

ACHIEVING BIOSAFETY LEVEL 3 THROUGH THE USE OF BIOSAFETY LEVEL 2 FACILITIES AND BIOSAFETY LEVEL 3 PRACTICES: A PREVALENCE SURVEY OF MEDICAL RESEARCH AND ACADEMIC INSTITUTIONS

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ABSTRACT

Heightened interest in pathogens with the potential for aerosol transmission and for which prevention and medical treatment is not readily available has resulted in a need for more work environments that meet Biosafety Level 3 (BSL 3) criteria. Recognizing that the facility-based criteria for BSL 3 cannot be achieved by some existing laboratories, the Centers for Disease Control and Prevention (CDC) and National Institutes of Health (NIH) biological safety guidelines provide an option for attaining BSL 3 status through the use of Biosafety Level 2 (BSL 2) facilities and strict adherence to BSL 3 practices (BSL 2/3). Inherent to this provision is a greater emphasis on safe work practices. Since the extent to which this approach is actually used in practice is not known, a nationwide mail survey of medical academic and research institutions was conducted to provide an objective indication of the proportion of BSL 3 operations actually being carried out in the BSL 2/3 mode. The results obtained indicate that 2% of activities designated as BSL 3 in the study population actually achieve this level of protection using the BSL 2/3 approach. The findings quantitatively estimate for the first time the proportion of BSL 3 activities being carried out in this fashion, and can serve as a reference point for future studies to evaluate usage trends. The results also demonstrate the utility of flexible, performance-based health and safety guidelines, as a significant amount of clinical and research work is being accommodated with the BSL 2/3 provision.

INTRODUCTION

The Centers for Disease Control and Prevention (CDC) and National Institutes of Health's (NIH) Biosafety in Microbiological and Biomedical Laboratories is perhaps one of the most widely recognized

references in the biosafety profession. This document categorizes infectious agents and activities into four general biosafety levels, each defined as a combination of safe practices, equipment, and laboratory facilities (CDC 1993). In general, biosafety level assignments are based on agent pathogenicity and route of transmission. Microorganisms not known to cause disease in healthy adults, such as *Bacillus subtilis* are assigned a Biosafety Level 1 (BSL 1). Agents assigned to BSL 2 environments include those whose common route of transmission is percutaneous or mucous membrane exposures, or ingestion of infectious materials, such as hepatitis B virus, *Toxoplasma* spp. and the salmonellae. Biosafety Level 3 designations are assigned to work with agents that are generally transmitted by aerosols, and which may cause serious and potentially lethal infection. Biosafety Level 4 (BSL 4) is assigned to high risk agents that pose a risk of life threatening disease. aerosol transmission and no vaccine or therapy.

The requirements to achieve BSL 1 and BSL 2 are minimal and can usually be met by most existing laboratories with very minor adjustments or modifications. However, the facility requirements for BSL 3 are more difficult for many existing laboratory facilities to attain, since features such as separate rooms, sealed penetrations, non-recirculated directional airflows, and filtered discharges may not be present. Recognizing this, the CDC/NIH guidelines include a caveat for existing facilities to permit low level and diagnostic work with agents designated for BSL 3:

"It is recognized, however, that many existing facilities may not have all of the facility safeguards recommended for Biosafety Level 3 (i.e., access zone, sealed penetrations, and directional airflow, etc.). In these circumstances, acceptable safety may be achieved for routine or repetitive operations

(i.e., diagnostic procedures involving the propagation of an agent for identification, typing, and susceptibility testing) in Biosafety Level 2 facilities. However, the recommended Standard Microbiological Practices, Special Practices, and Safety Equipment for Biosafety Level 3 must be rigorously followed. The decision to implement this modification of Biosafety Level 3 recommendations should be made only by the laboratory director" (CDC 1993).

Since the intent of this provision is to permit low level and diagnostic work, the CDC/NIH guidelines reflect an emphasize on the need for full BSL 3 containment facilities when larger volumes and higher concentrations of infectious materials are used.

The BSL 3 work practices described in the CDC/NIH manual are summarized in Table 1.

In recent years, the need for BSL 3 work environments has increased due primarily to research efforts directed towards the control and prevention

TABLE 1
Summary of Biosafety Level 3 Work Practices as Described by the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories.

- Closed doors during operations
- Restrict access to lab
- Establish policies and procedures for entry, including hazard communication
- Display of hazard warning signs
- Receipt of proper immunizations, where applicable
- Collection of baseline serum samples
- Creation or adoption of a biosafety manual
- Provision of appropriate training to lab personnel
- Demonstration of proficiency in standard practices and techniques
- Methods for safe handling of sharps
- Manipulations conducted in containment devices such as biosafety cabinets
- Routine cleaning and disinfection of work surfaces
- Proper storage and transport container that prevent leakage
- Decontamination of waste materials prior to leaving lab
- Proper handling of spills
- Proper reporting of spills and other exposure incidents
- Exclusion of unnecessary animals and plants

of two significant public health threats (Party 1996). Medical academic and research institutions have been challenged to provide adequate facilities to persons wishing to handle, propagate, and manipulate *Mycobacterium tuberculosis* and retroviruses such as the human immunodeficiency virus (HIV) or simion immunodeficiency virus (SIV), each of which are assigned to the BSL 3 category. With the impetus to accommodate such research and clinical activities, many institutions may be relying on the BSL 2/3 provision to permit BSL 3 work. Inherent to the BSL 2/3 provision is an increased emphasis on safe work practices, which is of interest to health

and safety professionals since the approach varies somewhat from the basic industrial hygiene adage of primary reliance on engineering controls (NSC 1988). A preliminary assessment of the extent to which this provision is being used would provide useful information to the entire biosafety community.

METHODS

To estimate the current proportion of BSL 3 operations conducted in the BSL 2/3 mode, a study population was identified that was considered likely

to host some form of BSL 3 activities. Since biomedical research and academic institutions regularly work with a wide variety of pathogenic agents, the 1996-1997 Directory of American Medical Education by the Association of American Medical Colleges was used as a source of institutions for inclusion in the study (AAMC 1996). This institutional listing was cross-referenced with the membership listings of the American Biological Safety Association (ABSA) and the American Industrial Hygiene Association (AIHA) in an attempt to identify a person responsible for, or associated with biosafety operations at each facility (ABSA 1997, AIHA 1996). With this cross-referencing, a total of 127 study participants were identified.

A simple survey questionnaire was developed and distributed via mail. Letters were specifically addressed to the identified or expected person responsible for biosafety at each institution. Survey questions were included at the bottom of the one page letter and were purposefully worded in an abbreviated format to ease completion and improve the rate of response. The survey questions included on the letter are shown in Table 2. Self-addressed stamped envelopes were also included, along with facsimile numbers and electronic mail addresses to expedite the return of information. The questionnaires were distributed in early July 1997 and data collected for a period of 45 days.

TABLE 2

Questions Included in Biosafety Level 3 (BSL 3) Survey of Medical Academic and Research Institutions.

How many laboratories are actively involved with Biosafety Level 3 (BSL 3) rated activities?

Of these BSL 3 activities, how many achieve this level by the use of BSL 2 facilities and BSL 3 practices?

Please provide an examples of the agent or agents being handled in these conditions.

In these situations, how is compliance with BSL 3 practices verified?

by a signed protocol?

mandatory training?

routine workplace monitoring?

other.

RESULTS

Of the 127 surveys initially distributed, 64 (50%) were returned within the 45 day study period. Of the respondent institutions, 39 (61%) reported the presence of BSL 3 rated activities, representing a total of 111 different laboratories. Of this total, 25 (22%) were reported to be achieving BSL 3 using the BSL 2/3 approach.

The agent most frequently reported to be handled in the BSL 2/3 settings was HIV, noted as the potential exposure agent in 22 of 39 BSL 3 settings (56%). *Mycobacterium tuberculosis* was identified as being used in 7 of the 39 settings (18%). A variety of other agents were also reported, such as han-

tavirus, typhus and rickettsia spp., with no notable trend or frequency.

Responding institutions indicated that a combination of methods are being used to ensure compliance with the safe work practice criteria inherent to BSL 2/3 operations. Thirty-four of 39 institutions (87%) reported that the submission of a signed protocol was used as a method of ensuring compliance. Routine workplace inspections were reported to be used in 35 of 39 (89%) institutions. Mandatory training was reported as required in 22 of 39 (56%) settings. Other miscellaneous methods, such as requiring the submittal of training documentation and mandatory quarterly activity reports, were indicated in 8 of 39 cases (20%).

DISCUSSION

The results obtained from this survey are interesting because the data assembled provide a quantitative estimate of the proportion of BSL 3 rated work currently being carried out in the BSL 2/3 mode. This estimation is based on the assumption that the data collected is representative of the survey's non-respondents as well. Using this estimate, future surveys can track changes in this proportion, providing valuable information for future editions of the CDC/NIH guidelines and other biosafety-related references. If, for instance, the proportion of BSL 2/3 operations increases, then perhaps additional guidance would be warranted on issues such as specific worker training issues and routine surveillance activities.

Several important parameters were not considered during this study which should be noted. No determination was made as to whether an institution was public or private, nor was any consideration given to the age of an institution's facilities. Certainly these parameters affect an institution's ability to maintain facilities that meet BSL 3 requirements, and should be considered for inclusion in any future surveys of this type. Additionally, information on the type of work performed in the designated settings, whether diagnostic or research, was not requested, and this should also be considered in any future studies of this kind.

This study also highlights the utility of flexible, performance-based health and safety guidelines. The authors of the CDC/NIH guidelines were insightful when they included provisions for such flexibility. If the guidelines had not permitted the BSL 2/3 adaptation, then perhaps a significant amount of clinical and research activities currently

conducted at academic medical centers would have been impeded. Health and safety professionals have for years been faced with regulations that were very prescriptive, allowing little room for professional judgement. Although this trend is changing with the promulgation of more performance-based standards, the authors of the CDC/NIH guidelines were very progressive in the development of their recommendations, and for this, their efforts are deserving of recognition.

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