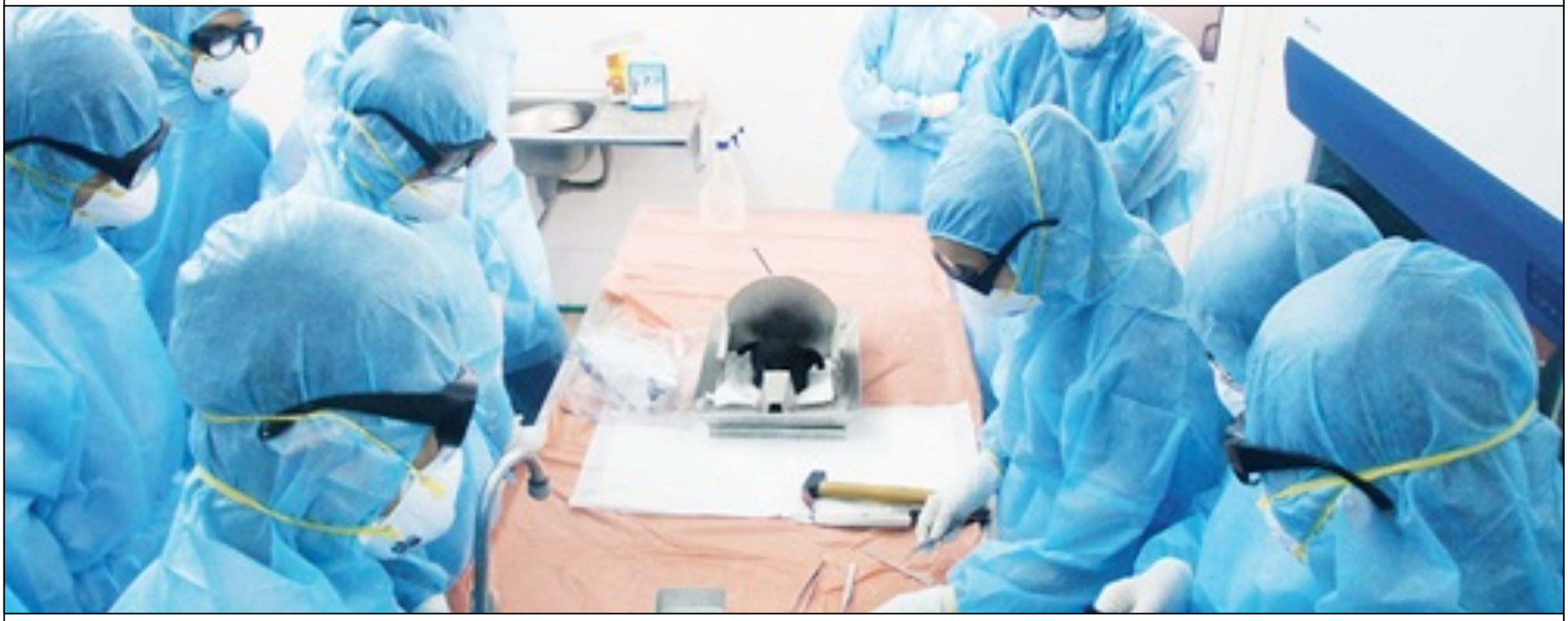
BIOCONTAINMENT ENGINEERING CONTROLS

Biocontainment Facility Manual

Cobeal™ Engineering For Biosafety

SECTION 1

Biosafety Levels at a Glance



Throughout this manual, references are made to biosafety levels (BSL-1, BSL-2, BSL-3, BSL-4), as well as to the relative hazards of infective microorganisms by risk group (WHO Risk Groups 1, 2, 3, and 4).

Biocontainment Facilities

Classification of infective microorganisms by risk group

1. (no or low individual and community risk) A microorganism that is unlikely to cause human or animal disease.
2. (moderate individual risk, low community risk) A pathogen that can cause human or animal disease but is likely to be a serious hazard to workers, the community, livestock or the environment. Exposures can cause serious infection, but effective treatment and preventative measures are available and the risk of spread of infection is limited.
3. (high individual risk, low community risk) A pathogen that usually causes serious human or animal disease but does not ordinarily spread from one infected individual to another. Effective treatment and preventative measures are available.
4. (high individual and community risk) A pathogen that usually causes serious human or animal disease and that can be readily transmitted from one individual to another, directly or indirectly. Effective treatment and preventive measures are not usually available.

Figure 1.1 Cobeal™ Bag In/Bag Out series

The Cobeal Bag In/Bag Out side access filter system is a safe, simple, reliable method for removing contaminated particulate filters and/or gas absorbers used for air purification in hazardous environments.

Biohazard containment areas are based on a composite of the design features, construction, containment facilities, equipment, practices and operational procedures required for working with agents from various risk groups.

Cobeal designs biosafety containment areas based on a risk assessment. Such an assessment will take the risk group as well as other factors into consideration in establishing the appropriate biosafety level. For example, a Level 2 Biohazard area will generally require Biosafety Level 2 facilities, equipment, practices and procedures for safe conduct of work. However, if particular pathogens or experiments require the generation

of high-concentration aerosols, then Biosafety Level 3 may be more appropriate to provide the necessary degree of safety, since it ensures superior containment of aerosols in the biohazard space. The biosafety level assigned for the specific work is done by Cobeal's professional Biosafety Risk Assessors and based on a professional risk assessment judgment, rather than by automatic assignment of a biosafety level according to the particular risk group designation of the pathogenic agent.

Summary of biosafety level requirements

	BIOSAFETY LEVEL			
	1	**2**	**3**	**4**
Isolation[a] of laboratory	No	No	Yes	Yes
Room sealable for decontamination	No	No	Yes	Yes
Ventilation:				
— inward airflow	No	Desirable	Yes	Yes
— controlled ventilating system	No	Desirable	Yes	Yes
— HEPA-filtered air exhaust	No	No	Yes/No[b]	Yes
Double-door entry	No	No	Yes	Yes
Airlock	No	No	No	Yes
Airlock with shower	No	No	No	Yes
Anteroom	No	No	Yes	—
Anteroom with shower	No	No	Yes/No[c]	No
Effluent treatment	No	No	Yes/No[c]	Yes
Autoclave:				
— on site	No	Desirable	Yes	Yes
— in laboratory room	No	No	Desirable	Yes
— double-ended	No	No	Desirable	Yes
Biological safety cabinets	No	Desirable	Yes	Yes
Personnel safety monitoring capability[d]	No	No	Desirable	Yes

a. Environmental and functional isolation from general traffic

b. Dependent on location of exhaust

c. Dependent on agent(s) used in biosafety space

d. For example, window, closed-circuit television, two-way communication

Biosafety Assessment

The assignment of a biosafety level takes into consideration the organism (pathogenic agent) used, the facilities available, and the equipment practices and procedures required to conduct work safely in the biosafety space.

Once performed, risk assessments should be reviewed routinely and revised when necessary, taking into consideration the acquisition of new data having a bearing on the degree of risk and other relevant new information from scientific literature and studies.

On the basis of the information ascertained during the risk assessment, a biosafety level can be assigned to the planned work, appropriate personal protective equipment selected, and standard operating procedures (SOPs) incorporating other safety interventions developed to ensure the safest possible conduct of the work.

Specimens for which there is limited information

On occasions, "outbreaks" occur for which there is inadequate or insufficient information available to perform an appropriate risk assessment. In these cases, it is prudent to take a cautious approach to biocontainment engineering controls.

For the purpose of this manual, guidance and recommendations are given as minimum requirements pertaining to biosafety levels. Although some precautious may appear to be unnecessary for organisms in lower risk groups, they are desirable for training purposes to promote good (i.e. safe) microbiological techniques (GMT).

Public health and safety spaces must all be designed for Biosafety Level 2 or above. As no public space has complete control over agents, individuals may be exposed to organisms in higher risk groups than anticipated. This possibility must be recognized in the development of safety plans and policies.

This manual provides basic guidelines. Biosafety Levels 1 and 2 presented here are comprehensive and detailed, as they are fundamental to all biosafety levels. Guidelines for Biosafety Level 3 and maximum containment areas - Biosafety Level 4 - are modifications of and additions to these guidelines, and designed to work with the more dangerous (hazardous) pathogens.

Biocontainment design and facilities

In designing a biocontainment space and assigning certain types of work to it, special attention should be paid to conditions that are known to safety problems. These include:

1. Formation of aerosols
2. Work with large volumes and/or high concentrations of microorganisms
3. Overcrowding with too much equipment
4. Infestation with rodents and arthropods
5. Unauthorized entrance
6. Workflow: use of samples

Design Features

1. Ample space must be provided for the safe conduct of workers and for cleaning and maintenance personnel.
2. Walls, ceilings and floors should be smooth, easy to clean, impermeable to liquids and resistant to the chemicals and disinfectants normally used in biocontainment spaces. Floors should be slip-resistant.
3. Bench tops should be impervious to water and resistant to disinfectants, acids, alkalis, organic solvents and moderate heat.
4. Illumination should be adequate for all activities. Undesirable reflections and glare should be avoided.
5. Facility furniture should be sturdy. Open spaces between and under benches, cabinets and equipment should be accessible for cleaning.
6. Storage space must be adequate to hold supplies for immediate use and thus prevent clutter on bench tops and in aisles. Additional storage space, conveniently located outside the biocontainment working areas, should also be provided.
7. Space and facilities should be provided for the safe handling and storage of solvents, radioactive materials, and compressed and liquefied gases.
8. Facilities for storing outer garments and personal items should be provided outside the biocontaminant working areas.
9. Facilities for eating and drinking and for rest should be provided outside the biocontainment working areas.

10.Hand-washing basins, with running water, should be provided in each room, preferably near the exit door.

11. Doors should have vision panels, appropriate fire ratings, and preferably by self-closing.

12. At Biosafety Level 2, an autoclave or other means of decontamination should be available in appropriate proximity to the biocontainment area.

13. Safety systems should cover fire, electrical emergencies, emergency shower and eyewash facilities.

14.First-aid areas or rooms suitably equipped and readily accessible should be available.

15. In the planning of permanent or temporary biocontainment facilities, consideration should be given to the provision of mechanical ventilation systems that provide an inward flow of air without recirculation. If there is no mechanical ventilation, windows should be able to be opened and should be fitted with arthropod-proof screens.

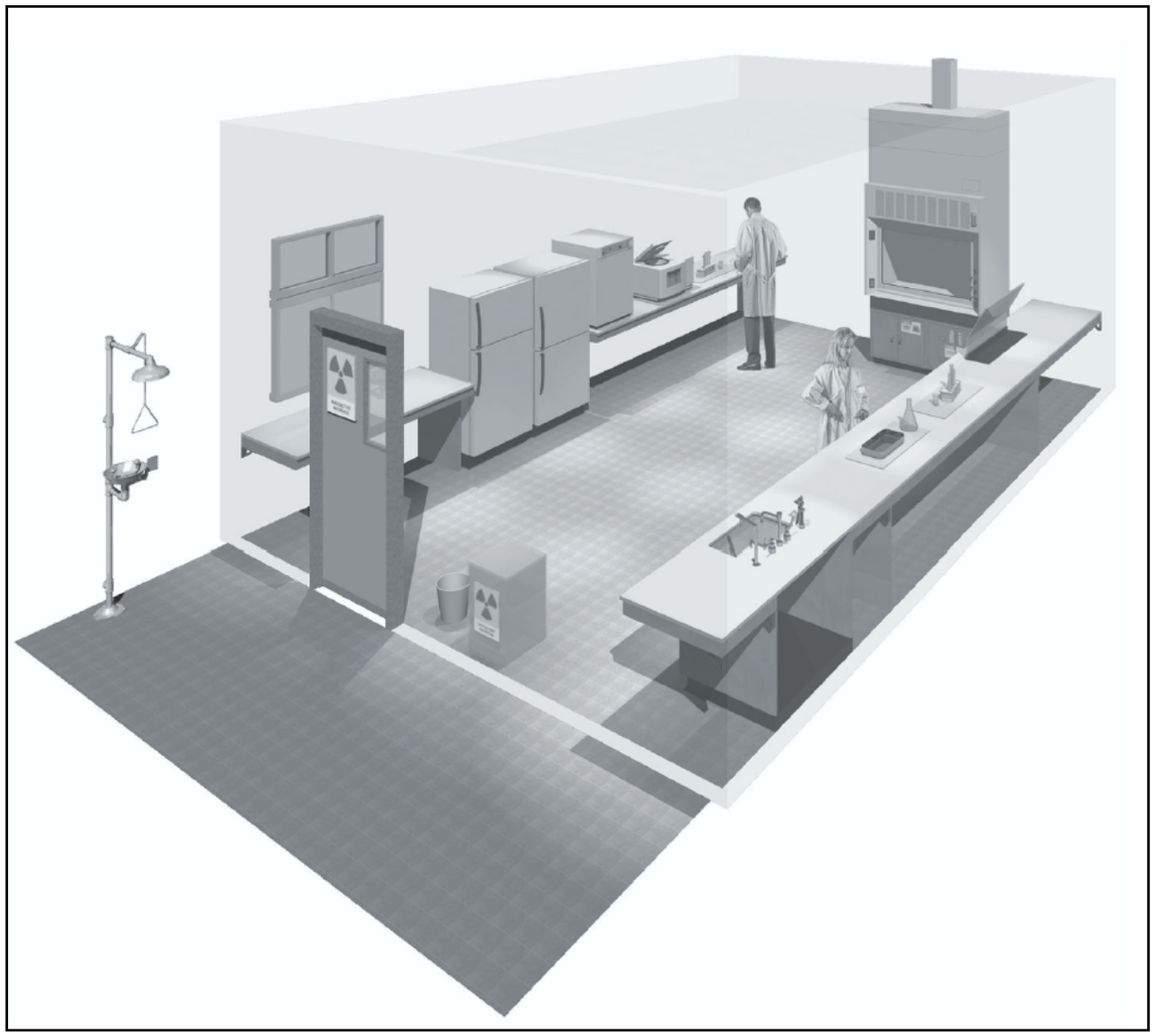
16. A dependable supply of good quality water is essential. There should be no cross-connections between sources of biocontainment areas and drinking-water supplies. An anti-backflow device should be fitted to protect the public water system.

17. There should be a reliable and adequate electricity supply and emergency lighting to permit safe exit. A stand-by generator is desirable for the support of essential equipment, such as incubators, biological safety cabinets, freezers, etc., and for ventilation of contained spaces.

18.There should be a reliable and adequate supply of gas. Good maintenance of the installation is mandatory.

19. Biocontainment areas are occasionally the targets of vandals. Physical and fire security must be considered. Strong doors, screened windows and restricted access are compulsory. Other measures should be considered and applied, as appropriate, to augment security.

A typical Biosafety Level 1 biocontaminat space



Biocontainment equipment

Together with good procedures and practices, the use of safety equipmnt will help to reduce risks when dealing with biosafety hazards. This section deals with basic principles related to equipment suitable for biocontainment spaces of all biosafety levels.

The biocontainment director should, after consultation with Cobeal and appropriate biosafety officers and safety committees (if designated), ensure that adequate equipment is provided and that it is used properly. Equipment should be selected to take account of certain general principles, such as:

1. Designed to prevent or limit contact between operator and the infectious agent or material

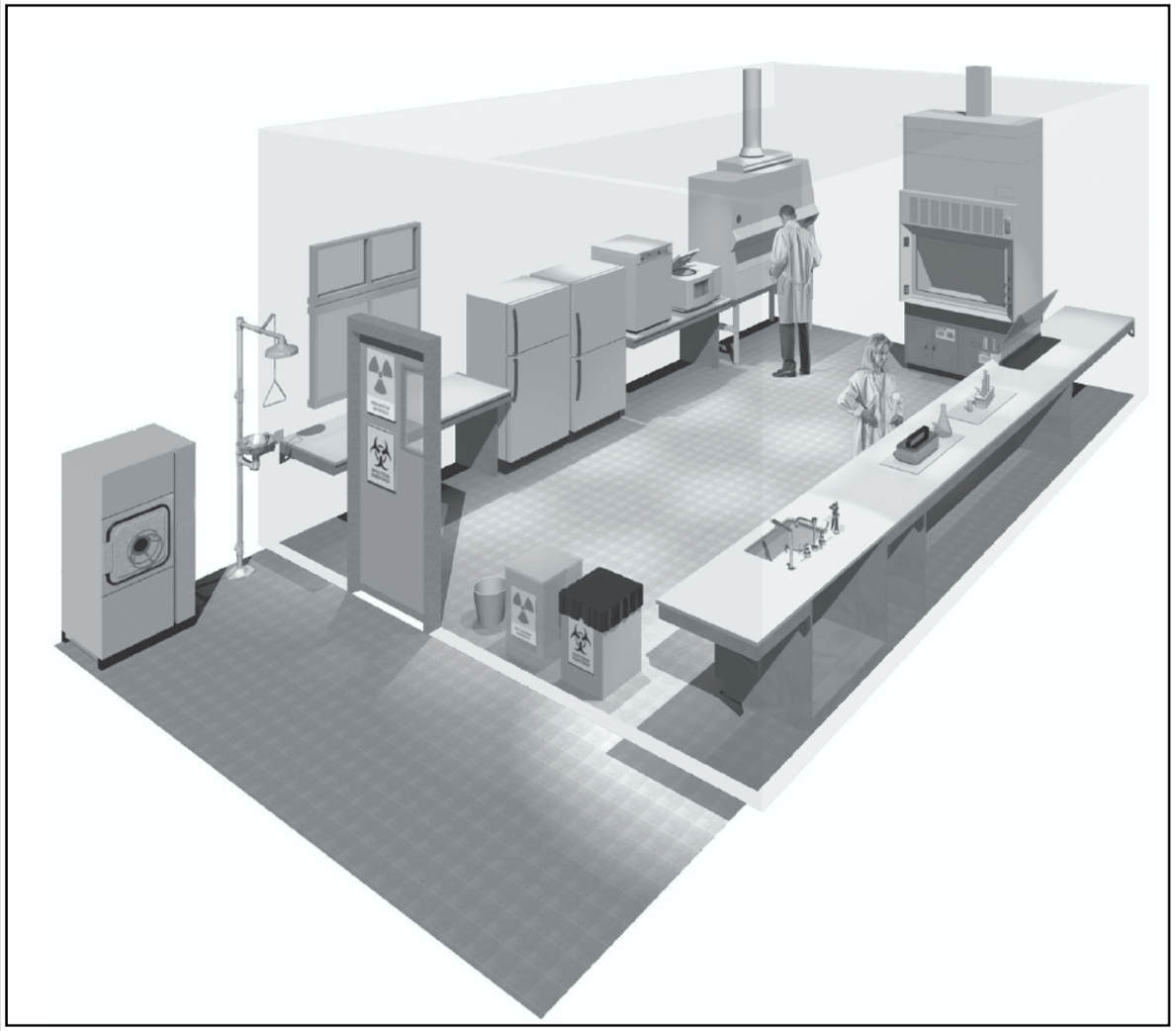
2. Constructed of materials that are impermeable to liquids, resistant to corrosion and meet structural requirements

3. Fabricated to be free of burrs, sharp edges and unguarded moving parts

4. Designed, constructed and installed to facilitate simple operation and provide for ease of maintenance, cleaning, decontamination and certification testing; glassware and other breakable materials should be avoided, whenever possible.

Cobeal will provide detailed performance and construction specifications to ensure that the equipment possesses the necessary safety features.

A typical Biosafety Level 2 biocontaminant space



Essential biosafety equipment, ***see Cobeal for full list***

1. Biological safety cabinets, to be used whenever:

   a. Infectious materials are handled; such materials may be centrifuged in the open biocontainment space if sealed centrifuge safety cups are used and if they are loaded and unloaded in a biological safety cabinet

   b. there is an increased risk of airborne infection

c. procedures with a high potential for producing aerosols are used; these may include centrifugation, grinding, blending, vigorous shaking or mixing, sonic disruption, and/or the opening of containers of infectious materials whose internal pressure may be different from the ambient pressure.

Waste handling

Waste is anything that is to be discarded.

In biocontainment facilities, decontamination of wastes and their ultimate disposal are closely related. In terms of daily use, few if any contaminated materials will require actual removal from the biocontainment facility or destruction. Most glassware, instruments and laboratory clothing will be reused or recycled. The overriding principle is that all infectious materials should be decontaminated, autoclaved or incinerated within the biocontainment facility.

The principal questions to be asked before discharge of any objects or materials from biocontainment facilities that deal with potentially infectious microorganisms are:

1. Have the objects ore materials been effectively decontaminated or disinfected by an approved procedure?

2. If not, have they been packaged in an approved manner for immediate on-site incineration or transfer to another facility for incineration capacity?

3. Does the disposal of the decontaminated objects or materials involve any additional potential hazards, biological or ortherwise, to those who carry out the immediate disposal procedures or who might come into contact with discarded items outside the facility?

Decontamination

Steam autoclaving is the preferred method for all decontamination processes. Materials for decontamination and disposal should be placed in containers, e.g. autoclavable plastic bags, that are color-coded according to whether the contents are to be autoclaved and/or incinerated.

Chemical, fire, electrical, radiation and equipment safety

A breakdown in the containment of pathogenic organisms may be the indirect result of chemical, fire, electrical or radiation accidents. It is therefore essential to maintain high standards of safety in these fields in an biocontainment area. Statutory rules and regulations for each of these will typically be provided by national or local authorities, whose assistance should be consulted.

Cobeal Guidelines for biocontainment facility commissioning

Biocontainment facility commissioning may be defined as the systematic review and documentation process signifying that specified biocontainment facility structural components, systems and/or system components have been installed, inspected, functionally tested and verified to meet national or international standards, as appropriate. The respective building systems design criteria and design function establish these requirements. In other words, biocontainment facilities designed as Biosafety Levels 1-4 will have different and increasingly complex commissioning requirements. Geographical and climatic conditions, such as geological fault lines or extreme heat, cold or humidity may also affect the biocontainment

facility design and therefore the commissioning requirements. Upon the completion of the commissioning process, the pertinent structural components and support systems will have been subjected to the various operating conditions and failure modes that can be reasonably expected, and will have been approved.

Cobeal's commissioning process and acceptance criteria is established early in the building process, preferably during the programming phase of the permanent or temporary construction or renovation project. By acknowledging the commissioning process early in the project, Cobeal's architects, engineers, safety and health personnel and ultimately the biocontainment occupants can understand the performance requirements and set uniform expectations for facility performance. The commissioning process provides the institution or agency and surrounding community with a greater degree of confidence that the structural, electrical, mechanical and plumbing systems, containment and decontamination systems, and security and alarm systems will operated as designed, to assure containment of any potentially dangerous microorganisms being introduced into the biocontainment facility.

Commissioning activities generally begin during the programming phase of the project and proceed through the construction and subsequent warranty period for a biocontainment facility. Warranty periods should generally extend for one year following occupancy.

In the case of more complex biocontainment facilities (Biosafety Levels 3 or 4), the institution may wish to retain an outside commissioning agent that has demonstrated experience and success in the commissioning of complex biosafety facilities. When an independent commissioning agent is used, the institution should still be a member of the commissioning agent, as well as Cobeal's representative, and a representative of the institution's Operations and Maintenance staff.

The following is a list of biocontainment facility systems and components that may be included in a commissioning plan for functional testing, depending on the containment level of the facility being constructed. The list is not exhaustive. The actual commissioning plan will reflect the complexity of the biocontainment facility being planned.

1. Building automation systems including links to remote monitoring and control sites
2. Electronic surveillance and detection systems
3. Electronic security locks and proximity device readers
4. Heating, ventilation (supply and exhaust) and air-conditioning (HVAC) systems
5. High-efficiency particulate air (HEPA) filtration systems
6. HEPA decontamination systems
7. HVAC and exhaust air system controls and control interlocks
8. Airtight isolation dampers
9. Refrigeration systems
10. Boilers and steam systems
11. Fire detection, suppression and alarm systems
12. Domestic water backflow prevention devices

13. Processed water systems (i.e., reverse osmosis, distilled water)

14. Liquid effluent treatment and neutralization systems

15. Plumbing drain primer systems

16. Chemical decontaminant systems

17. Medical laboratory gas systems

18. Breathing air systems

19. Service and instrument air systems

20. Cascading pressure differential verification of biocontaminant and support areas

21. Local area network (LAN) and computer data systems

22. Normal power systems

23. Emergency power systems

24. Uninterrupted power systems

25. Emergency lighting systems

26. Lighting fixture penetration seals

27. Electrical and mechanical penetration seals

28. Telephone systems

29. Airlock door control interlocks

30. Airtight door seals

31. Window and vision-panel penetration seals

32. Barrier pass-through penetration

33. Structural integrity verification: concrete floors, walls and ceilings

34.Barrier coating verification: floors, walls and ceilings

35.Biosafety containment envelope pressurization and isolation functions

36. Biological safety cabinets

37. Autoclaves

38. Liquid nitrogen systems and alarms

39.Water detection systems (e.g. in case of flooding inside biocontainment zone)

40. Decontamination shower and chemical additive systems

41. Cage-wash and neutralization systems

42. Waste management

Cobeal biocontainment facility certification

Biocontainment facilities are complex and dynamic environments. Today's biocontainment facility must be able to adapt quickly and to continuously increase public health needs and pressures. An example of this is the need for biocontainment facilities to adjust priorities to meet the challenges of emerging or re-emerging infectious diseases. In order to assure that adaptation and maintenance are undertaken promptly and in an appropriate and safe manner,

Cobeal provides biocontainment facility certification services to ensure that:

1. Proper engineering controls are being used and are functioning adequately as designed
2. Appropriate site and protocol specific administrative controls are in place
3. Personal protective equipment is appropriate for the tasks being performed
4. Decontamination of waste and materials has been adequately considered and proper waste management procedures are in place
5. Proper procedures for general laboratory safety, including physical, electrical and chemical safety are in place.

Biocontainment facility certification differs from biocontainment facility commissioning activities in several important ways. Biocontainment facility certification is the systematic examination of all safety features and processes within the facility (engineering controls, personal protective equipment and administrative controls). Biosafety practices and procedures are also examined. Biocontainment facility certification is an ongoing quality and safety assurance activity that should take place on a regular basis.

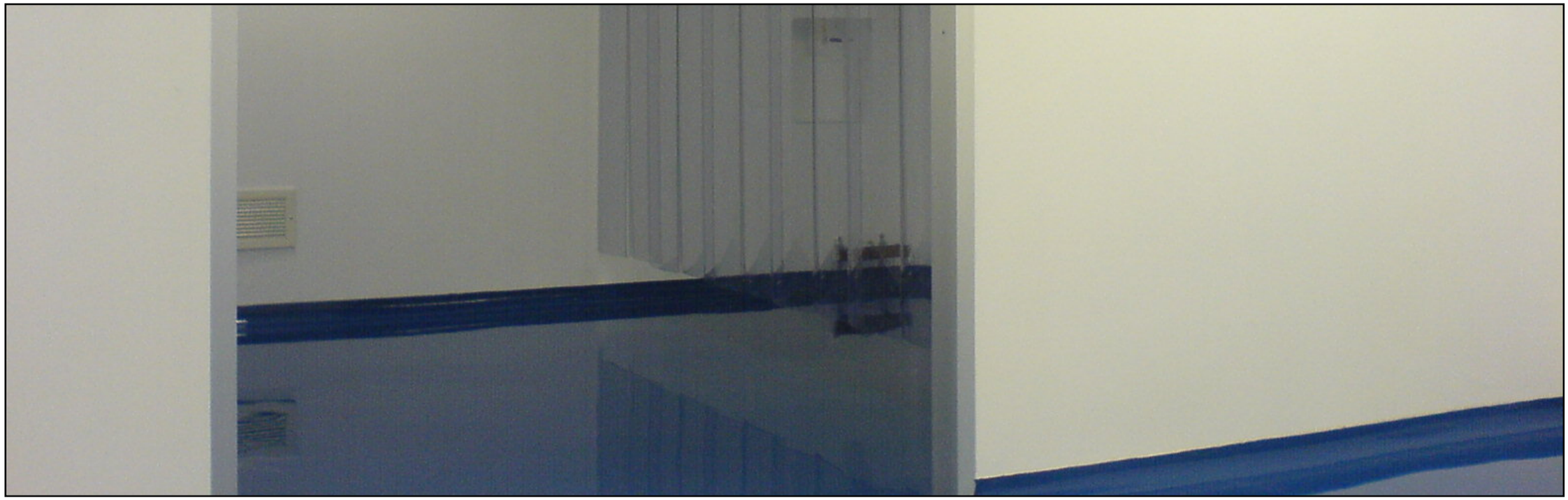
Cobeal has developed audit, survey and inspection tools to help ensure consistency in the biocontaminant facility certification process. These tools are flexible enough allow for the physical and procedural differences between biocontainment facilities necessitated by the type of work being conducted and the environmental conditions of the location, while at the same time providing a consistent approach.

Cobeal discusses findings of the audit, survey or inspection with the institution's personnel and management. Within the biocontainment facility, corrective actions are taken for all deficiencies identified during the audit process. Certification of the biocontainment facility will not provided and declared functional until all deficiencies have been adequately addressed.

The complexity of biocontainment certification goes beyond the scope of this manual. For details and further information, please contact the COBEAL Biosafety program.

Biocontainment Equipment

Biocontainment facilities



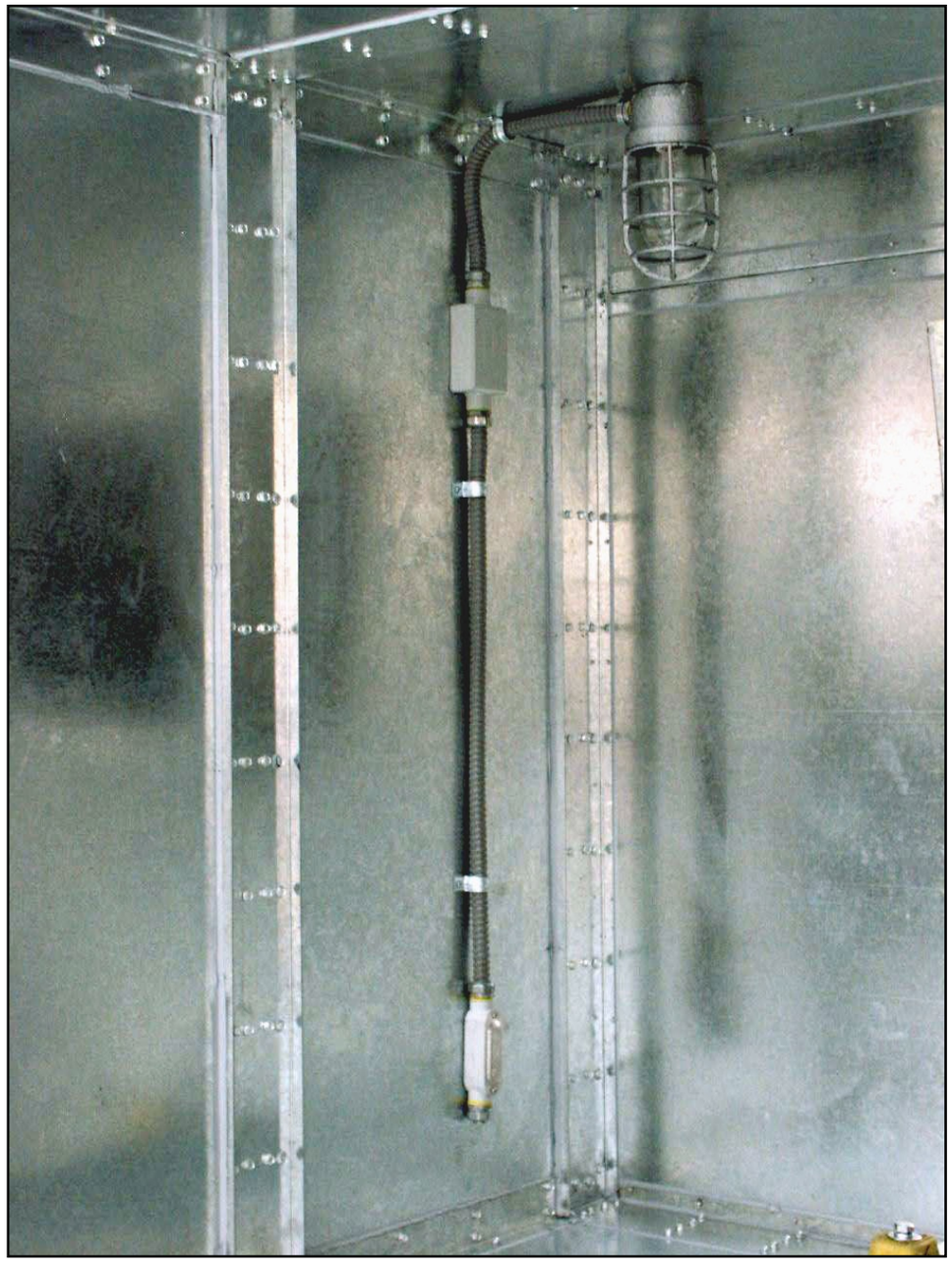
Laminar Flow equipment

The design of biocontaminant facility systems to meet biosafety level requirements presents special challenges. Cobeal closely designs and studies all equipment and systems for safety, capital and operating cost, maintenance, accessibility, construction and validation schedule goals, as well as any additional client requirements. Cobeal coordinates its efforts with those of the process and architectural design teams in the early conceptual and preliminary phases of the project to meet these critical factors.

Cobeal's biocontaminant facility design provides the primary barrier protection from the accidental release of infectious agents or toxins outside the biocontainment facility to the environment. The design and construction of the equipment contributes to the facility's efficiency as well as the workers' protection. It also provides a

barrier to protect people, and the environment outside of the biocontainment facility from infectious agents or toxins that may be accidentally released from the biocontainment facility. Biocontainment facility design is one element of “engineering controls” Cobeal uses in biocontainment facility design and biosafety.

Cobeal biocontaminant equipment

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