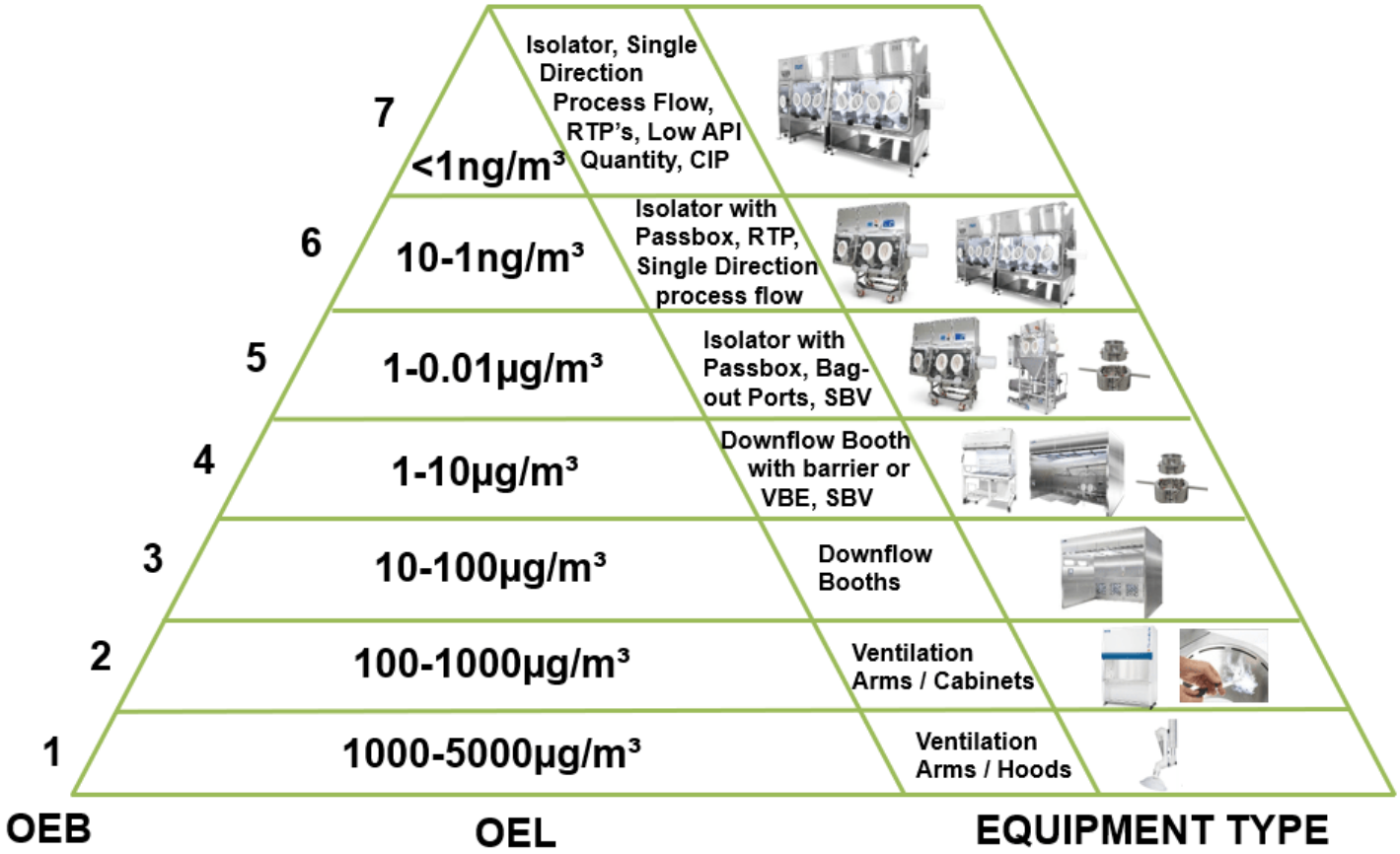
Handling HPAPIs: Choosing the Best Containment Strategies



The determination of personnel and environmental potential exposure is usually required for the safe handling of high potency active pharmaceutical ingredients (HPAPIs). A selective process in selecting the most appropriate strategies is also a must for the assurance of containment. HPAPIs are characterized by the occupational exposure limit (OEL) of at or lower than 10 micrograms per cubic meter of air (µg/m3). The lower the value, the more potent the compound; and the greater need for a higher level of containment is required. Their ability to target pathogens are more precise and more selective in comparison with the other conventional medicines in the market.

Antibody drug conjugates (ADCs), which use very toxic molecules specifically targeting cancer cells serve as one example for HPAPIs. These compounds represent an advancement in oncology treatment being highly potent cytotoxic drugs that do not harm the healthy cells unlike conventional chemotherapy.

As the number of potent compounds in the pharmaceutical development continues to increase, the opportunities for HPAPI manufacturers will rise as well. At Esco Pharma, the provision of the best product and service delivery is taken seriously. As we take on newer challenges, we are continuously soaring towards a greater progress. The issues regarding contamination for pharmaceutical, agricultural, medical, and production operations can be eliminated as we yield protection with containment.

In the manufacture of these highly potent compounds, specialized considerations are needed to be deliberated for the facility design, equipment, operation, and safety to achieve the best level of containment of the drug product. The assurance of environmental and employee safety exposure would require specialized containment. The following factors show the facility design of a typical kilo-laboratory for HPAPI handling:

- Room pressure controls designed for containment, including monitoring and verification, with the main HPAPI-handling area (negatively pressured area to the surrounding rooms)
- Airlocks around the manufacturing and laboratory spaces must provide gowning and degowning area with proper pressure controls
- Misting showers must be included in the degowning and exit areas to purge the personnel of any unwanted contaminants prior to the removal of personal protective equipment (PPE)
- Only important trained employees must have access to the HPAPI-handling areas
- Heating, ventilation, and air conditioning (HVAC) systems must be designed for single-pass air with temperature, humidity, and particle controls
- Safe-change filters inside isolators, ventilated enclosures, general HVAC exhaust system, etc., must be used in the filtration and capture of contaminants
- Preventive maintenance and proper change-control procedures for the assurance of an effective operating equipment

Engineering controls are also a must in using HPAPIs, as they are the primary source of containment and isolation of potent compounds. There are five stages in the hierarchy of controls that define the best level of protection and it is as follows:

- Product isolation: closed-system glassware and reactors, α/β valves
- Containment equipment: isolators, ventilated laminar flow enclosures, rapid-transfer ports, local exhaust ventilation, closed-system cleaning via clean-in-place
- Facility design: air pressurization, high number of air changes, single-pass air, restricted access, airlocks, safe-change filters, misting showers
- PPE: chemical suits needed for solvents and reagents, coveralls and hoods, powered air-purifying respirator (PAPR), proper glove selection
- Personnel: proper training, procedures and policies, education, health monitoring

BAND	OEB 1	OEB 2	OEB 3	OEB 4	OEB 5	OEB 6	OEB 7
OEL	>1000 - 5000 µg/m³	>100 - ≤1000 µg/m³	>10 - ≤100 µg/m³	>1 - ≤10 µg/m³	<1.0 - 0.01 µg/m3	0.01 - 0.001 µg/m3	<0.001 µg/m³ - <1 ng/m³
Equipment to Use	Ventilation Containment	Ventilation Containment or Flowhoods without downflow (single pass Fume cabinets)	Downflow Booths or VBEs, Flowhoods	VBEs or DFBs with higher containment, Flowhoods with downflow and inflow for small volume	Isolators recommended however if handling less than 3kg and short task duration, low dust cloud potential reverse oRABs possible	Isolators	Isolators

Production OSD				VBEs DFB with high containment screen	WDCI DFB with flexible isolator	WDCI	WDCI
Production common application		Fume Hoods	Downflow Booths	Isolators			
Production Injectable If Aseptic needed (with HPV)				ACTI (Aseptic Containment Isolator) CBI-U (Containment Barrier Isolator Unidirectional) GPPI (General Processing Platform Isolator)	ACTI (Aseptic Containment Isolator) CBI-U(Containment Barrier Isolator Unidirectional) GPPI (General Processing Platform Isolator) with closed transfer	ACTI (Aseptic Containment Isolator) With complete closed transfer (RTPs)	ACTI (Aseptic Containment Isolator) With complete closed transfer (RTPs)
R&D Qc/ IPQC Sampling		FHs (Fume Hoods) EFF (Esco Frontier® Floor) EFA (Esco Frontier® Acela™) CYT (Cytoculture ™ Cytotoxic Safety Cabinets)	FHs (Fume Hoods) EFF (Esco Frontier® Floor) EFA (Esco Frontier® Acela™) CYT (Cytoculture ™ Cytotoxic Safety Cabinets)		GPPI (General Processing Platform Isolator) CBI-T (Containment Barrier Isolator Turbulent) roRABs (Reverse open RABs) VBEs (if small quantity)	CBI-T (Containment Barrier Isolator Turbulent)	CBI-T (Containment Barrier Isolator Turbulent)

Table 1. OEB/OEL with further recommendations of Esco containment equipment.

Margaret Stava

562 355-5859

margaret@biopharmequip.com