

## CHAPTER 7

### RECOMMENDED BIOSAFETY LEVELS FOR INFECTIOUS AGENTS AND INFECTED ANIMALS

Selection of an appropriate biosafety level for work with a particular agent or animal study depends upon a number of factors (see Section V, Risk Assessment). Some of the most important are: the virulence, pathogenicity, biological stability, route of spread, and communicability of the agent; the nature or function of the laboratory; the procedures and manipulations involving the agent; the endemicity of the agent; and the availability of effective vaccines or therapeutic measures.

Agent summary statements in this section provide guidance for the selection of appropriate biosafety levels. Specific information on laboratory hazards associated with a particular agent, and recommendations regarding practical safeguards that can significantly reduce the risk of laboratory-associated diseases, are included. Agent summary statements are presented for agents which meet one or more of the following criteria: the agent is a proven hazard to laboratory personnel working with infectious materials (e.g., hepatitis B virus, *M. tuberculosis*); the potential for laboratory-associated infections is high, even in the absence of previously documented laboratory-associated infections (e.g., exotic arboviruses); or the consequences of infection are grave.

Recommendations for the use of vaccines and toxoids are included in agent summary statements when such products are available, either as licensed or Investigational New Drug (IND) products (see Appendix B, Immunoprophylaxis). When applicable, recommendations for the use of these products are based on current recommendations of the Public Health Service Advisory Committee on Immunization Practice, and are specifically targeted to at-risk laboratory personnel and others who must work in or enter laboratory areas. These specific recommendations should in no way preclude the routine use of such products as diphtheria-tetanus toxoids, poliovirus vaccine, influenza vaccine and others, because of the potential risk of community exposures irrespective of any laboratory risks. Appropriate precautions should be taken in the administration of live attenuated virus vaccines in individuals with altered immunocompetence or other medical condition (e.g., pregnancy), in which a viral infection could result in adverse consequences.

Risk assessments and biosafety levels recommended in the agent summary statements presuppose a population of immunocompetent individuals. Persons with altered immunocompetence may be at an increased risk when exposed to infectious agents. Immunodeficiency may be hereditary, congenital, or induced by a number of neoplastic or infectious diseases, by therapy, or by radiation. The risk of becoming infected or the consequence of infection may also be influenced by such factors as age, sex, race, pregnancy, surgery (e.g., splenectomy, gastrectomy), predisposing diseases (e.g., diabetes, lupus erythematosus) or altered physiological function. These and other variables must be

considered in applying the generic risk assessments of the agent summary statements to specific activities of selected individuals.

The biosafety level assigned to an agent is based on the activities typically associated with the growth and manipulation of the quantities and concentrations of infectious agents required to accomplish identification or typing. If activities with clinical materials pose a lesser risk to personnel than those activities associated with manipulation of cultures, a lower biosafety level is recommended. On the other hand, if the activities involve large volumes and/or concentrated preparations ("production quantities"), or manipulations which are likely to produce aerosols or which are otherwise intrinsically hazardous, additional personnel precautions and increased levels of primary and secondary containment may be indicated.

"Production quantities" refers to large volumes or concentrations of infectious agents considerably in excess of those typically used for identification and typing activities. Propagation and concentration of infectious agents, as occurs in large-scale fermentations, antigen and vaccine production, and a variety of other commercial and research activities, clearly deal with significant masses of infectious agents that are reasonably considered "production quantities." However, in terms of potentially increased risk as a function of the mass of infectious agents, it is not possible to define "production quantities" in finite volumes or concentrations for any given agent. Therefore, the laboratory director must make an assessment of the activities conducted and select practices, containment equipment, and facilities appropriate to the risk, irrespective of the volume or concentration of agent involved.

Occasions will arise when the laboratory director should select a biosafety level higher than that recommended. For example, a higher biosafety level may be indicated by the unique nature of the proposed activity (e.g., the need for special containment for experimentally generated aerosols for inhalation studies) or by the proximity of the laboratory to areas of special concern (e.g., a diagnostic laboratory located near patient care areas). Similarly, a recommended biosafety level may be adapted to compensate for the absence of certain recommended safeguards. For example, in those situations where Biosafety Level 3 is recommended, acceptable safety may be achieved for routine or repetitive operations (e.g., diagnostic procedures involving the propagation of an agent for identification, typing and susceptibility testing) in laboratories where facility features satisfy Biosafety Level 2 recommendations, provided the recommended standard microbiological practices, special practices, and safety equipment for Biosafety Level 3 are rigorously followed.

One example involves work with the Human Immunodeficiency Virus (HIV). Routine diagnostic work with clinical specimens can be done safely at Biosafety Level 2, using Biosafety Level 2 practices and procedures. Research work (including co-cultivation, virus replication studies, or manipulations involving concentrated virus) can be done in a BSL-2 facility, using BSL-3 practices and procedures. Virus production activities, including virus concentrations, require a BSL-3 facility and use of BSL-3 practices and procedures (see Agent Summary Statement).

The decision to adapt Biosafety Level 3 recommendations in this manner should be made only by the laboratory director. This adaptation, however, is not suggested for agent production operations or activities where procedures are frequently changing. The laboratory director should also give special consideration to selecting appropriate safeguards for materials that may contain a suspected agent. For example, sera of human origin may contain hepatitis B virus, and therefore, all blood or blood-derived fluids should be handled under conditions which reasonably preclude cutaneous, mucous membrane or parenteral exposure of personnel. Sputa submitted to the laboratory for tubercle bacilli assay should be handled under conditions which reasonably preclude the generation of aerosols during the manipulation of clinical materials or cultures.

The infectious agents that meet the previously stated criteria are listed by category of agent in Section VII. To use these summaries, first locate the agent in the listing under the appropriate category of agent. Second, utilize the practices, safety equipment, and type of facilities recommended in the agent summary statement as described in Section VII for working with clinical materials, cultures or infectious agents, or infected animals. The laboratory director is also responsible for appropriate risk assessment and for utilization of appropriate practices, containment equipment, and facilities for agents not included in the agent summary statements.