Bespoke Biosafety:

Building a Custom Biosafety Cabinet Around Your Laboratory Automation Equipment

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What happens when your risk assessment identifies that the large equipment (3D bioprinters, cell sorters, automated liquid handlers, etc.) you plan to use requires a primary containment device, such as a biosafety cabinet (BSC)? *Will it safely fit inside a standard 6 ft. (1.8 m) BSC while still providing adequate containment?* In some cases, a custom BSC designed specifically to fit around your equipment and your laboratory processes may be necessary to provide sufficient personnel, product, and environmental protection. In this article, we will discuss:

1. How to determine if your equipment needs to be placed inside a custom biosafety cabinet
2. What equipment features and user requirements are important discussion points for custom BSC design
3. Where to physically install a custom BSC in your lab space
4. Considerations for performance testing and field certification to ensure proper BSC airflow, operations, and containment with the equipment inside

Standard Class II Type A2 Biosafety Cabinet

Custom Biosafety Cabinet Risk Assessment

When conducting a risk assessment for laboratory work involving biological materials, one important aspect is to review the procedural risk factors and laboratory processes that are going to be performed with the hazardous agent(s).[1-4] This should include a review of specific laboratory equipment where biohazardous materials will be handled or processed. Additionally, the use of chemicals or radiological materials simultaneously along with the biological agents or in the same piece of equipment should be considered as part of a complete risk assessment. For more detailed information about conducting thorough risk assessments, especially those involving risk mitigation using BSCs, consider reviewing references 1-4.

Small bench-top aerosol generating equipment such as blenders, sonicators, vortexers, grinders, and microcentrifuges may easily fit inside a primary containment device, like a BSC, without any necessary modifications to the containment device. However, other larger equipment used to work with biological materials may be too large or uniquely shaped to be placed inside a standard, off-the-shelf BSC model. The BSC selected must not only be able to physically contain the device but also be large enough to allow for adequate airflow around the equipment and provide the product, personnel, and environmental protections afforded by that type of BSC. Review of this equipment prior to purchase by laboratory users and safety subject matter experts will facilitate consideration of the options for risk mitigation strategies for the work with this device. These discussions may also involve the equipment manufacturer and containment device manufacturer, however, ultimately the risk assessment and selected control measures are the responsibility of the user. These large pieces of equipment may present additional safety concerns including the spillage of fluids that are added to or produced by the equipment, the moving parts of the equipment, and ergonomic issues associated with manipulating materials or the equipment itself. Therefore, early consultation with safety professionals should be part of the risk assessment process for the use of new or large equipment that may be used with biological agents or multiple types of hazardous materials.

Depending on the needs of the researcher, the equipment requiring containment, and the hazards associated, BSCs may require smaller modifications (such as an altered front sash to accommodate the eyepieces of a microscope, changes to the work surface to accommodate small equipment or containers, or the placement of a plate or shield in the center of the front sash and the BSC's air intake opening such as for use with radiological materials[2]), or the BSC may need to be built from scratch for the equipment and research process(es). Examples of pieces of equipment, depending on their size and shape, that may require custom BSCs include 3D bioprinters, syringe or capsule fillers, cell sorters or flow cytometers, fermenters or bioreactors, bulk weighing devices, and automated liquid handling equipment.

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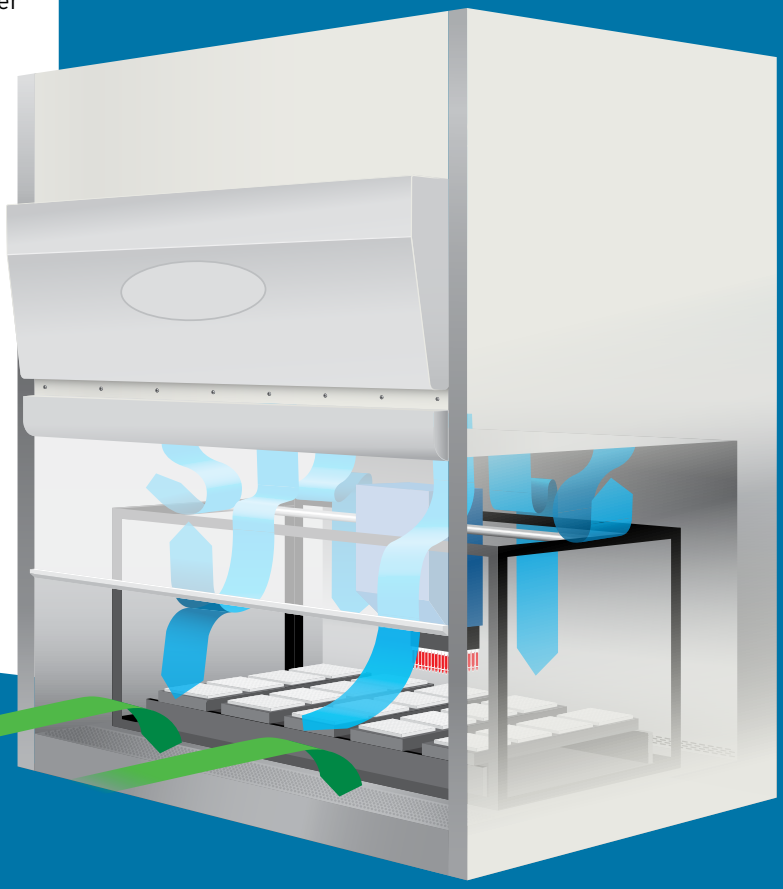
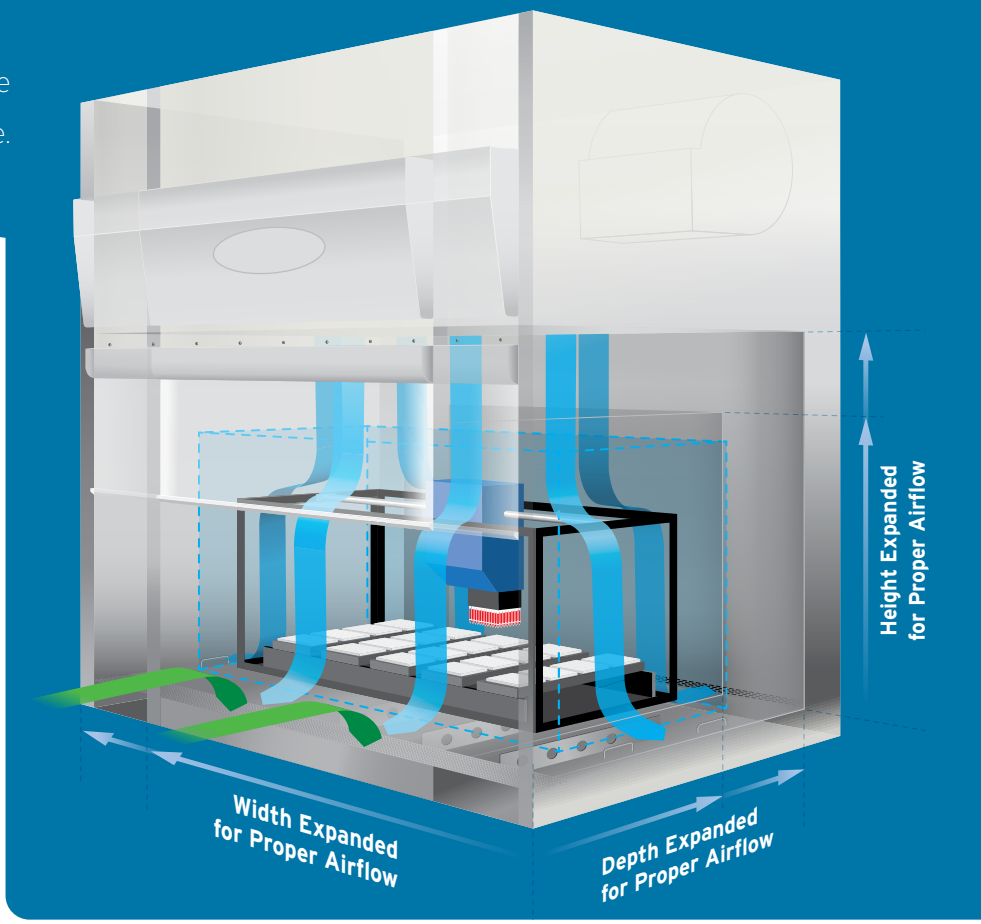


Standard biosafety cabinet with obstructed airflow caused by overcrowding the work zone.



Augmented biosafety cabinet to accommodate the oversized equipment inside the work zone.

Considerations for Your Equipment and BSC Design

Once it has been determined that the equipment needs a biocontainment solution and will not fit inside a standard biosafety cabinet, you should reach out to your selected BSC manufacturer to begin the custom design process. You should be ready to discuss the specifications and needs of the equipment, processing steps, and requirements of the biological or other hazardous materials to be safely handled. **You should get assistance from the equipment manufacturer and your safety subject matter experts to help consider the following items:**

Equipment Specifications

Likely the first consideration for a custom BSC is the dimensions of the equipment that needs to be contained inside the work zone. As mentioned previously, the custom BSC needs to not only adequately fit the piece or pieces of equipment but also still allow for proper functionality and the level of protection afforded by a Class II cabinet. This means that the equipment cannot impact the BSC's air curtain or the HEPA-filtered downward laminar airflow provided to the BSC's work surface. Additionally, some of these larger pieces of equipment may be of substantial weight and exceed the recommended capacity of a traditional cabinet's work surface or base stand. The NSF/ANSI 49 – 2020 Informative Annex 1 notes that the base stand and supports for the BSC should be considered as part of the initial requirements assessment.[3] In the custom BSC design process, the weight of the equipment may therefore lead the BSC manufacturer to install reinforcements to the work surface and/or base to accommodate the equipment.

In addition to its size and weight, the equipment may have additional specifications or requirements that must be evaluated during the custom design process. *Is the equipment particularly sensitive to vibrations? Does the device need to be run at a particular temperature or does it generate significant amounts of heat?* The work surfaces can be designed to provide additional stabilization against vibrations or to include heating or cooling coils to maintain the necessary temperature to run the equipment. Additionally, utility services such as electrical outlets and vacuum or compressed air systems, should be carefully considered for use in BSCs.[2,3] The equipment may need to be plugged into the BSC and this supply of power could be impacted by the BSC's own electrical needs for its proper function.[3] The electricity needs of the custom BSC with the equipment inside of it should be reviewed to ensure the laboratory facility can provide an adequate source of power with the right voltage and amperage to support the performance of both the BSC and the equipment running within it.

Work Processes

Another topic to consider is the process or workflow that needs to be performed with the equipment contained inside the BSC. Mapping out a benchtop space with simulated equipment and materials and performing a test run of the laboratory process may be useful in determining the appropriate width and depth of work surface that is needed.[3] *Would it be useful to have space next to the equipment inside the BSC to prepare materials or samples that need to go into the equipment? Will biohazardous waste produced by the equipment need to be collected and stored in the BSC before being treated or prepared for disposal?* This additional work surface width should be planned into the custom BSC design. *Are there other pieces associated with, or connected to, the equipment that do not need to be housed within the BSC but should be nearby?* For example, a computer tower or monitor that runs the equipment or displays the output may need to be

Custom Class II Biosafety Cabinet designed specifically to house a robotic liquid handler for a pharmaceutical manufacturing application. This one-of-a-kind BSC model is outfitted with a reinforced work surface, hinged access opening, and additional cord pass-through ports.

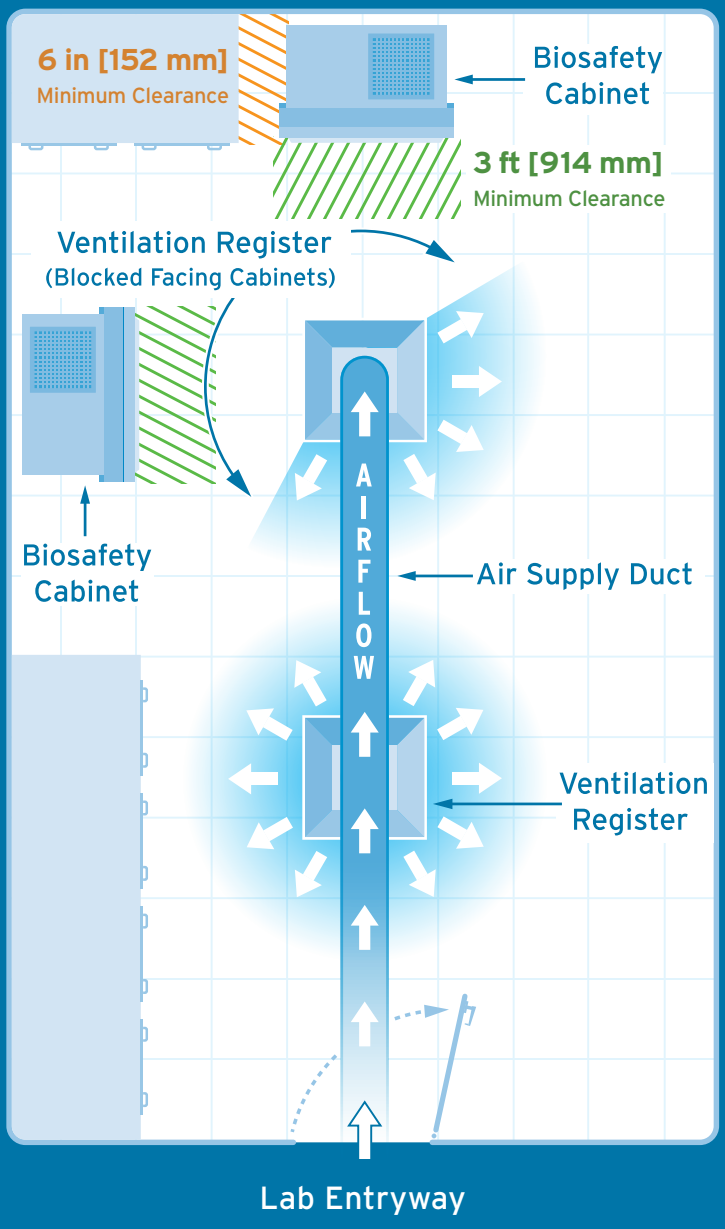
connected to the equipment in the BSC work zone but may not itself require containment. It is possible to have negative pressure pass-throughs on the side(s) of the custom BSC to port tubing, power cables, data cables, or other types of connections to non-contained, associated equipment. These ported devices may be placed on a lab bench next to the cabinet, depending on the lab's layout. However, a shelf can be built on the exterior wall(s) of the custom BSC that can support this additional equipment if there is no existing casework, or if it is more convenient for the BSC user.

The need to access the equipment should also be evaluated when designing your custom BSC. *Once the equipment is installed in the custom BSC work zone, does it ever need to be removed or will it remain permanently installed?* If the equipment must be moved frequently or is particularly cumbersome to move, it may be possible to design the work surface in such a way that it can slide or roll out of the work zone, allowing access to the equipment. Alternatively, the front of the BSC can be designed to open with double doors that swing outward, and the work surface can be placed on wheels so it can be easily removed from the cabinet with the equipment on it. The accessibility and removability of the equipment may also be important to ensure the device can be properly maintained, cleaned, or decontaminated. Additionally, consider whether the equipment needs to be accessible from multiple sides during normal operations and/or maintenance. It may be possible to allow for access to the equipment from several sides while it is in operation by having additional openings such as back or side access panels that are built into the BSC design, provided that it is still possible to maintain adequate containment with these additional access openings.

This custom Class II walk-in biosafety cabinet utilizes a modular design to allow for on-site assembly and an isolation table to minimize vibration on the contained automation equipment.

Custom Biosafety Cabinet Placement in the Laboratory

Now that the dimensions, shape, technical specifications, and equipment adjacencies for the custom biosafety cabinet have been determined, it is important to consider the laboratory space this BSC is proposed to be installed into. There are several facility considerations for both the transportation through existing elevators, hallways, and doors[3], as well as the connection to existing building mechanical and electrical systems.[2,3] Depending on the size of the equipment contained inside, a custom BSC can become quite large. It is essential to evaluate whether the custom BSC can be moved into the laboratory as one, completely built device or if the BSC needs to be constructed in smaller modules that will require assembly once in place within the laboratory.



Also, for any BSCs that must be hard ducted or canopy connected to the building's exhaust system, both the physical location and placement of those connection points along with the capacity of the building's HVAC system must be considered before installing the cabinet.[2,3] The location of existing supply and exhaust vents in the laboratory may limit the placement of the custom BSC or necessitate construction activities to provide a new exhaust connection that is in a more ideal location for the installation of this piece of equipment. The user should review the proposed custom BSC's overall dimensions with their facilities management and/or engineering teams and the BSC manufacturer to come up with the best solution for the construction and installation of the cabinet into the laboratory.

When considering the optimal location for custom BSC installation, remember that generally biosafety cabinets should be installed:

1. Away from areas of personnel traffic, doors, air supply ventilation, windows, fans or air conditioning units, and chemical fume hoods or other equipment that may impact the BSC's airflow
2. Such that there is adequate clearance on all sides of the BSC to access the equipment, access the cabinet itself for maintenance, allow for adequate airflow into and out of the BSC, and allow for airflow and filter testing of the BSC
3. Close to the location of an electrical outlet that can support the BSC and its internal equipment load[2,3,5]

The access needs for the equipment inside the custom BSC were discussed in the previous section, but these considerations will also impact the location and placement of the cabinet within the laboratory. If the work surface was designed to be moved in and out of the custom BSC, the BSC's front face can be opened widely, or there are added back or side access panels or shelving permanently integrated into the structure of the BSC, the custom cabinet must be installed in the laboratory somewhere that these designed aspects can be appropriately utilized and operated.

When deciding where in the laboratory to place your BSC, ensure a minimum clearance of 3 ft. (914 mm) in front of the cabinet and 6 in. (152 mm) from each side.

If possible, it may also be beneficial to consider the need for a custom BSC when designing or renovating your laboratory space to allow for the necessary clearances, utilities, and access points to the cabinet. Additionally, since both the custom BSC and the equipment inside of it are likely to be difficult, if not logistically implausible, to remove from the lab once installed these devices need to be accounted for during whole room decontamination or fumigation. The compatibility of the custom BSC and its enclosed equipment with your proposed chemical disinfectants should be evaluated and reviewed by the lab user, a safety professional, and the equipment and/or BSC manufacturer(s).

Certification and Smoke Testing

During the custom BSC design process, it is critical to ensure the cabinet will provide the necessary personnel, product, and environmental protection that it is being designed for once the equipment is installed in the BSC. The cabinet manufacturer can perform testing using bacterial spores, aerosol tracers, or smoke to evaluate and visualize the custom BSC design and performance with a mock-up of the equipment inside. This may be requested by the user or considered by the BSC manufacturer if there are concerns about the custom BSC's design. This equipment mock-up testing and visualization may lead to changes to the design to ensure adequate protection is provided by the device or to allow for easier certification of the cabinet. For example, the access openings of the custom BSC may need to be moved or altered to accommodate the equipment and maintain aerosol containment. Additionally, the BSC manufacturer may find that they need to segment the downflow diffuser screen that covers the HEPA filter located above the work surface so the screen can be more easily removed to allow a BSC field certifier to scan this HEPA filter while the equipment is in place.

As with standard Class II biosafety cabinets, once these custom BSCs are installed by the manufacturer or the user, they should be field certified by an accredited field certifier to ensure they are functioning properly and maintaining containment based on testing instructions provided by the manufacturer.[2,5] These instructions will often include mapping the downflow velocity, testing the BSC's particle containment, measuring the airflow velocities, and the expected smoke patterns.[5] Due to the complexity of custom cabinet design, the manufacturer will need to provide testing instructions and certification requirements both for when the custom BSC is empty and also a methodology for certification when the equipment is installed in the custom BSC. The field certifier will need to evaluate and certify the custom BSC with an empty work zone and again with the equipment installed since the equipment's placement will change the downflow grid for airflow testing. Subsequent custom BSC field certifications and any necessary maintenance may warrant surface decontamination of the equipment housed inside of the BSC or fumigation of the entire custom BSC prior to manipulating or disassembling it. As mentioned above, the material compatibility and disinfectant's efficacy on biological agents in use in the BSC needs to be reviewed and evaluated before releasing the equipment for certification or maintenance activities. If the custom BSC will be used in the future for new or different equipment than it was designed for, additional smoke testing and consultation with the manufacturer may be required by the certifier to evaluate and certify the new configuration.[2]

Conclusions

The risk assessment and overall process necessary to design a custom BSC for a piece of equipment that requires containment involves many considerations about the contained equipment, the laboratory environment, the custom BSC, and BSC testing and field certification. These considerations include:

1. The equipment's dimensions and weight, its sensitivity to vibrations, operating temperature requirements, necessary electrical voltage and amperage, and connection to electricity or other utilities
2. The location of associated equipment and need for processing space
3. The need to access to different sides of the equipment and whether the equipment is permanently installed in the BSC or should be easily removed
4. The need for connection to the building's exhaust system and optimal location within the laboratory room
5. The custom BSC's ability to contain aerosols and have its performance field certified

Common considerations for custom BSC design, placement, and certification are presented and detailed above, however, each custom cabinet design and installation will be different and unique based on the equipment, facility, and user needs. **This article is intended to facilitate discussions and considerations between the user, safety subject matter experts, the equipment manufacturer, and the BSC manufacturer.** The goals of these discussions are to ensure the custom BSC is:

1. Designed to provide adequate containment, functionality, and access to the equipment installed within the BSC
2. Located in the lab where it can properly function, connect to the building's utilities, and be operated by the user
3. Able to be field certified with the desired equipment inside the custom cabinet's work zone

Given the many literal and metaphorical moving parts in the installation, operation, and certification of a custom biosafety cabinet, it is critically important that you approach the design process with an adequate understanding of each part and consult with the necessary experts from the very start.

References:

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