

ILLINOIS DEPARTMENT OF PUBLIC HEALTH  
OFFICE OF HEALTH PROTECTION  
DIVISION OF INFECTIOUS DISEASES

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GUIDELINES FOR ACCIDENTAL  
LABORATORY EXPOSURE TO BRUCELLOSIS

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SEVENTH FLOOR  
CHICAGO, ILLINOIS 60603  
312-814-4846

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## INTRODUCTION

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Since 1986, fewer than 150 cases of brucellosis have been reported annually in the United States; however, brucellosis is the most commonly reported laboratory-acquired infection. *Brucella*, the causative agent of brucellosis, is easily aerosolized and has the potential to cause acute and chronic illness. Human illness associated with the vaccine strain RB51 has been documented from inadvertent needle sticks or inoculation of conjunctiva or open wounds with RB51.

Definitions for laboratory exposure risk to *Brucella* spp. and recommendations for post-exposure prophylaxis (PEP) have been developed by the U.S. Centers for Disease Control and Prevention (CDC). Brucellosis has occurred following laboratory accidents, such as dropped culture plates or ruptured centrifuge tubes. Laboratory procedures that result in the generation of aerosols containing *Brucella* can transmit the organism and result in infection. People not directly working with a culture isolate may still be exposed to aerosols generated during a procedure if they are in close proximity to the culture while it is being manipulated. For these reasons, CDC recommends that *Brucella* isolates are manipulated in class II or higher biological safety cabinets.

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## WHEN SUSPECTED EXPOSURE OCCURS

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When exposure occurs:

1. Conduct risk assessment, determine dates of exposure and determine the risk.
2. Notify infection control, occupational health or designees.
3. Notify local health authorities as soon as possible.
4. Perform follow-up testing and surveillance as described below.
5. Refer exposed individuals to occupational health for prophylaxis or treatment.

The risk levels are:

High-risk exposure:

- Work conducted on an open bench (i.e. outside of BSL3 conditions) with an opened culture plate containing a *Brucella* isolate, or in close proximity to such work (e.g. across an open bench top, within arm's length, or within five feet).
- Individuals present in the laboratory during a *Brucella* aerosol-generating event should be considered as having a high-risk exposure.
- The risk for accidental exposure is highest for procedures or manipulations that occur outside the biological safety cabinet and that have the potential for creating aerosols or splashes; examples of such procedures include pipetting, centrifuging, grinding, blending, shaking, mixing, sonicating, and opening containers of infectious materials.

Low-risk exposures - other workers present in the lab, but who do not have high-risk exposures:

- *Brucella*-exposed worker - any microbiology laboratory worker present in the microbiology laboratory during work-up and identification of a *Brucella* isolate, from the time growth was first recognized on a culture plate until all culture isolates were destroyed or removed from the lab.

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## LOCAL HEALTH AUTHORITY NOTIFICATION

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Notification will be as follows:

- Laboratory will notify local health authority by phone or fax as soon as possible when an exposure is known to have occurred.
- Local health authority will notify the Illinois Department of Public Health Communicable Disease section.
- The Department Communicable Disease section will notify the Department Laboratory.
- After notification, laboratory will work directly with the Department laboratory to coordinate sequential serological testing at CDC.

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## LABORATORY TESTING

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Serological testing is recommended as follows:

- Sequential serologic testing on all *Brucella*-exposed workers at baseline, two and four weeks post exposure. These samples should be batched and sent together at four weeks to the Department's laboratory. (Hospital will coordinate with the laboratory).
- Sequential serologic testing on all *Brucella*-exposed workers at six and 24 weeks post exposure. These samples should be batched and sent at 24 weeks to Public Health laboratory (Hospital will coordinate with the Department's Laboratory).
- Results will be sent to submitter and the Department's Communicable Disease section.

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## TREATMENT

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Referral to occupational health for PEP for *Brucella*-exposed workers with high-risk exposures:

- Doxycycline 100 mg twice daily and rifampin 600 mg once daily for three weeks.
- Consider trimethoprim-sulfamethoxazole for contraindications to doxycycline.

- Pregnant workers with high-risk exposures should consider PEP in consultation with their obstetricians.

Refer to occupational health for discussion regarding PEP with *Brucella*-exposed workers with only low-risk exposures.

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## POST EXPOSURE SURVEILLANCE

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Arrange with occupational health active surveillance (e.g. weekly) for development of febrile illness or other signs and symptoms of brucellosis among all *Brucella*-exposed workers (see table 1).

Table 1: Post-Exposure Surveillance

SIGN/SYMPTOM	YES	NO	UNSURE	IF YES, DATE OF ONSET
Fever (Temp > 100.4°F)				
Chills				
Sweating				
Severe or persistent headache				
Joint pains				
Muscle pains				
Fatigue				
Unintended weight loss				

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## INFORMATION SHEET FOR LABORATORY EXPOSURE

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**What is brucellosis?** Brucellosis is a bacterial infection caused by pathogenic species of the genus *Brucella*, including *melitensis*, *abortus*, *suis* and *canis*. These bacteria are primarily passed among animals, such as sheep, goats, cattle, deer, elk, pigs, and dogs. Typically, humans become infected by coming in contact with infected animals or by eating or drinking contaminated pasteurized milk or other contaminated dairy products, such as cheese, when these products are produced in a country which has endemic *Brucella* in livestock.

In humans, brucellosis can cause a range of symptoms that are similar to the flu and may include fever, sweats, headaches, back pain, and physical weakness. Brucellosis can be a chronic disease, causing recurrent fevers, chronic joint pain, and fatigue. Although rare, severe infections and death may occur. Brucellosis is uncommon in the United States, where 100 to 200 cases are reported each year, but brucellosis can be common in countries that have significant amounts of disease in animals.

**How is brucellosis transmitted?** Humans are generally infected in one of three ways: eating or drinking unpasteurized dairy products that contain *Brucella*, having the bacteria enter the body through skin wounds, or inhaling aerosolized organisms. The most common way to be infected is by eating or drinking contaminated milk products. Inhalation of *Brucella* organisms is not a common route of infection, but it can be a significant hazard for people working in laboratories where the organism is cultured. Direct person-to-person spread of brucellosis is extremely rare.

**Can brucellosis be transmitted in the laboratory?** Brucellosis is the most commonly reported laboratory-acquired infection. More than 400 cases and five deaths have been reported in the literature. Brucellosis has occurred following laboratory accidents, such as dropped culture plates or ruptured centrifuge tubes. It also has been reported following routine laboratory work outside of biological safety cabinets, and sniffing of culture plates has been implicated in some laboratory acquired cases. Laboratory procedures that result in the generation of aerosols containing *Brucella* can transmit the organism and result in infection. People not directly working with a culture isolate may still be exposed to aerosols generated during a procedure if they are in close proximity to the culture while it is being manipulated. For these reasons, the Centers for Disease Control and Prevention recommends that *Brucella* isolates are manipulated in class II or higher biological safety cabinets.

**What are the signs and symptoms of brucellosis?** Infection with *Brucella* can cause intermittent and recurring fever, chills, malaise and sweats. Joint and lower back pain, headaches, depression, anorexia and fatigue are also common. Without appropriate treatment, brucellosis may result in localized abscesses in any organ and can last from several weeks to several years. Brucellosis is rarely fatal. In an infected person, clinical signs and symptoms of brucellosis will usually develop in two to four weeks following exposure to the organism. However, the incubation period can range from a few days to six months.

**How is brucellosis diagnosed?** For people with active infection, brucellosis is diagnosed by culturing *Brucella* organisms from samples of blood or bone marrow. Serology also can be used to detect antibodies against the bacteria. This method is often used to detect sub-clinical or early infections before the development of clinical signs. To evaluate antibody levels, a minimum of two blood samples should be collected two weeks apart. Following a laboratory exposure to a *Brucella* culture, antibody levels are assessed serially for six months.

**Can prophylactic treatment be used to prevent an infection?** Prophylactic antibiotics are recommended for people who have participated in activities at high risk for transmitting brucellosis, such as following a laboratory exposure. In several studies prophylaxis has been effective in preventing the development of clinical disease following laboratory exposure to *Brucella* organisms. Oral doxycycline (100 mg twice daily) and rifampin (600 mg once daily) are used in combination for three to six weeks to prevent reoccurring infection. In people unable to take this medication, other antibiotics may be prescribed. Women who are pregnant or breast-feeding should consider post-exposure prophylaxis in consultation with their health care provider.

**How is disease due to brucellosis treated?** The same antibiotics that are used to prevent brucellosis are used to treat people with clinical disease, but treatment may be for a longer duration. In patients with severe infections or complications, antibiotics therapy may be continued for months and surgical therapy may be required.

**If I may have been exposed to *Brucella* organisms, should I watch for signs of brucellosis?** Yes, you should watch for signs of brucellosis for six months following your exposure. If you experience a fever, with or without any of the other symptoms of brucellosis (chills, malaise, sweats, joint and lower back pain, headaches, depression, anorexia and fatigue), for an unknown reason during that time, contact your employee health office or your health care provider. Be sure to inform your physician that you were exposed to *Brucella* organisms, so that he or she can consider brucellosis when making a diagnosis.

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## RECOMMENDATIONS FOR SAFE LABORATORY PRACTICES FOR *BRUCELLA* SPP.

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- When brucellosis is suspected, clinicians should note “suspect or rule out brucellosis” on the laboratory submission.
- Review laboratory containment methods and microbiological procedures to ensure compliance with recommendations in the Biosafety in Microbiological and Biomedical Laboratories (BMBL), Fifth edition.
- Use primary barriers: use safety centrifuge cups, personal protective equipment, and class II or higher biological safety cabinets (BSCs) for procedures with a high likelihood of producing droplet splashes or aerosols.

- Use secondary barriers: restrict access to the laboratory when work is being performed and maintain the integrity of the laboratory's air handling system by keeping external doors and windows closed.
- Perform all procedures on unidentified isolates carefully to minimize the creation of splashes or aerosols.
- Prohibit sniffing of opened culture plates to assist in the identification of isolates.
- Manipulate isolates of small ram-negative or ram-variable rods within a BSC.

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## SUBMISSION OF SERUM FOR BRUCELLA SEROLOGY

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1. Acute- and convalescent-phase serum specimens should be batched together unless otherwise indicated (1<sup>st</sup> batch: 0-, 2-, and 4-week specimens; 2<sup>nd</sup> batch: 6- and 24-week specimens).
2. Please send serum, not whole blood.
3. Serum should be sent in Sarstedt 2 ml micro tube with an O-ring in the lid (ref #72.694.006). The O-ring helps to prevent leaking or drying of sample. These tubes may be purchased from commercial vendors.
4. Serum drawn at zero and two weeks post exposure should be frozen. After obtaining the four-week specimen, ship all specimens (0, 2, and 4 weeks) on ice packs to the IDPH laboratory. Similarly, the six-week specimen should be frozen until the 24-week specimen is obtained, and then they should be sent together on ice packs to the Department laboratory.
5. A separate CDC Form 50.34 should be filled out for each specimen from each patient. A line list should not be used, since the CDC will not issue individual reports from submissions made with a line list.
6. When filling out Form 50.34, be sure to indicate the following: test requested (*Brucella* serology), submitter's name and address, type of specimen (including its week of collection). Include patient information (name, date of birth, sex).
7. Ship specimens overnight to:
 

Illinois Department of Public Health Chicago Laboratory  
Bacteriology Unit  
2121 W. Taylor St.  
Chicago, IL 60612

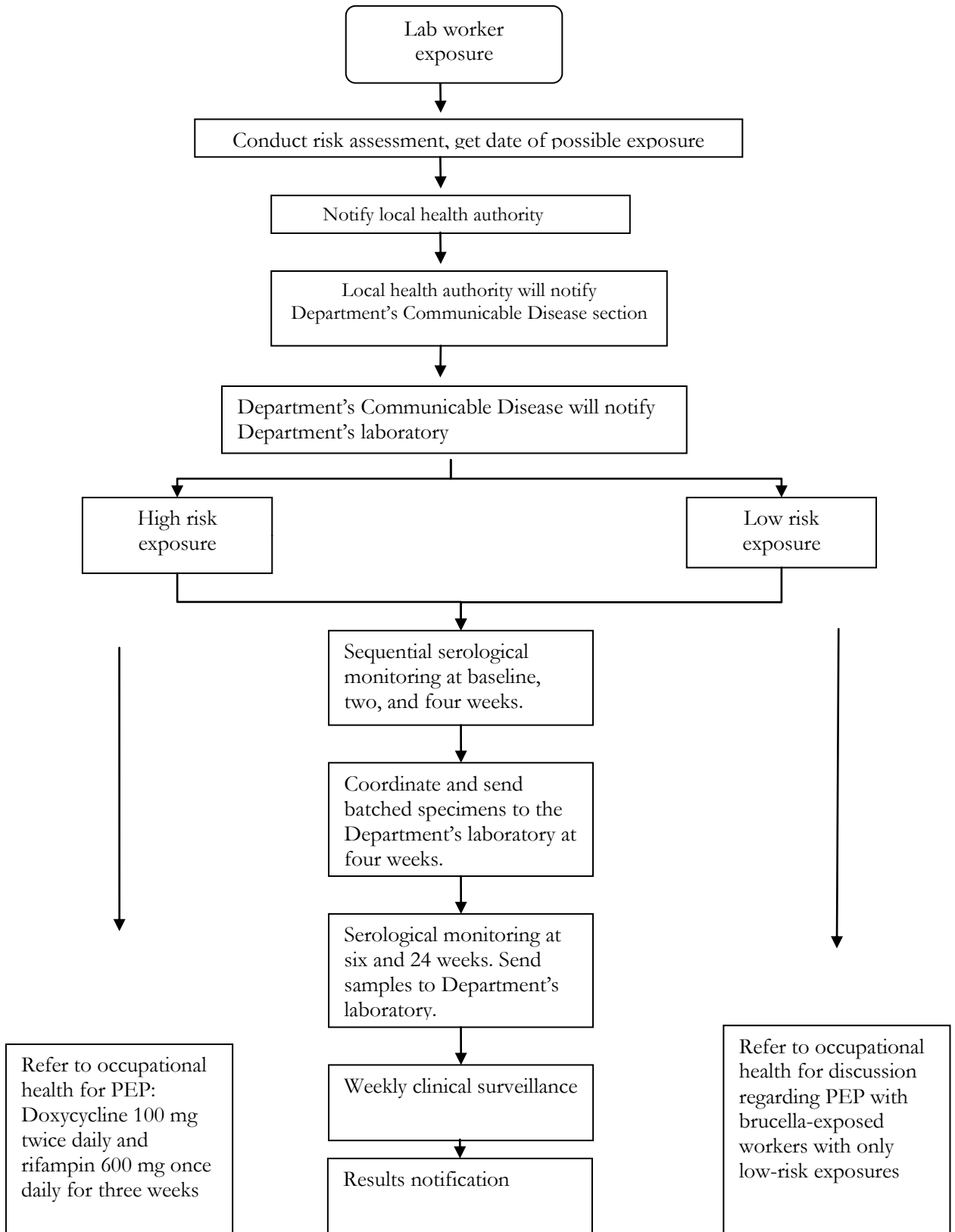
Do not ship on a Friday or before a holiday. The Department's Laboratory will forward the specimens to the CDC for testing.

8. CDC Form 50.34 should accompany the specimens; the form is included.
9. When filling out the form, the more complete the form the better. The minimal information should include the following: test requested (*Brucella* serology), submitter's name and address, patient's name/sex/ DOB, type of specimen, collection dates, date of onset of symptoms, and history of travel, water or animal exposures.
10. Please contact:
 

Roman Golash  
Bacteriology Unit Supervisor

Illinois Department of Public Health Chicago Laboratory  
312-793-1571 or 312-793-4747





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## ACRONYMS

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BMBL: Biosafety in Microbiological and Biomedical Laboratories

BSCs: Biological safety cabinets

BSL: Bio-safety level

CD: Communicable Disease

CDC: U.S. Centers for Disease Control and Prevention

DID: Division of Infectious Diseases

PEP: Post-exposure prophylaxis

RB51: Attenuated vaccine strain