Update: Potential Exposures to Attenuated Vaccine Strain *Brucella abortus* RB51 During a Laboratory Proficiency Test—United States and Canada, 2007

IN NOVEMBER 2007, NEW YORK STATE DEPARTMENT of Health (NYSDOH) officials notified CDC of potential exposures to attenuated vaccine strain *Brucella abortus* RB51 (RB51) in multiple clinical laboratories that participated in a Laboratory Preparedness Survey (LPS) proficiency test.1 NYSDOH conducted a survey of participating laboratories and identified 17 laboratories that reported handling the RB51 sample in a manner placing lab workers at potential risk for exposure. Subsequently, CDC recommended that public health officials conduct a review of biosafety practices at all LPS-participating laboratories to identify any additional RB51 exposures. This report summarizes the results of investigations in 36 states, two cities, one county, and the District of Columbia. As of January 14, 2008, follow-up by public health officials with LPS-participating laboratories throughout the United States identified a total of 916 laboratories with potential RB51 exposure. The results highlight the need for routine adherence to recommended biosafety practices when working with infectious organisms, particularly during widespread infectious-disease events, including bioterrorism attacks.

LPS is a voluntary proficiency-testing survey developed in partnership with the College of American Pathologists, the Association of Public Health Laboratories, and CDC. The survey is designed to simulate a scenario in which presence of a bioterrorism agent is suspected in a clinical laboratory and to exercise Laboratory Response Network (LRN) sentinel laboratory protocols6 for “rule-out” or “referral” of potential bioterrorism agents. RB51 is an attenuated vaccine strain of *B. abortus* used to vaccinate cattle against brucellosis; human illness is known to have resulted from RB51 vaccine–related exposures.2 During October-November 2007, an LPS kit containing simulated or modified strains (i.e., attenuated) of pathogens identified as potential bioterrorism agents, including RB51 for the first time, was distributed to 1,316 laboratories throughout the United States and Canada. The LPS kit included written instructions stating that all samples should be handled inside a Class II biological safety cabinet (BSC) with biosafety level 3 (BSL-3) primary barriers and safety equipment. The extent of identification and degree of manipulation of the LPS samples within each laboratory was determined by the laboratory’s analytic capabilities. Basic laboratory procedures performed included preparing specimens for culture by reconstitution and inoculation onto appropriate media, preparing and performing a Gram stain, and possibly performing biochemical spot/slide tests (e.g., oxidase, indole, or catalase).

On November 27, 2007, CDC was notified by NYSDOH officials of potential RB51 exposures during the LPS exercise. The exposures reported initially occurred after an RB51 specimen was mislabeled as a routine patient specimen and submitted by an LPS-participating laboratory to the New York state bacteriology laboratory. As a result, routine benchtop procedures were used by NYSDOH laboratory personnel to handle the isolate, resulting in 24 laboratory workers potentially exposed to RB51. Further investigation by NYSDOH determined that 16 LPS-participating laboratories in the state had not handled the RB51 samples properly, despite correct labeling of the samples. CDC then recommended that all state health departments review biosafety practices used by LPS-participating laboratories in their states while working with the RB51 sample to identify any additional persons who were potentially exposed. Canadian health officials also were notified of the event because Canadian laboratories participated in LPS. To facilitate this review, CDC provided a set of questions identifying the types of manipulations and widespread aerosol-generating procedures that might result in exposure.

Risk-assessment definitions were developed by CDC, categorizing the level of exposure risk (e.g., high, low, or none) based on the specific laboratory practices performed and the proximity of workers to any manipulations or aerosol-generating procedures. RB51 exposure was deemed to have occurred if the specimen was handled in a manner other than the established recommended practice (i.e., working inside a Class II BSC using BSL-3 primary barriers and safety equipment).3,4 Persons with high-risk exposure were defined as those who either (1) performed a potentially high-exposure practice (e.g., sniffing bacteriologic cultures), (2) were within 5 feet of any manipulation of RB51 on an open bench, or (3) were present in the laboratory during a widespread aerosol-generating event (e.g., vortexing) involving RB51. Persons with low-risk exposure were defined as those present in the laboratory when a high-risk exposure occurred. Postexposure prophylaxis (PEP) was recommended only for persons identified as having high-risk exposures but also was offered to those categorized as having low-risk exposures.
To assess the magnitude of this event at the national level, on December 11, CDC requested information from state health departments regarding the number of LPS-participating laboratories in which exposures occurred, the number of persons categorized with high- and low-risk exposures, and the number of persons recommended to receive PEP. States also were asked whether any illnesses that occurred in potentially exposed persons were consistent with brucellosis symptoms.

Voluntary reports from 36 states, two cities, one county, and the District of Columbia identified 254 laboratories that had handled the RB51 specimen under conditions that resulted in potential exposures. These areas reported 916 laboratory workers with exposure to RB51, including 679 (74%) with high-risk exposures and 237 (26%) with low-risk exposures. Data regarding the percentage of persons who received PEP were not available. As of January 14, no cases of brucellosis related to these exposures had been reported to CDC.

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CDC Editorial Note: Laboratory-proficiency testing is an accepted assessment tool, not unique to bioterrorism preparedness, designed to measure performance and improve the diagnostic and biosafety expertise of participating laboratories. Proficiency-testing samples containing nonattenuated pathogenic agents such as Mycobacterium tuberculosis and other organisms requiring biosafety precautions are sent routinely from the College of American Pathologists to approximately 1,000 laboratories. In 2006, LPS was revised to include attenuated organisms such as RB51 that more closely mimic those on the CDC list of category A, B, or C bioterrorism agents† after participating LRN sentinel laboratories indicated a need for a more realistic exercise. Because some of the attenuated vaccine strains can cause infection if not handled appropriately, the LPS kit shipped to participating laboratories included written instructions stating that all samples should be handled inside a Class II BSC with BSL-3 primary barriers and safety equipment. All participating laboratories confirmed that they had a functioning Class II BSC.

Clinical laboratories routinely encounter hazardous organisms (e.g., Neisseria meningitidis or Mycobacterium tuberculosis) that require biosafety precautions. Brucellosis is the most commonly reported laboratory-acquired bacterial infection, is easily aerosolized, and has the potential to cause acute and chronic illness.5-7 Human illness associated with the vaccine strain RB51 has been documented from inadvertent needle sticks or inoculation of conjunctiva or open wounds with RB51.2,7 Definitions for laboratory exposure risk to Brucella spp. and recommendations for PEP have been developed by CDC† and were applied to the laboratory-acquired brucellosis cases that occurred in Indiana and Minnesota in 2006.8

The numerous exposures identified during this LPS highlights the importance of adhering to biosafety practices when handling samples during proficiency testing and when handling specimens routinely entering clinical laboratories for identification. Biosafety practices minimize the risk for exposure; however inadvertent exposures still can occur when infectious agents enter the laboratory. All clinical laboratories that handle and test unknown specimens should establish and adhere to written diagnostic test protocols (e.g., American Society of Microbiology guidelines for avian influenza or sentinel laboratory guidelines to rule out suspected agents of bioterrorism8). These protocols should be incorporated directly into routine bench procedures and should indicate laboratory findings that signal the need for increased biosafety precautions.9

One lesson from this event is the potential vulnerability of laboratorians during large-scale events (e.g., bioterror or widespread illness) involving highly lethal infectious agents, even when the agent is recognized. During such events, additional recommendations for higher-level biosafety practices might be needed. When such events occur, exposures to highly lethal agents can be minimized by rapid communication among laboratories and by rapid implementation of situation-specific recommendations.8

Because CDC category A, B, or C bioterrorism agents are not often associated with naturally occurring disease, laboratory professionals might be less familiar with these agents than more commonly identified organisms. Laboratory readiness should include annual review of biosafety protocols with particular attention to training laboratory personnel in the characteristics of particular agents and the biosafety practices recommended for their handling and testing. For example, in routine practice, observance of small, gram-negative coccobacilli on Gram stain should alert laboratorians to the potential presence of Brucella spp. or Francisella tularensis, especially when a patient has symptoms compatible with illness caused by those organisms. Clinicians should alert laboratory personnel when specimens are submitted from patients with clinical findings suggestive of infectious agents that pose a threat to laboratorians during handling.

Exercises such as LPS designed to test skills and procedures in laboratories are an important part of overall preparedness. LPS is one of the few exercises specifically designed to test laboratory response to bioterrorism agents. CDC is continuing to review the event described in this report to further understand the factors that led to the variations in biosafety practices during this laboratory proficiency test. This review will provide additional insights that should improve proficiency-testing programs and biosafety training.

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Interim Recommendations for the Use of Haemophilus influenzae Type b (Hib) Conjugate Vaccines Related to the Recall of Certain Lots of Hib-Containing Vaccines (PedvaxHIB® and Comvax®)

ON DECEMBER 19, THIS REPORT WAS posted as an MMWR Dispatch on the MMWR website (http://www.cdc.gov/mmwr).

On December 13, 2007, Merck & Co., Inc. (West Point, Pennsylvania) announced a voluntary recall of certain lots of two Haemophilus influenzae type b (Hib) conjugate vaccines, PedvaxHIB® (monovalent Hib vaccine) and Comvax® (Hib/hepatitis B vaccine). Providers should return unused vaccine from these recalled lots using procedures outlined on the Merck website at http://www.merckvaccines.com/PCHRecall.pdf. Additional information regarding the affected lots is available online from the Food and Drug Administration (FDA) at http://www.fda.gov/consumer/updates/hib121307.html. Merck has suspended production of its Hib conjugate vaccines and does not expect to resume distribution of these vaccines until the fourth quarter of 2008. The recall of PedvaxHIB and Comvax and suspension of production are expected to result in short-term disruption to the Hib vaccine supply in the United States.

Merck issued this voluntary recall as a precautionary measure because the company cannot assure the sterility of equipment used during manufacture of these lots. However, the potency of the vaccine in the recalled lots was not affected, and Merck reported that no contamination of vaccine has been detected. Therefore, children who received Hib conjugate vaccine from the recalled lots do not need revaccination or any special follow-up.

Two other Hib conjugate vaccines manufactured by Sanofi Pasteur (Swiftwater, Pennsylvania) and currently licensed and available for use in the United States, ActHIB® (monovalent Hib vaccine) and TriHIBit® (diphtheria and tetanus toxoids and acellular pertussis [DTaP]/Hib vaccine), are unaffected by the recall. However, Sanofi Pasteur likely will not be able to immediately provide adequate Hib vaccine to vaccinate fully all children for whom the vaccine is recommended.

The recommended vaccination schedule for all available Hib-containing vaccines consists of a primary series (consisting of 2 or 3 doses, depending on the formulation) administered beginning at age 2 months and a booster dose at age 12-15 months. Because of the short-term reduction in available doses of Hib-containing vaccines, CDC, in consultation with the Advisory Committee on Immunization Practices (ACIP), the American Academy of Family Physicians, and the American Academy of Pediatrics, recommends that providers temporarily defer administering the routine Hib vaccine booster dose administered at age 12-15 months except to children in specific groups at high risk, which are described in this report. Providers should register and track children for whom the booster dose is deferred to facilitate recalling them for vaccination when supply improves.

Sustained high levels of coverage with Hib conjugate vaccine have resulted in a substantial decline in the incidence of Hib disease in the United States. In 2006, the incidence of Hib disease in children aged <5 years was 0.21 per 100,000, representing a greater than 99% reduction in disease compared with incidence in the prevaccine era. Population immunity is