no significant dust is generated in these research laboratories, the use of pre-filters in the exhaust is generally not necessary. If pre-filters are placed in the HEPA filter housing, if and when they load, the same decontamination process that is used for the HEPA filter housing in the animal biosafety facility must be used to change them. Again, the problems and costs associated with changing these filters far outweigh the benefit of providing them.

Biosafety Tips

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Biosafety Tips brings you practical approaches to biosafety or "news you can use." If you are looking for a useful and sensible solution to a biocontainment problem or perhaps a reference to help convince a skeptical researcher of the need for caution, this is the place to look. In this column I will share some biosafety insights for managing a variety of workplace situations. I welcome feedback or suggestions for future topics. Please e-mail any comments or suggestions to karen_byers@dfci.harvard.edu or to Co-Editor Barbara Johnson at barbara_johnson@verizon.net.

Is the Community at Risk to Exposure from Microbes in the Lab?

Publications past and present indicate that laboratory biosafety containment practices work well to protect the outside community from exposure to the human pathogens. Lapses in research containment practices are extremely rare, and the accounts are guideposts for biosafety practice. In identified cases, the incidents have been investigated and reported to prevent re-occurrence. This column will review the few community exposures that have occurred, the associated lapses in proper biosafety containment practices, and the lessons we've learned from them. The deliberate criminal acts of 2001, in which the mailing of anthrax spores caused 5 deaths and 17 infections, are being excluded because this tragic biosecurity lapse did not originate from authorized laboratory research (Federal Bureau of Investigation). The same exclusion applies to the contamination of restaurant salad bars by a religious commune in Oregon. This resulted in 751 cases of Salmonellosis; an investigation identified the same strain of *S. typhimurium* in a laboratory at the commune (Torok et al., 1997).

Failure to Limit Research with High-consequence Pathogens to Appropriate Laboratory Facilities

Smallpox was eradicated from the world population in 1977. Unfortunately, in 1978 two more cases occurred in Birmingham, England. The index case was a photographer who became infected by aerosol air leaked into her office from an exhaust duct. The photographer survived; however, the secondary infection of her mother resulted in a fatality. The smallpox laboratory director committed suicide after learning about the two infections (Collins, 1999; Heymann et al., 2004).

Failure to Decontaminate Vaccine Before Disposal

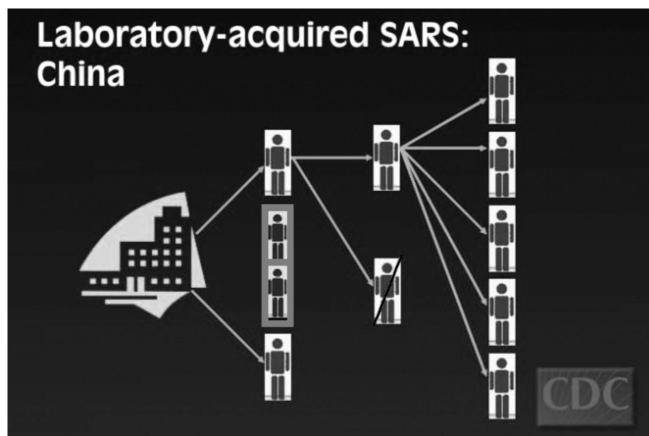
In 2000, eight children in Vladivostock, Russia became infected while playing with discarded vials of smallpox vaccine. The community initially feared that the children had been exposed to smallpox, since they were not aware that the live virus in smallpox vaccine is vaccinia (ProMED-mail, 2000).

Inadequate Decontamination of Materials Removed from the Laboratory

Six cases of Q fever occurred in commercial laundry staff that cleaned linens and uniforms from a laboratory working with *C. burnetii* (U.S. Department of Public Health and Human Services et al., 1999). It is not clear whether that number also includes the infection of a laundry worker in 1948 and a case in a household contact of a laboratory worker in 1950 (Collins et al., 1999).

In 2004, nine cases of SARS occurred in Beijing, China. The two index cases were identified as graduate students at the University of Virology who worked in a BSL-2 laboratory with samples that were inactivated and then removed from the BSL-3 SARS lab. Unfortunately, the virus inactivation procedures for SAR Co-V were not verified and were later proven to be insufficient. The mother of one student was fatally infected. The nurse who cared for both the infected student and the student's mother also became infected and transmitted SARS Co-V to five other patients. This is the only reported instance of tertiary transmissions from laboratory-associated infections. A subsequent analysis of stored serum samples identified two previous cases among the BSL-2 laboratory staff; the illnesses were self-limiting cases that were not diagnosed

Figure 1
Samples removed for analysis at Biosafety Level 2 without decontamination. See www.wpro.who.int/sars/docs/update/update07022004.asp



as SARS at the time the students were ill. All of these cases are represented in the graphic from the CDC web site (Figure 1) (CDC, 2004).

Infection of Medical Personnel

In addition to the nurse infected with SARS in Beijing, three additional transmissions to medical personnel have occurred because of treating staff infected in the laboratory. One pathologist was fatally infected while conducting an autopsy of a scientist who died of a laboratory-acquired Marburg infection (Alibek et al., 1999), and the other two were cases of laboratory-acquired Brucella infections in clinical laboratory technicians who were infected when culturing blood from infected clinical laboratory technicians (Chusid et al., 1993; Noviello et al., 2004).

Failure to Restrict Access to the Laboratory

Several incidents of visitors to the laboratory becoming infected have been documented.

- In 1973, a visitor to a smallpox laboratory in London became infected and transmitted smallpox to two contacts (Collins et al., 1999, p. 30).
- There was also a case of Q fever in a laboratory visitor (Collins et al., 1999).

Eight cases of *B. pertussis* in adults occurred in staff who did not directly work with the organism but had access to common laboratory spaces where the *B. pertussis* was manipulated; there was one secondary case of transmission to a family member (U.S. Department of Public Health and Human Services et al., 1999).

- Two index laboratory-acquired cases of *B. pertussis* at a large university resulted in one documented case of secondary transmission to a household contact (U.S. Department of Public Health and Human Services et al., 1999).
- A 6-year-old child visiting a clinical microbiology laboratory on "take-your-daughter-to-work day" was shown an agar plate with bacterial colonies. The child put her finger on a colony; her mother immediately washed the child's hands, but the child sustained a serious infection with *E. coli* O157: H7 (Salerno et al., 2004).
- An immunosuppressed student visited a mycology laboratory and became infected with *Penicillium marneffi* (Hilmarsdottir et al., 1994).

Transmission to Household Contacts by Laboratory Personnel

- A microbiology laboratory director re-isolated the laboratory stock cultures that included *S. typhi* and *S. agona* strains from previous proficiency testing samples. The *S. typhi* and the *S. agona* strains were provided to a student in the clinical laboratory as "unknowns" to identify. After work, the director's usual routine was to prepare dinner for his wife and two children. The wife was hospitalized and blood cultures yielded both *S. typhi* and *S. agona*; her infection was fatal. The son's blood cultures were positive for *S. typhi*, but he survived. The *S. typhi* and *S. agona* strains isolated from the wife and the *S. typhi* from the son were identical to the laboratory stock strains. The clinical lab director and a student in the lab assigned the same strains as an exercise in identification did not become ill (Blaser & Loftgren, 1981).
- A reference strain of poliovirus was isolated from the fecal sample of a child with diarrhea. The viral isolate was identical to the strain used in the polio vaccine production facility where the child's father worked. The father remained well, although he had been involved in an accident in the facility which may have contaminated his clothing. Fortunately, the child had been immunized and recovered, but the case is cited in the global action plan for the laboratory containment of polioviruses, since, in the absence of immunization, the outcome could have been different (Heymann et al., 2004; Mulders et al., 2003).
- Two household contacts of a rickettsologist became infected with Q fever (U.S. Department of Public Health and Human Services et al., 1999).
- A clinical laboratory worker worked with a proficiency test sample, then ate half of her sandwich. She brought the other half of the sandwich home for her child to eat. The child developed typhoid, and the cultures and the proficiency test sample were both phage strain C1 (Blaser & Lofgren, 1981).

Transmission to Household Contacts by Unanticipated Routes

These cases were the first report in the literature of this mode of transmission for this agent.

- Marburg infection by sexual transmission occurred two months after the index case was released from the hospital (U.S. Department of Public Health and Human Services et al., 1999).
- *Brucella melitensis* infection by sexual transmission was documented in the wife and the fiancée of clinical laboratory workers infected in the laboratory (Goosens

et al., 1983; Ruben et al., 1991). This route of transmission had not been reported previously.

- Twelve days after conducting a necropsy on a cow infected with *L. interrogans serovar hardjo*, the veterinarian became ill. Her infant was infected with the same organism through breast milk (Bolin & Koellner, 1988).
- An animal caretaker was bitten by a rhesus monkey and herpetic lesions appeared at the site. His wife applied non-prescription creams to the lesions and to her contact dermatitis. The shared tubes of zinc oxide and hydrocortisone creams were thought to be the medium that transmitted the infection. B virus was isolated from a punch biopsy of her dermatitis; she was successfully treated with intravenous and then daily oral acyclovir (Holmes et al., 1990).

This review of community-acquired infections only reinforces the need for errors to be disclosed and remediated. The Sverdlosk epidemic of 1979 is the only "outbreak" scenario—the only instance of airborne transmission of disease resulting in a community outbreak. Seventy-seven infections, with 68 fatalities, occurred downstream of an anthrax bioweapon factory (Meselson et al., 1994). This is an important case study of the aerosol transmission of disease along the plume resulting from emissions and the effect of prevailing wind patterns. Of course, the scale of modern research operations is many orders of magnitude less than operations in a bioweapons factory, and the containment practices as described in this facility do not meet modern standards. However, the incident description serves as a reminder that human error can have dire consequences. According to Ken Alibek, in his book *Biohazard*, a technician left a note indicating that he had removed a clogged exhaust filter at the end of a work shift. The supervisor did not record the information in the log book, so the next supervisor was unaware of the problem and began operations as usual. Several hours later, the missing filter was noticed, and procedures were halted for filter replacement. Since the plant was operating in violation of the Biological Weapons Convention of 1972, the incident was kept a secret, and prophylactic antibiotics were not administered to the general population. According to Alibek, the number of casualties was not anticipated. In the rare incident with *any* potential to affect the outside community, laboratory directors must assume the responsibility of disclosing the details and immediately launching preventive medicine efforts.

While a few infections have occurred, clinical and research laboratories have an outstanding record in terms of minimizing risk to the community outside the laboratory. Every biosafety professional, director, and bench scientist share the responsibility for minimizing that risk. The subject is frequently debated in the public media and even recently on the biosafety listserve (www.absa.org). To quote a recent post by R. Fink:

> To say we must have zero risk is not logical. Nothing has zero risk; it is always a question of whether the benefit outweighs the risk. If zero risk was the criteria prior to research on pathogens, then we would have no vaccines and no antimicrobial agents, and we would be plunged back to a time when any infection was life-threatening and good genes and luck were required to live beyond the mid-40s. What is remarkable is how rarely the community is adversely impacted by research organisms. Despite the thousands of research labs, clinical labs, hospital labs, and large-scale fermentations, the occurrence of an infection in the community is extremely rare.

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Capsule

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What's new? What's hot? What's timely? If you don't have time to search the Internet for the latest developments that might impact your work environment, you just might find some of this information in the "Capsule" column. Please e-mail any comments or suggestions to ekrisiunas@aol.com or to Co-Editor Barbara Johnson at barbara_johnson@verizon.net or Co-Editor Karen B. Byers at karen_byers@dfci.harvard.edu.

Recommendations for the Selection and Use of Respirators and Protective Clothing for Protection Against Biological Agents

This document is based on current understandings of the potential agents and existing recommendations for biological aerosols and is oriented toward acts of terrorism. The recommendations provided here do not address, and are not applicable to, controlled use of biological agents in biosafety laboratories. Available at: www.cdc.gov/niosh/docs/2009-132/

Plan to Combat Extensively Drug-resistant Tuberculosis: Recommendations of the Federal Tuberculosis Task Force—*MMWR,* February 13, 2009/58(03):1-43

The recommendations provided in this report include specific actions and new activities that will require additional funding and a renewed commitment by government and non-government organizations involved in domestic and international TB control efforts to be implemented effectively. The Federal TB Task Force will coordinate the activities of various federal agencies and partner with state and local health departments, nonprofit agencies, and TB advocacy organizations to implement this plan to control and prevent XDR TB in the United States and to contribute to global efforts in the fight against this emerging public health crisis. Available at: www.cdc.gov/mmwr/preview/mmwrhtml/rr5803a1.htm

Hepatitis C Virus Transmission at an Outpatient Hemodialysis Unit—New York, 2001–2008 *MMWR*, March 6, 2009/56(08):189-194

In July 2008, the New York State Department of Health (NYSDOH) received reports of three hemodialysis patients seroconverting from anti-hepatitis C virus (HCV) negative to anti-HCV positive in a New York City hemodialysis unit during the preceding 6 months. This report summarizes the results of that investigation, which found that six additional patients had HCV seroconversion during 2001-2008 and that the hemodialysis unit had numerous deficiencies in infection control policies, procedures, and training. Available at: www.cdc.gov/mmwr/preview/mmwr html/mm5808a2.htm

National Bio- and Agro-Defense Facility—Update

The proposed National Bio- and Agro-Defense Facility (NBAF) in Manhattan, Kansas, will research high-consequence biological threats involving zoonotic (i.e., transmitted from animals to humans) and foreign animal diseases. It will allow basic research; diagnostic development, testing, and validation; advanced countermea-