthrax countermeasures as described in the EUA. CDC is having proposed doxycycline crushing instructions, proposed doxycycline recipient fact sheets, and proposed ciprofloxacin recipient fact sheets translated into Spanish.

11. Will Project Area planners have the opportunity to access the proposed language in the fact sheets?

Yes. CDC intends to make available to Project Area planners the fact sheets as proposed in the pre-EUA submission. These fact sheets, however, will not be authorized to accompany countermeasures under an EUA unless FDA ultimately authorizes them under an EUA.

12. Could FDA make last minute changes to the fact sheets as part of the EUA?

Yes. It is possible that FDA could make changes to the fact sheets as part of any EUA that might be issued if, for example, new information with respect to risks and benefits became available prior to issuance of the EUA. CDC has submitted a pre-EUA submission with proposed fact sheets for FDA review. CDC and FDA are coordinating closely to limit to the extent possible the need for last minute changes.

13. Will states be allowed to distribute their own state-developed fact sheets for doxycycline and/or ciprofloxacin deployed from the SNS?

It depends on the conditions imposed by any EUA that might be issued. CDC has submitted a pre-EUA submission with proposed fact sheets for FDA review. The

only fact sheets that may lawfully accompany ciprofloxacin and/or doxycycline under an EUA are those ultimately authorized by any EUA that might be issued.

14. Why is an EUA needed to distribute doxycycline and ciprofloxacin accompanied by fact sheets?

FDA has approved new drug applications and abbreviated new drug applications for doxycycline and ciprofloxacin for post-exposure prophylaxis against inhalational anthrax. The written emergency information (including facts sheets) that would accompany doxycycline and ciprofloxacin in an emergency is not part of the drug applications and has not been approved by FDA. As a general matter, dispensing of doxycycline and ciprofloxacin accompanied by written information that is not part of the FDA-approved labeling renders the drugs unapproved in certain respects as well as misbranded under the law. An EUA would allow the drugs to be legally distributed for the unapproved uses for which they would be authorized. An EUA could be needed for other reasons depending on the circumstances.

Labels

15. Will Project Areas need to plan to include information required under section 503(b)(2) of the Act on the label of the dispensed doxycycline or ciprofloxacin or the required Medication Guide label statements for ciprofloxacin?

CDC's pre-EUA submission proposes that not all of the information required under section 503(b)(2) of the Act would appear on the label of the distributed doxycycline and ciprofloxacin. CDC also proposes that the required Medication Guide label statement for ciprofloxacin not appear on the label. SNS doxycycline and ciprofloxacin will be dispensed with pre-printed labels on the bottles. CDC is proposing that additional information would need to be added to the label of oral suspensions when dispensing product directly to recipients. CDC is not proposing that additional information be added to labels of unit of use bottles of tablets. Project Area planners should plan to dispense ciprofloxacin and doxycycline with labels authorized under any EUA that might be issued.

Post Exposure Prophylaxis Course

16. Pharmacies dispense partial quantities of medication as common practice. Why is dispensing an initial 10-day supply of medication considered to be different?

The duration of therapy for post-exposure prophylaxis (PEP) for inhalation anthrax in the FDA-approved labeling for ciprofloxacin and doxycycline is 60 days. CDC's pre-EUA submission proposes that additional written information be distributed regarding the dispensing of a 10-day supply of doxycycline and ciprofloxacin as well as written information regarding the remaining course of treatment, if needed, as part of a mass dispensing strategy. Fact sheet information

on the partial 10-day supply is outside the scope of the approved drug applications (where the prophylaxis course is described as 60 days). The only written information that can be legally distributed is that approved as part of the drug applications or that authorized under an EUA that might be issued.

Crushing Instructions

17. The pre-EUA submission covers crushing instructions for doxycycline tablets. Will additional crushing instructions also be made available for ciprofloxacin tablets?

No, not at this time. The federal government is working to develop palatable crushing instructions for ciprofloxacin.

18. Will states be allowed to use their state developed crushing guidance for doxycycline? For ciprofloxacin?

States can only lawfully distribute doxycycline and ciprofloxacin accompanied by crushing instructions authorized by any EUA that might be issued. Drugs that are accompanied by crushing instructions that are not authorized under the EUA may not be legally distributed under the EUA. CDC's pre-EUA submission proposes that certain FDA-developed 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.

Non-SNS Assets

19. What if states/local areas want to distribute ciprofloxacin and/or doxycycline that are not deployed from the SNS?

CDC's pre-EUA submission generally covers doxycycline and ciprofloxacin anthrax countermeasures *deployed from the SNS*. Countermeasures that are not deployed from the SNS are outside the scope of CDC's pre-EUA submission. If the ultimate EUA is similarly limited, PREP Act protections may not apply with respect to products not deployed from the SNS.