October 2011

Mass Dispensing of Prophylactic Antibiotic Medication Following a Bioterrorism Attack

Part 1: General Policy

Part 2: Model Standing Orders

Part 3: Additional Information and Suggested Guidance

Appendices

Appendix A: Missouri Strategic National Stockpile Public Health Dispensing Assessment Form

Appendix B: Doxycycline EUA Fact Sheet for Recipients

Appendix C: Doxycycline EUA Fact Sheet for Recipients - Home Preparation Instructions for Children or Adults Who Cannot Swallow Pills

Appendix D: In an Emergency: How to Prepare Doxycycline for Children and Adults Who Cannot Swallow Pills

Appendix E: Doxycycline EUA Fact Sheet for Health Care Professionals

Part 1: General Policy

Following a large-scale bioterrorism attack with an agent such as *Bacillus anthracis*, *Yersinia pestis*, or *Francisella tularensis*, prophylactic antibiotics (and in the case of *B. anthracis*, vaccine) would be provided from the **Strategic National Stockpile** to persons with potential exposure to aerosolized organisms. Depending on the nature of the attack, the total number of persons with possible exposure could be extremely large, and antibiotic prophylaxis would need to be initiated in these individuals as quickly as possible. Antibiotic dispensing would occur at dispensing sites (e.g., Point of Dispensing, or POD, sites).

Following exposure to *Bacillus anthracis*, the recommended period of antibiotic prophylaxis is currently 60 days. However, potentially exposed persons (who will initially be identified based on imprecise estimates of how widely the organism was disseminated) will, when they first present to a dispensing site, only be given a 10-day supply of medication. Then, during the following days, public health officials will be able to obtain a more precise estimate of who was actually at risk of exposure. This will allow a more accurate determination of who will need to receive additional medication to complete the full 60-day course of prophylaxis, and these persons will then be notified where and when to come to receive their remaining medication (and possibly their initial dose of anthrax vaccine).

Standing Orders

Standing orders will be needed for nurses at the dispensing sites so that they have the authority to dispense prophylactic antibiotic medications to potentially-exposed persons. **The model standing orders provided in Part 2, below, are specifically intended for use at dispensing sites in mass antibiotic prophylaxis situations (following a bioterrorism attack) during a governor-declared state of emergency.**

The content of these orders (e.g., medication dosages, duration of treatment) might need to be changed in the context of a specific event based on updated recommendations from the Centers for Disease Control and Prevention (CDC), and possibly other expert groups. The Missouri Department of Health and Senior Services (DHSS) will continue to provide medical professionals, local public health agencies (LPHAs), and dispensing sites with the most current recommendations throughout the event.

In addition, the physician who will sign the standing orders for a dispensing site may decide to make modifications to the model standing orders provided here. However, any such modifications must be consistent with the provisions of the Food and Drug Administration (FDA) Emergency Use Authorization (EUA), described in the next section. Also, any modifications to the standing orders must be consistent with the most current prophylactic treatment guidelines from CDC and DHSS.

During the period when prophylactic antibiotics are being dispensed at a dispensing site, the physician who has signed the standing orders (or another physician who is his/her designee) must be immediately available to dispensing site staff, either by being present at the dispensing site, or by phone.

Emergency Use Authorization (EUA)

If medications are dispensed for prophylaxis in a bioterrorism emergency, their usage would likely not, because of the special requirements of the situation, be consistent with current FDA-approved labeling. To address this issue, the distribution and dispensing of prophylactic medications during a bioterrorism event would take place under an FDA-issued EUA. The purpose of this EUA would be to ensure that medications are distributed and used legally in responding to the event, that dispensers and recipients have the information they need regarding the use of these drugs in an emergency, and that liability protections afforded by the Public Readiness and Emergency Preparedness (PREP) Act (see next page) with respect to these medical countermeasures are in place. More information on EUAs is available at http://www.naccho.org/topics/emergency/SNS/upload/PREP-EUA_Final-CDC-Q-and-A-1-15-09.pdf.

An EUA covering the emergency use of doxycycline products for post-exposure prophylaxis of inhalational anthrax in the event of a public health emergency involving *B. anthracis* has been issued. If FDA issues additional EUAs, all relevant documents (including recipient and health care professional's fact sheets) will be provided to LPHAs, and to dispensing sites, as soon as they become available.

It is imperative that all provisions of the EUA be followed in the dispensing of medication during the response to the event.

Public Readiness and Emergency Preparedness (PREP) Act

The Public Readiness and Emergency Preparedness Act ("PREP Act") enacted as Division C of the Defense Appropriations Act for fiscal year 2006, Pub. L. No. 109-148, added new authorities under the Public Health Service (PHS) Act to alleviate concerns about liability related to the manufacture, testing, development, distribution, administration and use of countermeasures against chemical, biological, radiological and nuclear agents of terrorism, epidemics, and pandemics.

The PREP Act authorizes the Secretary of the Department of Health and Human Services ("Secretary") to issue a declaration ("PREP Act declaration") that provides immunity from tort liability (except for willful misconduct) for claims of loss caused, arising out of, relating to, or resulting from administration or use of countermeasures to diseases, threats and conditions determined by the Secretary to constitute a present, or credible risk of a future public health emergency to entities and individuals involved in the development, manufacture, testing, distribution, administration, and use of such countermeasures. A PREP Act declaration is specifically for the purpose of providing immunity from tort liability, and is different from, and not dependent on, other emergency declarations. The PREP Act also authorizes an emergency fund in the United States Treasury to provide compensation for injuries directly caused by administration or use of a countermeasure covered by the Secretary's declaration.

For more information on the PREP Act, go to http://www.phe.gov/Preparedness/legal/prepact/Pages/prepqa.aspx.

Evaluation and Referral of Symptomatic Persons to a Medical Facility or Medical Professional for Evaluation and Necessary Treatment

All individuals presenting to a dispensing site to receive prophylactic antibiotic medication should first be asked whether they have a febrile illness before being allowed into the dispensing area. Any person who reports having a febrile illness should be taken to an evaluation area and further assessed. If, based on this assessment, it is judged the person could be experiencing signs/symptoms of the disease, then that individual should be given an initial dose of the appropriate prophylactic medication, provided with a 10-day supply of the medication, and immediately referred to medical care, or immediately transported to a designated medical facility. More information is provided below in "Part 3: Additional Information and Suggested Guidance for Mass Antibiotic Prophylaxis Dispensing Sites."

Health Assessment of Persons Receiving an Initial Supply of Prophylactic Antibiotic Medication

Individuals presenting to a dispensing site to receive prophylactic antibiotic medication and/or to pick up medication for potentially-exposed family members will be asked to complete the appropriate sections of the form entitled *Public Health Model: Health Assessment Template/Drug Dispensing Protocol* (contained in Appendix A) or a similar form used for health assessment which captures required information. Medication will be provided according to the protocol contained in this form.

Emergency Use Information Fact Sheets for Medication Recipients

All persons receiving prophylactic antibiotic medication at a dispensing site will be given an appropriate emergency use information fact sheet containing information on the medication they received. An example is the recipient's fact sheet for doxycycline (for use in the context of *B. anthracis* exposure) shown in the Appendix B. This fact sheet was developed and approved by CDC/FDA for use under an EUA.

In order to ensure accuracy and consistency, dispensing sites should only use recipient's fact sheets that have been endorsed by FDA/DHSS.

If necessary, medication recipients will also receive a fact sheet with home preparation instructions for children or adults who cannot swallow pills. One of the two fact sheets shown in Appendix C and Appendix D must be used to provide such instructions for doxycycline pills.

Emergency Use Information Fact Sheets for Health Care Professionals

All health care professionals associated with a dispensing site will be given appropriate emergency use information fact sheets containing information on the medications being provided. An example is the health care professional's fact sheet for doxycycline (for use in the context of *B. anthracis* exposure) shown in the Appendix E. This fact sheet was developed and approved by CDC/FDA for use under an EUA.

In order to ensure accuracy and consistency, dispensing sites should only use health care professional's fact sheets that have been endorsed by FDA/DHSS.

Part 2: Model Standing Orders

- **Antibiotic Prophylaxis Against *Bacillus anthracis* (Anthrax)**

- **Antibiotic Prophylaxis Against *Yersinia pestis* (Plague)**

- **Antibiotic Prophylaxis Against *Francisella tularensis* (Tularemia)**

The physician who will sign the standing orders for a dispensing site may decide to make modifications to the model standing orders provided here.

However, any such modifications must be consistent with the provisions of the Emergency Use Authorization (EUA) that has been issued for the current event, and with the most current prophylactic treatment guidelines from the Centers for Disease Control and Prevention (CDC) and the Missouri Department of Health and Senior Services (DHSS).

Standing Orders for a Mass Antibiotic Prophylaxis Dispensing Site Following a Bioterrorism Attack With *Bacillus anthracis* (Anthrax)

Date and time this order was implemented:

_____

_____

I direct nurses employed by, or serving as volunteers for, the

_____ (name of Agency/Organization) to dispense medications to individuals presenting for prophylactic treatment to *Bacillus anthracis*.

All medications must be dispensed in accordance with the following prophylactic treatment guidelines and within the restrictions of the guidelines of the Strategic National Stockpile program.

Recommended Therapy for Inhalational Anthrax Infection for Post-Exposure Prophylaxis (PEP)

Category	Initial Oral Therapy+	Therapy if Strain is Susceptible#	Total Duration of PEP Therapy
Adults	Ciprofloxacin, 500 mg orally every 12h **Or** Doxycycline, 100 mg orally every 12h		60 days (A 10 day-supply of medication will be provided at the initial visit to the dispensing site.)
Children	Ciprofloxacin Weight < 31 kg (67 lbs): 10–15 mg/kg orally every 12 h* Weight ≥ 31 kg (67 lbs): adult dose **Or** Doxycycline Weight < 40 kg (89 lbs): 2.2 mg/kg orally every 12 h* Weight ≥ 40 kg (89 lbs): adult dose	Amoxicillin Weight < 20 kg (44 lbs): 80 mg/kg to be taken orally in 3 divided doses every 8 hr Weight ≥20 kg (44 lbs): 500 mg orally every 8 hr	60 days (A 10 day-supply of medication will be provided at the initial visit to the dispensing site.)
Pregnant Women	Ciprofloxacin, 500 mg orally every 12 h **Or** Doxycycline, 100 mg orally every 12h	Amoxicillin, 500 mg orally every 8 h	60 days (A 10 day-supply of medication will be provided at the initial visit to the dispensing site.)
Immunosuppressed persons	Same as for nonimmunosuppressed adults and children		

+ The Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics (AAP) have stated that when no information is available about the antimicrobial susceptibility of the implicated strain of *Bacillus anthracis*, initial PEP with ciprofloxacin or doxycycline is recommended for adults and children. The Food and Drug Administration (FDA) has approved ciprofloxacin and doxycycline for use as PEP against anthrax.

CDC recommends that as soon as the organism's susceptibility to penicillin has been confirmed, prophylactic therapy for children and pregnant women should be changed to oral amoxicillin. Amoxicillin is not FDA-approved for anthrax PEP.

* Maximum daily dose for ciprofloxacin is 500mg BID, and for doxycycline is 100mg BID.

References:

1. CDC. Update: Investigation of anthrax associated with intentional exposure and interim public health guidelines. *MMWR* 2001; 50(41):893.
2. Inglesby TV, O'Toole T, Henderson DA, et al. Anthrax as a biological weapon, 2002: updated recommendations for management. *JAMA* 2002; 287:2236-52. Includes corrections from *JAMA* 2002; 288:1849.
3. CDC. Responding to detection of aerosolized *Bacillus anthracis* by autonomous detection systems in the workplace. *MMWR* 2004;53(RR-7):9.
4. AAP. Anthrax. In: Pickering LK, et al (eds). *Red Book: 2009 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009:214.

Individuals presenting to a dispensing site to receive prophylactic medication will be asked to complete the appropriate sections of the attached form entitled *Public Health Model: Health Assessment Template/Drug Dispensing Protocol*. Medication will be provided according to the protocol contained in this form. This order will terminate _____
date

_____ _____

Physician Date of Signature

Standing Orders for a Mass Antibiotic Prophylaxis Dispensing Site Following a Bioterrorism Attack With *Yersinia pestis* (Plague)

Date and time this order was implemented:
_____
_____

I direct nurses employed by, or serving as volunteers for, the _____ (name of Agency/Organization) to dispense medications to individuals presenting for prophylactic treatment to *Yersinia pestis* (Plague).

All medications must be dispensed in accordance with the following prophylactic treatment guidelines and within the restrictions of the guidelines of the Strategic National Stockpile program.

Recommended Post-exposure Prophylaxis for Pneumonic Plague

Table 2. Working Group Recommendations for Treatment of Patients With Pneumonic Plague in the Contained and Mass Casualty Settings and for Postexposure Prophylaxis*

Patient Category	Recommended Therapy
	Mass Casualty Setting and Postexposure Prophylaxis#
Adults	Preferred choices Doxycycline, 100 mg orally twice daily†† Ciprofloxacin, 500 mg orally twice daily‡ Alternative choice Chloramphenicol, 25 mg/kg orally 4 times daily§**
Children‖	Preferred choice Doxycycline,†† If ≥45 kg, give adult dosage If <45 kg, then give 2.2 mg/kg orally twice daily Ciprofloxacin, 20 mg/kg orally twice daily Alternative choices Chloramphenicol, 25 mg/kg orally 4 times daily§**
Pregnant women¶	Preferred choices Doxycycline, 100 mg orally twice daily†† Ciprofloxacin, 500 mg orally twice daily Alternative choices Chloramphenicol, 25 mg/kg orally 4 times daily§**

*These are consensus recommendations of the Working Group on Civilian Biodefense and are not necessarily approved by the Food and Drug Administration. See "Therapy" section for explanations. One antimicrobial agent should be selected. Therapy should be continued for 10 days. Oral therapy should be substituted when patient's condition improves. IM indicates intramuscularly; IV, intravenously.

‡Other fluoroquinolones can be substituted at doses appropriate for age. Ciprofloxacin dosage should not exceed 1 g/d in children.

§Concentration should be maintained between 5 and 20 µg/mL. Concentrations greater than 25 µg/mL can cause reversible bone marrow suppression.[35,62]

‖Refer to "Management of Special Groups" for details. In children, ciprofloxacin dose should not exceed 1 g/d, chloramphenicol should not exceed 4 g/d. Children younger than 2 years should not receive chloramphenicol.

¶Refer to "Management of Special Groups" for details and for discussion of breastfeeding women. In neonates, gentamicin loading dose of 4 mg/kg should be given initially.[63]

#Duration of treatment of plague in mass casualty setting is 10 days. Duration of postexposure prophylaxis to prevent plague infection is 7 days.

**Children younger than 2 years should not receive chloramphenicol. Oral formulation available only outside the United States.

††Tetracycline could be substituted for doxycycline.

Reference: Inglesby TV, et al. Plague as a Biological Weapon: Medical and Public Health Management. *JAMA* 2000; 283:2281

Individuals presenting to a dispensing site to receive prophylactic medication will be asked to complete the appropriate sections of the attached form entitled *Public Health Model: Health Assessment Template/Drug Dispensing Protocol*. Medication will be provided according to the protocol contained in this form. This order will terminate _____
date

_____ _____
Physician Date of Signature

Standing Orders for a Mass Antibiotic Prophylaxis Dispensing Site Following a Bioterrorism Attack With *Francisella tularensis* (Tularemia)

Date and time this order was implemented:

_____

_____

I direct nurses employed by, or serving as volunteers for, the _____ (name of Agency/Organization) to dispense medications to individuals presenting for prophylactic treatment to *Francisella tularensis*.

All medications must be dispensed in accordance with the following prophylactic treatment guidelines and within the restrictions of the guidelines of the Strategic National Stockpile program.

Recommended Post-Exposure Prophylaxis for Tularemia

Table 3. Working Group Consensus Recommendations for Treatment of Patients With Tularemia in a Mass Casualty Setting and for Postexposure Prophylaxis*

Mass Casualty Recommended Therapy
Adults
Preferred choices
Doxycycline, 100 mg orally twice daily
Ciprofloxacin, 500 mg orally twice daily†
Children
Preferred choices
Doxycycline; if ≥45 kg, give 100 mg orally twice daily; if <45 kg, give 2.2 mg/kg orally twice daily
Ciprofloxacin, 15 mg/kg orally twice daily†‡
Pregnant Women
Preferred choices
Ciprofloxacin, 500 mg orally twice daily†
Doxycycline, 100 mg orally twice daily

*One antibiotic, appropriate for patient age, should be chosen from among alternatives. The duration of all recommended therapies in Table 3 is 14 days.
†Not a US Food and Drug Administration–approved use.
‡Ciprofloxacin dosage should not exceed 1 g/d in children.

Reference: Dennis DT, et al. Tularemia as a Biological Weapon: Medical and Public Health Management. *JAMA* 2001; 285:2763-73-90.

Individuals presenting to a dispensing site to receive prophylactic medication will be asked to complete the appropriate sections of the attached form entitled *Public Health Model: Health Assessment Template/Drug Dispensing Protocol*. Medication will be provided according to the protocol contained in this form.

This order will terminate _____
date

_____ _____
Physician Date of Signature

Part 3: Additional Information and Suggested Guidance

Changes to Recommendations

The Missouri Department of Health and Senior Services (DHSS) provides health care professionals access to current information and clinical recommendations regarding potential bioterrorism-related diseases on its website (see http://health.mo.gov/emergencies/ert/biomed.php).

Once a bioterrorism event is recognized and specific information on that event starts to become available, clinical recommendations (including recommendations for post-exposure prophylaxis) may change in order to optimize the response to this particular situation. As new recommendations from the Centers for Disease Control and Prevention (CDC), and possibly other expert groups, become available, they will immediately be provided to health care professionals, local public health agencies (LPHAs), and dispensing sites.

Additional Consideration Regarding Ciprofloxacin

The ciprofloxacin package insert states that concomitant administration of ciprofloxacin and tizanidine (Zanaflex®) is contraindicated. Concomitant use of ciprofloxacin and tizanidine can significantly increase tizanidine levels and may result in serious side effects.

If a person is given ciprofloxacin at the dispensing site, they should also be provided with instructions (verbally and/or in writing) stating that, if they are currently taking tizanidine (Zanaflex®), they should begin taking the ciprofloxacin, but should immediately contact their medical provider for instructions regarding the tizanidine (the provider may switch them from tizanidine to another medication).

Alternatively, before providing ciprofloxacin, the person who is to receive it (or the family member picking up the medication) can be questioned as to whether tizanidine is currently being taken. If the answer is yes, then doxycycline, rather than ciprofloxacin, should be used if possible. If ciprofloxacin must be used, then the individual should be provided with instructions, as described above, to start the ciprofloxacin but immediately contact a medical provider for instructions regarding the tizanidine.

Suggested General Guidelines for Management of Symptomatic Persons Who Present to a Dispensing Site

Persons with symptoms of illness will be presenting to dispensing sites. Management of these symptomatic individuals will have to take into consideration available resources and other factors specific to the event, remembering that the main purpose of the dispensing site is to rapidly provide prophylactic medication to large numbers of asymptomatic persons who have potentially been exposed to a dangerous pathogen. The following are some options for management of symptomatic persons which dispensing sites can consider. Regardless of the option chosen, if the terrorist attack resulted in potential exposure to *Y. pestis* (plague, which in its pneumonic form is transmissible from person-to-person), all persons presenting to the dispensing site should be asked whether they have a febrile illness before they are allowed into the building. Anyone who indicates that he/she has a febrile illness should immediately be separated from other persons seeking medication, put on a surgical mask, and then be taken to an evaluation area or immediately referred to a medical facility.

A. If resources are limited and/or other factors require, persons with a febrile illness who present to the dispensing site may, once identified, have to simply be told to immediately obtain medical evaluation without receiving any further evaluation at the site. This is not the optimal approach, but it may have to be used in some circumstances.

(If exposure to *Y. pestis* is suspected, all persons presenting to the dispensing site should be asked whether they

have a febrile illness before they are allowed into the building. Anyone who indicates that he/she has a febrile illness should immediately be separated from other persons seeking medication. The febrile individual should put on a surgical mask and be told to immediately obtain medical evaluation at a medical facility.)

If at all possible, the person should quickly be provided with a 10-day supply of appropriate prophylactic medication (and take the first dose) before leaving the dispensing site. They should be told that even though they have been given antibiotics for preventive treatment, it remains absolutely essential that they obtain immediate medical evaluation followed by further treatment as necessary.

One reason it is important to provide an initial supply of prophylactic medication to these individuals is that if, when they present to a medical facility, it is determined that they do not have the disease of concern (and thus do not need to be placed on a more appropriate treatment regimen and likely hospitalized), they will – very importantly – have already started their prophylactic medication, and will have enough of this medication to complete 10 days of prophylaxis.

A second reason for providing prophylactic medication is that if such individuals do have the disease of concern (anthrax, plague, or tularemia), then giving them this medication (and having them take the first dose) at the dispensing site may actually be providing some immediate treatment for their illness. Note that in a mass-casualty situation (i.e., one in which there are limited medical resources), the recommended treatment regimens for anthrax, plague, and tularemia are the same oral regimens recommended for prophylaxis. However, also be aware that treatment in a contained-casualty situation (i.e., where there are adequate resources) is with parenteral medications, and thus the treatment regimen in this situation would not be the same as the prophylaxis regimen. Which particular medication(s) a given symptomatic individual needs to receive will be determined by a medical provider after that person is evaluated at a medical facility.

If possible, the dispensing site should have mechanisms for transporting symptomatic persons needing further evaluation to a medical facility. If, as may be likely, the resources are not available to transport all such symptomatic persons, then it would be highly desirable to at least be able to transport to medical care persons with no other form of transportation, along with those who appear to be significantly ill and in need of immediate evaluation and treatment.

B. More preferably, if resources and other factors allow, all individuals presenting to a dispensing site should be asked whether they have a febrile illness before they are allowed into the dispensing area (or, if exposure to *Y. pestis* is suspected, before they are allowed into the building). Any person who reports having a febrile illness should be taken to an evaluation area and further assessed. By doing a simple assessment at the dispensing site, it is hoped that those individuals who are unlikely to be displaying manifestations of the disease in question (anthrax, plague, or tularemia) can be identified and, as a result, not be sent to a medical facility (which very likely could already be overwhelmed with ill and worried persons).

The following are meant to provide general guidance. If possible, measurement of the symptomatic person's temperature should be done to assist in the evaluation.

1. Where exposure to *Bacillus anthracis* (anthrax) is suspected, any person who has fever **plus** one or more of the following symptoms should be given an initial dose of the appropriate prophylactic medication, provided with a 10-day supply of the medication, and immediately referred to medical care:
   - muscle aches
   - cough, chest discomfort, or difficulty in breathing
   - vomiting or diarrhea
   - intense sweating
   - severe headache or mental confusion
   - skin ulcer, possibly with a blackened surface

2. Where exposure to *Y. pestis* (plague) is suspected, all persons presenting to the dispensing site should be asked whether they have a febrile illness before they are allowed into the building. Anyone who indicates that he/she has a febrile illness should immediately put on a surgical mask and be taken to the evaluation area. All persons who will be within 6 feet of the symptomatic person during the evaluation/disposition process should also wear a surgical mask. For purposes of evaluation, any person who has fever **plus** one or

more of the following symptoms should be given an initial dose of the appropriate prophylactic medication, provided with a 10-day supply of the medication, and immediately referred to medical care:

- cough (especially bloody)
- chest discomfort
- difficulty in breathing
- tachypnea (particularly in young children)
- nausea, vomiting, abdominal pain

For symptomatic individuals who will be transported to medical care: if there will be any delay in the transport process, the person should be placed in an "isolation area" to minimize exposure to others.

3. Where exposure to *Francisella tularensis* (tularemia) is suspected, any person who has fever **plus** one or more of the following should be given an initial dose of the appropriate prophylactic medication, provided with a 10-day supply of the medication, and immediately referred to medical care:
   - cough
   - muscle pain
   - vomiting
   - diarrhea
   - conjunctivitis (red, painful eyes)
   - pharyngitis (sore throat)

As indicated above, all symptomatic persons who are referred for immediate medical evaluation should, before leaving the dispensing site, quickly be provided with a 10-day supply of appropriate prophylactic medication (and take the first dose). In addition, they should be told that even though they have been given antibiotics for preventive treatment, it remains absolutely essential that they obtain immediate medical evaluation followed by further treatment as necessary.

Symptomatic persons who, after assessment at the dispensing site, are not referred for further medical evaluation should be provided with a 10-day supply of appropriate prophylactic medication (and take the first dose). They should be informed that they need to immediately seek medical evaluation if they subsequently experience fever plus any of the other signs/symptoms listed above for the disease of concern.

If possible, the dispensing site should have mechanisms for transporting symptomatic persons needing further evaluation to a medical facility. If, as may be likely, the resources are not available to transport all such symptomatic persons, then it would be highly desirable to at least be able to transport to medical care persons with no other form of transportation, along with those who appear to be significantly ill and in need of immediate evaluation and treatment.

C. Other mechanisms for managing symptomatic persons in the context of a specific event may be developed by dispensing sites (with the direction and approval of the dispensing site physician). However, the development of other approaches should take into consideration the issues mentioned above.

Additional Information on Clinical Presentations

Inhalational Anthrax. Initial phase: non-specific symptoms such as low-grade fever, nonproductive cough, headache, nausea, vomiting, malaise, fatigue, myalgias, profound sweats, chest discomfort (upper respiratory tract symptoms are rare); maybe rhonchi on chest exam, otherwise normal; chest x-ray may show mediastinal widening and/or pleural effusion; infiltrates might be present. Subsequent, fulminant phase: 1–5 days after onset of initial symptoms; may or may not be preceded by 1–3 days of improvement; abrupt onset of high fever and severe respiratory distress (dyspnea, stridor, cyanosis), shock, death within 24–36 hours. Hemorrhagic meningitis can be present.

[Note that direct skin contact with anthrax spores can result in **cutaneous anthrax** (11 confirmed or probable cases of cutaneous anthrax, in addition to 11 cases of inhalational anthrax, were associated with the 2001 anthrax attacks). In cutaneous anthrax, an area of local edema becomes a pruritic macule or papule, which progresses to a vesicle in 1-2 days, followed by an ulcer with subsequent development of a depressed black eschar within 7–10 days of the initial lesion.

There is usually surrounding local edema, and small (1-3 mm) vesicles may surround the ulcer. The lesion is usually painless, but patients may also have fever, malaise, headache, lymphangitis, and painful regional lymphadenopathy.]

For more information, go to http://www.cidrap.umn.edu/cidrap/content/bt/anthrax/biofacts/anthrax_clindx.html.

Pictures of clinical manifestations are available at http://www.cidrap.umn.edu/cidrap/content/bt/anthrax/images/index.html.

Pneumonic Plague. Fever, headache, weakness, and rapidly developing severe pneumonia with cough, chest pain, dyspnea, and tachypnea (particularly in young children). Cough can be productive of bloody, mucoid, or (less commonly) purulent sputum. Prominent gastrointestinal symptoms – including nausea, vomiting, diarrhea, and abdominal pain – may be present. Chest x-ray findings are variable but bilateral infiltrates or consolidation is common; pleural effusions may be present. Massive mediastinal adenopathy occurs rarely. Complications include septicemia and meningitis.

For more information, go to http://www.cidrap.umn.edu/cidrap/content/bt/plague/biofacts/plague_clindx.html.

Pictures of clinical manifestations are available at http://www.cidrap.umn.edu/cidrap/content/bt/plague/images/index.html.

Inhalational Tularemia. May see abrupt onset of fever, chills, malaise, headache, myalgias, joint pain, nonproductive cough, and progressive weakness. Persons with pneumonia can develop chest pain, dyspnea, bloody sputum, and respiratory failure. However, inhalational exposures can commonly result in an initial clinical picture of systemic illness without prominent signs of respiratory disease. The earliest chest x-ray findings may be peribronchial infiltrates, typically advancing to bronchopneumonia in >1 lobes, and often accompanied by pleural effusions and hilar lymphadenopathy – such signs may, however, be minimal or absent. Aerosol exposures to *F. tularensis* can incapacitate some persons in the first 1-2 days of illness, and pulmonary infection can sometimes rapidly progress to severe pneumonia, respiratory failure, and death. Although exposure to aerosolized *F. tularensis* is expected to principally cause primary pleuropneumonic infection, some exposures might contaminate the eye (resulting in ocular tularemia with conjunctivitis), penetrate broken skin (resulting in ulceroglandular or glandular disease), or cause oropharyngeal disease (with pharyngitis and cervical lymphadenitis).

For more information, go to
http://www.cidrap.umn.edu/cidrap/content/bt/tularemia/biofacts/tularemiafactsheet.html#_Clinical_Syndromes_and.

Pictures of clinical manifestations are available at
http://www.cidrap.umn.edu/cidrap/content/bt/tularemia/images/index.html.

For questions related to these standing orders, or guidance regarding the provision of prophylactic antibiotics during a mass dispensing event, please contact the Center for Emergency Response and Terrorism at 573/526-3798.

Appendix A

Missouri Strategic National Stockpile
Public Health Dispensing Assessment Form

Missouri Strategic National Stockpile Public Health Dispensing Assessment Form

Head of Household
Name:
Address:
City, State, Zip
Phone #

Step 1. List all household members for whom you are picking up medicine today; place your name in the first line.

Step 2. For each person listed, answer all three questions.

Question 1	Question 2	Question 3
Is this person allergic to or should not take: Doxycycline? Tetracycline? (Vibramycin) Minocycline?	Is this person allergic to or should not take: Ciprofloxacin (Cipro)? Levofloxacin (Levaquin)? Other foxacin?	Is this person: In 2nd half of pregnancy? Breastfeeding? A child under 8 years old?

Decision Chart – STAFF USE ONLY			
Answer 1 **Allergic or not to take Doxycycline?**	**Answer 2** **Allergic or not to take a floxacin?**	**Answer 3** **Child, Pregnant, or Breastfeeding?**	**Provide**
No / DK	No / DK	No	Doxy
No / DK	No / DK	Yes / DK	Cipro
No / DK	Yes	Any	Doxy
Yes	No / DK	Any	Cipro
Yes	Yes	Any	Refer
DK = Don't Know		**Any = Any Answer (Y, N, DK)**	

Last Name, First Name	Yes, No, Don't Know?	Yes, No, Don't Know?	Yes, No, Don't Know?	Check medicine to be provided STAFF USE ONLY				Affix Labels here if not referred	
				Doxy		Cipro		Referral Reason	
				Doxy		Cipro		Referral Reason	
				Doxy		Cipro		Referral Reason	
				Doxy		Cipro		Referral Reason	
				Doxy		Cipro		Referral Reason	
				Doxy		Cipro		Referral Reason	
				Doxy		Cipro		Referral Reason	
				Doxy		Cipro		Referral Reason	
				Doxy		Cipro		Referral Reason	
Add totals under Doxy and Cipro columns									

Step 3: Each person should take the medicine checked in the row following his/her name.

Appendix B

Doxycycline EUA Fact Sheet for Recipients

Doxycycline EUA Fact Sheet for Recipients

You are receiving doxycycline because you may have been exposed to the anthrax germ, which can be deadly. You do not have to take this drug, but taking doxycycline to treat anthrax will reduce your risk of getting sick and dying. If possible, you may want to discuss with a health care professional the benefits and risks described in this fact sheet, or any available alternatives.

The full course of treatment is usually 60 days. If you have received a partial supply, public officials will announce where you can get the rest of the medicine.

What is anthrax?

Anthrax is a serious disease caused by the germ *Bacillus anthracis*. People who breathe in (inhale) anthrax germs are at risk of serious illness, ***including death***. However, you can't get anthrax from another person.

- First symptoms are cold-like or flu-like symptoms, e.g., a sore throat, mild fever, muscle aches.
- Later symptoms are cough, chest discomfort, shortness of breath, tiredness, muscle aches.

Symptoms usually occur within 7 days of inhaling anthrax germs, but can take up to 42 days to appear. See a doctor immediately if you have symptoms.

What is doxycycline?

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. If you take doxycycline as directed and begin to feel sick anyway, ***get medical care right away***.

How do I take doxycycline?

- Adults and those 8 years and older and children 89 lbs (40 kg) or more – take one pill (100 mg) in the morning and one pill in the evening on an empty stomach with a full glass of water.
- If you get an upset stomach or indigestion, take it with some food or milk. Be sure to drink lots of fluids.
- Children under 89 lbs (40 kg) and adults who can't swallow a pill – ***follow the directions provided to you on crushing and mixing doxycycline.***
- If you have received the liquid form, follow the directions on the bottle; you can store it at room temperature for up to 14 days.
- If you miss a dose, take only next scheduled dose – ***Do not take two doses at one time.***
- Doxycycline may not work as well when taken with some medicines. Take it 2 hours before or 2 hours after taking: antacids; multivitamins or supplements with calcium, iron, magnesium, or sodium bicarbonate; Sucralfate (Carafate); Colestipol (Colestid); cholestyramine; Didanosine; Bismuth subsalicylate (Helidac) (Pepto Bismol) (Kaopectate); or any other products to treat indigestion, nausea, or diarrhea.
- Doxycycline may affect dosing of certain blood thinners or seizure medicines; call your doctor if you are on these medications.
- Keep the pills dry; store them between 68–77°F (20–25°C).
- Keep containers out of the reach of children and pets; call the poison control center if accidental ingestion occurs (1-800-222-1222).

Who should NOT take doxycycline?

STOP taking the medicine if you get any of these serious, but rare, side effects; get medical help right away (go to the Emergency Room or call 911):

- swelling of the tongue, hands, or feet
- closing of the throat
- trouble breathing
- severe itching or rash, especially hives and whelps
- severe stomach cramps with high fever or bloody diarrhea
- yellowing of the eyes or skin or dark-colored urine
- pain when swallowing
- unusual bleeding or bruising
- severe headaches, dizziness, or double vision

Keep taking the medicine if you have:

- mild nausea or vomiting, upset stomach, loose stools
- vaginal yeast infection

Do not take doxycycline if you have had a severe allergic reaction to doxycycline or another tetracycline drug.

Are there other possible severe side effects?

- Serious liver problems (liver failure)
- Sensitivity to the sun
- Discolored teeth, poor tooth enamel in children under the age of 8 or when taken by their mothers during the last half of pregnancy or while nursing
- Slowed bone growth in children
- Birth control pills stop working. Use another form of birth control until you finish taking all of your doxycycline

What is unknown about the emergency use of doxycycline?

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 post-exposure prophylaxis (PEP), or what the impact of dispensing without an individual prescription will be.

How do I report side effects or errors?

Tell your doctor right away and report side effects or medication errors to MedWatch at www.fda.gov/medwatch (1-800-FDA-1088).

CONTACTS: If you have any questions, please contact XXXXX (placeholder for stakeholder's specific contact information).

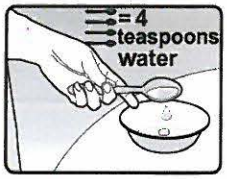
** If you have received doxycycline with an expired date on the package, FDA has authorized its use. Testing of the medicine found it is safe to use past the expiration date.*

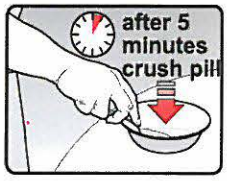
Appendix C

Doxycycline EUA Fact Sheet for Recipients - Home Preparation Instructions for Children or Adults Who Cannot Swallow Pills

Doxycycline EUA Fact Sheet for Recipients—
Home Preparation Instructions for Children or Adults Who Cannot Swallow Pills

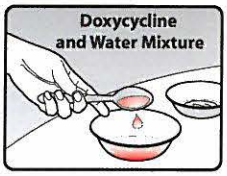
1. Put 1 doxycycline pill (100 mg) in a small bowl.
2. Add 4 full teaspoons (1 teaspoon=5 cc; 4 teaspoons=20 cc) of water to the same bowl.
3. Let the pill soak in the water for 5 minutes so it will be soft.
4. Use the back of a metal teaspoon to crush the pill in the water. Crush the pill until you can't see any pieces.
5. Stir the pill and water to mix it well. Find your child's weight on the left side of the chart below.
6. Next, look on the right side of the chart below to find the amount of doxycycline and water mixture to mix with food. The chart shows you the amount to give your child for 1 dose. *For a ½ teaspoon dose, fill the metal teaspoon half way. It is better to give a little more of the medicine than not enough.*

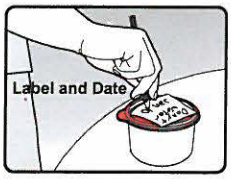




Child's Weight	Amount of Doxycycline and Water Mixture	Teaspoons
12 pounds or less	½ teaspoon	
13 to 25 pounds	1 teaspoon	
26 to 38 pounds	1½ teaspoons	
39 to 50 pounds	2 teaspoons	
51 to 63 pounds	2½ teaspoons	
64 to 75 pounds	3 teaspoons	
76 to 88 pounds	3½ teaspoons	
89 pounds or more and adults	Use the entire mixture	Entire Mixture

7. Add the recommended amount of the doxycycline and water mixture from the chart above to a second bowl. **NOTE:** for adults and children 89 pounds and more, use the entire mixture.
8. Add 3 teaspoons of milk **or** chocolate milk **or** chocolate pudding **or** apple juice to the second bowl to make it taste better. If you use apple juice, also add 4 teaspoons of sugar to the second bowl.
9. Stir well. Give all of the doxycycline, water, and food mixture in the second bowl. This is one dose.
10. Each child or adult should take 1 dose in the morning and 1 dose at night each day.
11. If you have enough leftover doxycycline and water mixture for another dose, keep it for the next dose. The doxycycline and water mixture can be stored in a covered bowl or cup at room temperature for up to 24 hours. Label and date the container. Keep the mixture in a safe place, out of the reach of children and pets.
12. Throw away any unused mixture after 24 hours and make a new doxycycline and water mixture before the next dose.





CONTACTS: If you have any questions, please contact XXXXX (placeholder for stakeholder's specific contact information).

Appendix D

In an Emergency: How to Prepare Doxycycline for Children and Adults Who Cannot Swallow Pills

In an Emergency:

How to Prepare Doxycycline for Children and Adults Who Cannot Swallow Pills

Mixing Doxycycline Hyclate 100mg Tablets with Food

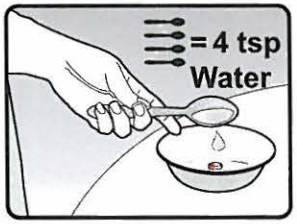
Once you have been notified by your federal, state or local authorities that you need to take doxycycline for a public health emergency, it may be necessary to prepare *emergency* doses of doxycycline for children and adults who cannot swallow pills.

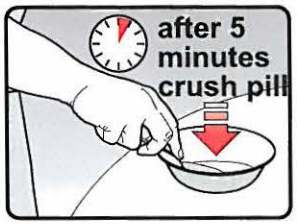
June 2008
Prepared by the U.S. Food and Drug Administration

1 Supplies You Will Need

You will need these items to make doses of doxycycline for adults and children who cannot swallow pills:

- 1 doxycycline pill (100 mg) *(Do not take doxycycline if you are allergic to tetracyclines)*
- a metal teaspoon
- 2 small bowls
- Water
- one of these foods or drinks to hide the bitter taste of crushed doxycycline:
  - milk or chocolate milk
  - chocolate pudding
  - apple juice and sugar





2 Crushing the Pill and Mixing with Water

1. Put 1 doxycycline pill in a small bowl.
2. Add 4 full teaspoons of water to the same bowl.
3. Let the pill soak in the water for 5 minutes so it will be soft.
4. Use the back of a metal teaspoon to crush the pill in the water. Crush the pill until no visible pieces remain.
5. Stir the pill and water so it is well mixed.

You have now made the Doxycycline and Water Mixture.

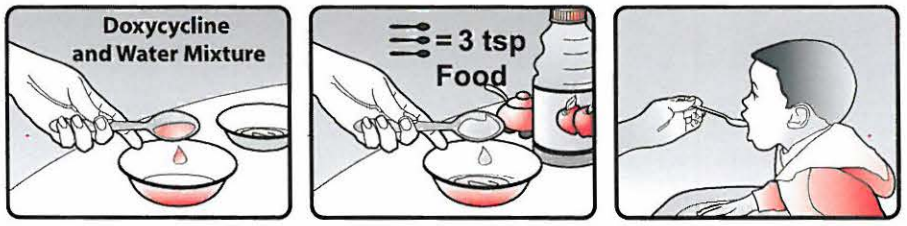
Child's weight: _____

3 Adding Food to the Doxycycline and Water Mixture to Make It Taste Better

1. Weigh your child.
2. Find your child's weight on the left side of the chart below.
3. Next, look on the right side of the chart to find the amount of the Doxycycline and Water Mixture to mix with food. The chart shows you the amount to give your child for 1 dose. *(For a ½ teaspoon dose, fill the metal teaspoon half way. It is better to give a little more of the medicine than not enough).*

Child's Weight	Amount of Doxycycline and Water Mixture	Teaspoons
12 pounds or less	½ teaspoon	
13 to 25 pounds	1 teaspoon	
26 to 38 pounds	1½ teaspoons	
39 to 50 pounds	2 teaspoons	
51 to 63 pounds	2½ teaspoons	
64 to 75 pounds	3 teaspoons	
76 to 88 pounds	3½ teaspoons	
89 pounds or more and adults	Use the entire mixture	Entire Mixture

4. Add the right amount of the Doxycycline and Water Mixture from the chart above to the second bowl. For adults and children 89 pounds and more, use the entire mixture.
5. Add 3 teaspoons of milk **or** chocolate milk **or** chocolate pudding **or** apple juice to the second bowl. If you use apple juice, also add 4 teaspoons of sugar to the second bowl.
   - Stir well.



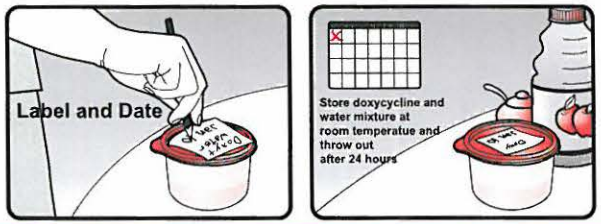
6. Go to Step 4 for dosing.

4 Dosing the Doxycycline and Water Mixture Mixed With Food

1. Give all of the Doxycycline and Water and food mixture in the second bowl. This is one dose.
2. **Each child or adult should take 1 dose in the morning and 1 dose at night each day.**

5 Storing the Doxycycline and Water Mixture (If There Is Enough for Another Dose)

- **If you have enough leftover doxycycline and water mixture for another dose, you can keep it for the next dose.**
- The doxycycline and water mixture can be stored in a covered bowl or cup. Label and date.
- Keep the mixture in a safe place out of the reach of children.
- Store the Doxycycline and Water Mixture at room temperature for up to 24 hours.
- Throw away any unused mixture after 24 hours and make a new Doxycycline and Water Mixture before the next dose.



Do not take doxycycline if you have an allergy to tetracyclines

Get emergency help if you have any signs of an allergic reaction including hives, difficulty breathing, or swelling of your face, lips, tongue or throat.

Doxycycline may cause diarrhea, skin reaction to the sun, loss of appetite, nausea and vomiting. Birth control pills may not work as well if you take doxycycline.

MedWatch

Report any reaction to the medication to MedWatch at www.fda.gov/medwatch or 1-800-FDA-1088

Appendix E

Doxycycline EUA Fact Sheet for Health Care Professionals

Doxycycline EUA Fact Sheet for Health Care Professionals

Dear Health Care Professional: If you have received this Fact Sheet, an event has occurred that calls for the emergency use of doxycycline. 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. Doxycycline is FDA-approved to reduce the incidence or progression of disease following exposure to aerosolized *B. anthracis*, including post-exposure prophylaxis (PEP) of inhalational anthrax. However, certain uses provided for under this EUA are not FDA-approved and would not be consistent with relevant statutes and regulations under normal circumstances, e.g., distribution without a prescription.[1] For more information on this EUA, see FDA's web page at www.fda.gov.

What are the symptoms of anthrax?

First symptoms are cold-like or flu-like symptoms, e.g., sore throat, mild fever, myalgias. Later symptoms are cough, chest discomfort, shortness of breath, fatigue, and myalgias. Symptoms usually occur within 7 days of inhaling anthrax germs, but can take up to 42 days to appear.

Who cannot take doxycycline?

Anyone allergic to doxycycline, or another tetracycline, must ***not*** be given doxycycline.

What is the usual dose of doxycycline?

- The full PEP regimen is usually 60 days. Patients may not have received a full PEP regimen in response to this anthrax incident; public officials will announce where and when they can get the rest of the medicine.
- Adults (≥18) who can swallow tablets or children who weigh 40 kg (89 lbs) or more and can swallow tablets should receive one tablet (100 mg) by mouth in the morning and one tablet in the evening.
- Adults who cannot swallow tablets and children under 40 kg (89 lbs) should follow the instructions on how to prepare doxycycline for children and adults who cannot swallow pills, which tell individuals how to crush tablets and prepare the dose (www.fda.gov/doxyprepare). These instructions are appropriate for tablet formulations, but not for capsules.
- Children weighing less than 14 kg (30 lbs) should receive priority for using doxycycline oral suspension, dosed by weight (see table below).
  - For the doxycycline powder for oral suspension (5 mg/mL) — Mix the doxycycline with water before you give the medication to the recipient, write the dose on the bottle, and mark the dose with a line on the syringe.
  - Tell the recipient to shake well the doxycycline oral suspension before each use.

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 60mL 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	

Recipients taking magnesium, aluminum antacids, sucralfate, Videx (didanosine), or products that contain calcium, iron, or zinc should take doxycycline at least 2 hours before, or 2 hours after, taking any of these other products.

[1] **For more information** about the benefits and risks of doxycycline, please see the FDA-approved package insert for doxycycline available at www.dailymed.nlm.nih.gov.

Tell patients to *STOP* taking the medicine and get medical help immediately if they get any of the following possible serious side effects:

- Serious allergic/hypersensitivity reactions sometimes fatal (anaphylactic and/or rashes)
- Severe stomach cramps with high fever or bloody diarrhea (antibiotic associated diarrhea and pseudomembranous colitis)
- Yellowing of the eyes or skin or dark-colored urine (liver failure)
- Pain when swallowing (esophageal ulcers). Tell recipients to drink a glass of water after taking doxycycline.
- Unusual bleeding or bruising
- Severe headaches, dizziness, or double vision

But tell patients to keep taking the medicine if they have:

- Mild nausea or vomiting
- Upset stomach, loose stools
- Vaginal yeast infection

What are other possible serious side effects of doxycycline?

- Doxycycline is safe to take during pregnancy, but if taken during the last half of pregnancy or when nursing, children may later have teeth problems (yellow-gray-brown permanent color changes and poor enamel formation); this may also occur in children under 8 years old who take doxycycline
- Slowed bone growth in children who take doxycycline
- Photosensitivity
- Birth control pills may not work as well. Recommend use of another form of birth control while taking doxycycline.

Risk-Benefit Statement

The significant known risks are those associated with the side effects described above. The expected benefits are prevention of disease, including death, associated with anthrax exposure. 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.

Available Alternatives

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.

Reporting Adverse Event or Medication Errors

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.

Give recipients the "Doxycycline EUA Fact Sheet for Recipients"

CONTACTS

If you have any questions, please contact XXXXX (*placeholder for stakeholder's specific contact information*).