

# Shielded BSCs in Radiopharmaceutical Practice under USP <825>: Regulatory Requirement or Risk-Based Engineering Solution?



## 1. Introduction

Radiopharmaceuticals occupy a unique position in pharmaceutical practice: they simultaneously require compliance with aseptic compounding standards under USP <825> and radiation protection requirements from the facility's Radioactive Material (RAM) License under NRC or Agreement State authority. No other class of drug product demands this dual compliance at every single dispensing event.

USP <825> (Radiopharmaceuticals Preparation, Compounding, Dispensing, and Repackaging) became compendially applicable on November 1, 2023, establishing uniform minimum standards for all practice settings. Its facility and engineering control requirements particularly the mandate for an ISO Class 5 Primary Engineering Control (PEC) for all sterile preparation have direct and practical implications for equipment selection in every nuclear medicine department and nuclear pharmacy in the United States.

This article explores a key consideration in radiopharmacy facility planning: whether Lead-Shielded Biological Safety Cabinets (Shielded BSCs) are required under USP <825> or adopted as part of a risk-based engineering approach. Drawing directly from the regulatory text of USP <825>, this paper demonstrates that while the lead shielding requirement originates from the RAM license rather than USP <825>, the two obligations are must be addressed concurrently in facility design and operations and an integrated Shielded BSC is the one of the most effective solution when both are considered together.

## 2. The Dual Hazard of Radiopharmaceutical Compounding

### 2.1 Classification and Regulatory Scope

USP <825> Section 1 defines radiopharmaceuticals as a subset of RAMs under NRC control and a subset of prescription drugs under FDA control. Critically, they are not classified as Hazardous Drugs under NIOSH, placing them outside USP <800> and within the specialised framework of USP <825>.

### 2.2 Balancing Aseptic Technique and Radiation Safety

USP <825> Section 1 explicitly acknowledges the fundamental tension in radiopharmaceutical practice:

*"Strict adherence to all typical aseptic handling practices is not possible in many scenarios where radiopharmaceuticals are handled. Thus, it is necessary to balance aseptic handling practices (patient safety) with radiation protection practices (worker safety)."*

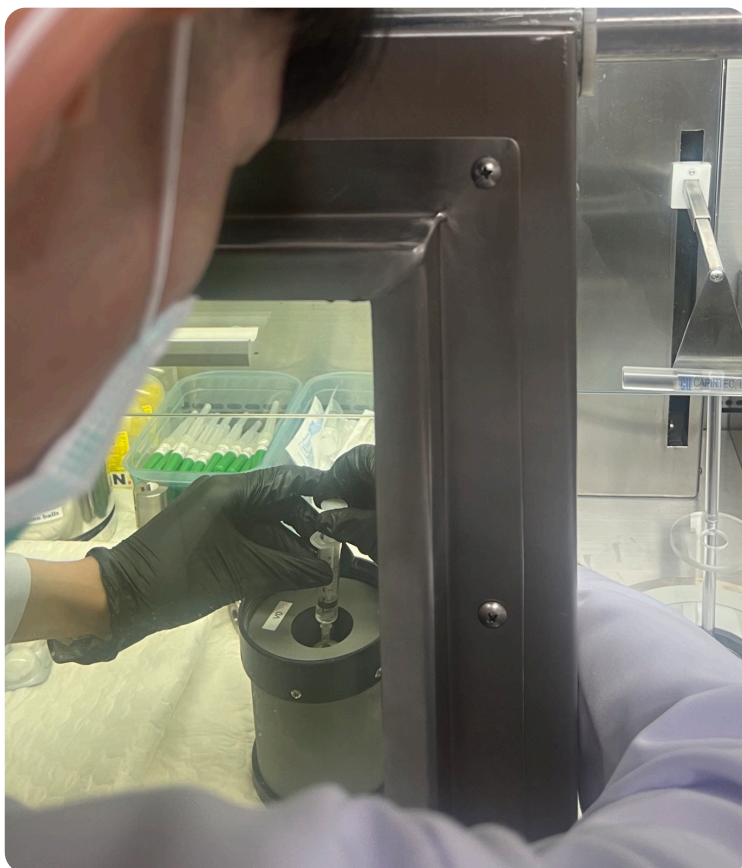
This tension is at the heart of every equipment decision in radiopharmacy. A Shielded BSC is the engineering solution that resolves it, providing ISO Class 5 aseptic conditions (patient safety) and integrated lead shielding (worker safety) within a single validated device.

### USP <825> Section 2 Four Principles of Radiation Safety (direct text)

2.1 Time: Minimise handling time. Personnel may work quickly in and out of the ISO Class 5 PEC. 2.2 Distance: Increase distance from RAM. Remote handling tools may be used within an ISO Class 5 PEC. 2.3 Shielding: The use of shielding (L-block, torso, vial, syringe shields) is usually required throughout handling, including within an ISO Class 5 PEC. 2.4 RAM Contamination Control: Vertical airflow (not horizontal) in a PEC is used to control contamination.



Nuclear Medicine workstation



Setting the standard in radiopharmaceutical safety with Shielded BSCs Class II

## 3. What USP <825> Actually Requires: Facilities and Engineering Controls

### 3.1 Primary Engineering Control (PEC): Definition and Approved Types

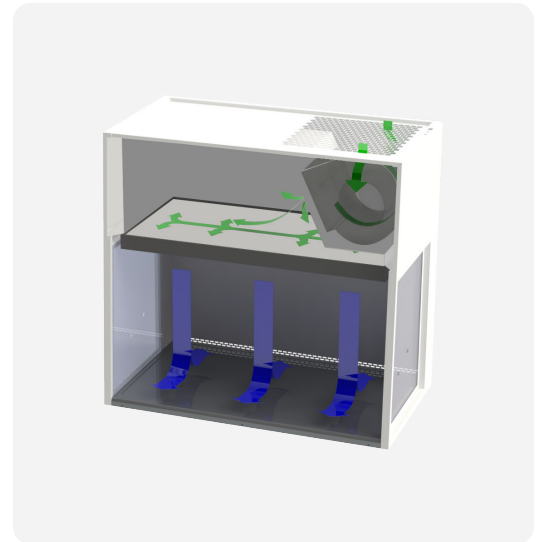
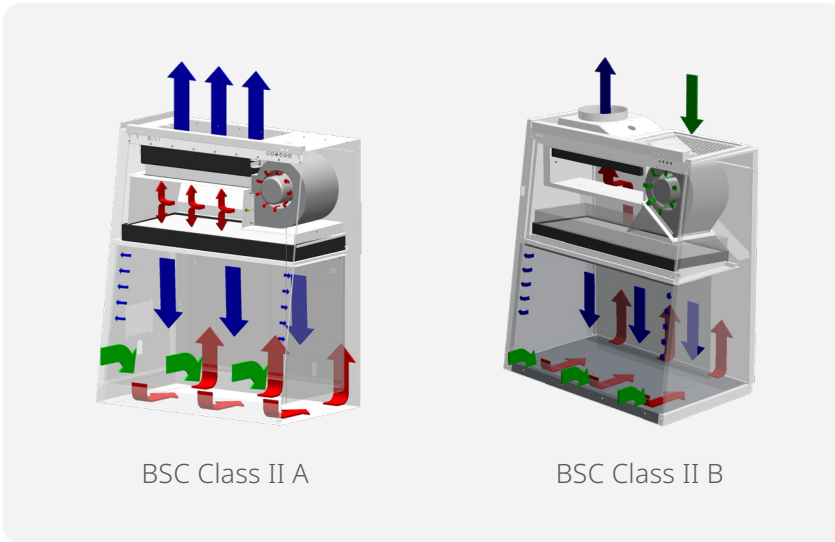
USP <825> Section 5.1 requires that all sterile radiopharmaceutical preparation be performed within a PEC that maintains ISO Class 5 or better air quality. The chapter defines approved PEC types explicitly:

### USP <825> Section 5.1 Biological Safety Cabinet (BSC) Class II (direct text)

A Class II BSC is a cabinet with an open front, inward airflow, downward unidirectional HEPA-filtered airflow, and HEPA-filtered exhaust. The BSC is designed to provide worker protection from exposure to biohazardous material and to provide an ISO Class 5 or better environment for preparing sterile radiopharmaceuticals.

## BSC Class II airflow Diagram

## Vertical Laminar Airflow cabinet Diagram



■ Room air (inflow)   
 ■ Unfiltered/potentially contaminated air   
 ■ ULPA-filtered air

■ ULPA-filtered air   
 ■ Room air/inflow air

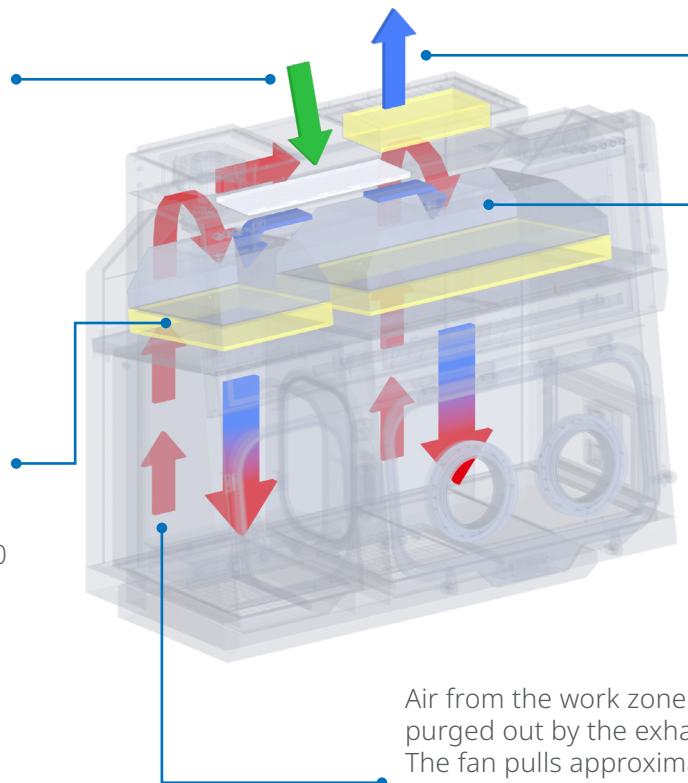
## Airflow Patterns For Streamline® Compounding Isolator Models

### Closed Systems (Isolator) Recirculating Airflow

Ambient air is pulled through the inlet pre-filter G4 and supply filter located on top of a laminar the isolator.

The downflow filter creates airflow providing ISO Class 5 air cleanliness (ISO 14644-1) to the main chamber and pass-through, with a down flow velocity of 0.40 m/s +/- 20%.

■ HEPA-filtered air   
 ■ Unfiltered/potentially contaminated air   
 ■ Room air/inflow air



Approximately **30% of the purged air is exhausted** through the filter to prevent heat build-up inside the isolator.

Exhausted air is **replenished by ambient air** coming from the top inlet pre-filter G4 that has 80% efficiency.

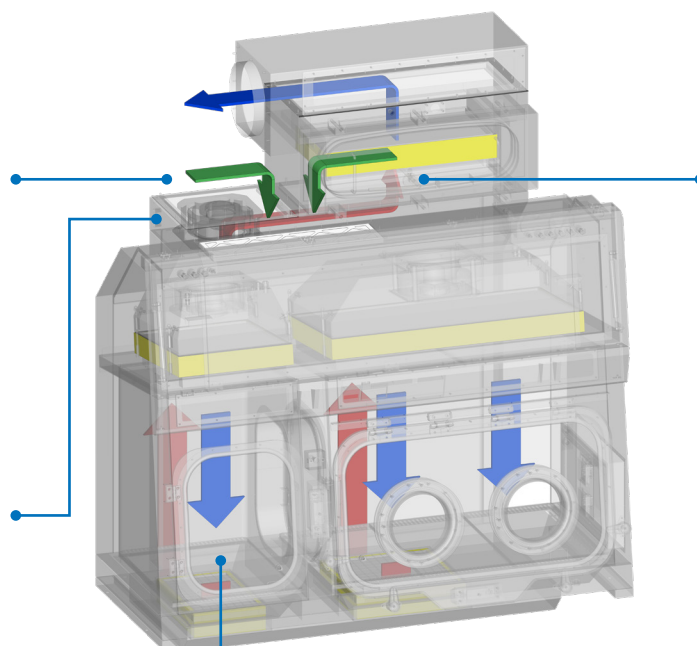
Air from the work zone and pass-through is quickly purged out by the exhaust fan to keep the area clean. The fan pulls approximately **70% of the purged air back to the plenum**, passes through the HEPA downflow filter again, and is recirculated back to the work zone and pass-through.

## Airflow Patterns For Streamline® Compounding Isolator Models

### Closed Systems (Isolator) Total Exhaust/Single Pass Airflow

Ambient air is pulled through the inlet pre-filter G4 and supply filter via the main fans at the top of the isolator. This creates positive pressure on the plenum which provides the downflow of air with a velocity of 0.40 m/s  $\pm$  20%.

The pre-filter extends the life of the filters by trapping larger particulates that can easily clog the main filters.



Air from the work zone and pass-through is then quickly purged by the fans to keep the area clean. The purge is completely exhausted through HEPA filters as well; ensuring that only clean air is exhausted back to the environment

- HEPA-filtered air
- Unfiltered/potentially contaminated air
- Room air/inflow air

This downflow supply then provides an ISO Class 5 environment and unidirectional airflow inside the isolator; thus, protecting the materials inside the main chamber and pass-through.

Other approved PEC types include:

- Laminar Airflow Workbench (LAFW) must provide vertical unidirectional HEPA-filtered airflow
- Hot Cell or Closed Systems integrated HEPA filtration systems certifiable to ISO Class 5

**A fume hood is explicitly excluded.** USP <825> FAQ confirms: a fume hood does not contain a HEPA filter, cannot protect the sterile radiopharmaceutical from microbial contamination, and cannot be considered a PEC for sterile drug preparation. It cannot be retrofitted into an ISO Class 5 device.

### 3.2 Radiation Shielding Within the PEC: What Section 2.3 Says

USP <825> Section 2.3 is the most directly relevant provision for the shielding question:

#### USP <825> Section 2.3 Shielding (direct text)

Radiation exposure to personnel decreases with the use of shielding materials. Therefore, handlers of radiopharmaceuticals may use various shielding materials (e.g., lead, tungsten) in various configurations. The use of shielding, such as L-block, torso, vial, and syringe shields, is usually required throughout the radiopharmaceutical handling process, including within an ISO Class 5 PEC.

The phrase "usually required" indicates that shielding is a commonly expected and widely implement control measure of radiopharmaceutical handling within the PEC. USP <825> further acknowledges shielding as a known constraint on airflow.

### 3.3 Airflow Acknowledgement: Shielding as a Known PEC Design Factor

USP <825> Section 2.3 is the most directly relevant provision for the shielding question:

#### USP <825> Section 5.1 The Radiopharmaceutical Processing Environment

HEPA-filtered air must be supplied in the direct processing area (DPA) at a velocity sufficient to sweep particles away from aseptic processing areas and maintain unidirectional airflow as much as possible during operations, given the limitations added from the radiation shielding in the DPA.

This is a significant provision: USP <825> explicitly recognises that radiation shielding is present inside the DPA and that it affects airflow. The standard does not prohibit shielding within the PEC — it accommodates it. An integrated Shielded BSC, where the shielding is engineered into the cabinet as a complete system, is consistent with the intent of USP <825>, which recognizes the presence of shielding within the DPA.

### 3.4 Secondary Engineering Control (SEC) and the SRPA

USP <825> Section 2.3 is the most directly relevant provision for the shielding question:

#### USP <825> Section 5.1 SRPA Definition

A PEC may be located within an unclassified area, without an ante-room or buffer area. This type of design is called an SRPA. Only sterile radiopharmaceutical preparation, preparation with minor deviations, dispensing, and repackaging may be performed in an SRPA. If the SRPA meets ISO Class 8 total airborne particle count specifications, it can also be used for storage and elution of non-direct infusion radionuclide generators (e.g., Tc-99m).

The SRPA is a unique provision of USP <825> that makes the standard practical for the majority of hospital nuclear medicine departments, which cannot build or maintain full ISO-classified cleanrooms.

## 4. BUD Implications: How PEC and SEC Choice Affects Beyond-Use Date

USP <825> Table 7 directly links the choice of PEC and SEC to the maximum permitted BUD. Where a Shielded BSC serves as the ISO Class 5 PEC, highlighted rows apply:

Manipulation	PEC	SEC	Max BUD
Immediate use	—	—	1 hr
Dispensing, repackaging, preparation, preparation with minor deviations	ISO Class 5 PEC e.g. Shielded BSC	SRPA	12 hr
Generator elution (Tc-99m, Ga-68) non-direct infusion	—	SRPA with ISO Class 8 total airborne particle count	12 hr
Generator elution (Tc-99m, Ga-68) non-direct infusion	—	ISO Class 8 buffer area + ISO Class 8 ante-room	24 hr
Dispensing, repackaging, preparation, minor deviations	ISO Class 5 PEC e.g. Shielded BSC	ISO Class 8 buffer area + ISO Class 8 ante-room	24 hr
Dispensing, repackaging, preparation, minor deviations, compounding (sterile components)	ISO Class 5 PEC e.g. Shielded BSC	ISO Class 7 buffer area + ISO Class 8 ante-room	96 hr
Radiolabeled blood components (e.g. leukocytes)	ISO Class 5 PEC e.g. Shielded BSC	ISO Class 7 buffer area + ISO Class 8 ante-room	6 hr (from blood draw)

Key takeaway: a Shielded BSC operating as the ISO Class 5 PEC within a compliant SRPA enables 12-hour BUD for dispensing and preparation, the standard operational window for hospital Tc-99m dispensing. Upgrading the SEC extends BUD further, with the same Shielded BSC throughout.

## 5. USP <825> Compliance Map: Shielded BSC Section by Section

The following table maps specific USP <825> requirements by section to how the Esco Radiopharmacy Hood (Lead-Shielded BSC) addresses each one:

USP <825> Requirement	Section	How Shielded BSC Addresses It
ISO Class 5 PEC required for all sterile radiopharmaceutical preparation	Sec. 5.1	Class II BSC is an approved PEC type; HEPA-filtered downflow and inward airflow maintain ISO Class 5 in the DPA
PEC must be located in a SEC (SRPA or classified buffer room)	Sec. 5.1	Shielded BSC placed within SRPA or classified area per facility design
Vertical downward unidirectional HEPA-filtered airflow and HEPA-filtered exhaust	Sec. 5.1 — Types of PECs	Class II BSC provides downward unidirectional HEPA-filtered airflow with HEPA-filtered exhaust by design
Shielding is “usually required” throughout handling including within ISO Class 5 PEC	Sec. 2.3	Integrated lead shielding provides torso protection at the cabinet level; additional syringe/vial shields used within the PEC as needed
Radiation shielding acknowledged as a known limitation on first air in the DPA	Sec. 5.1 — Processing Environment	Integrated shielding is a designed-in feature; smoke study performed at certification confirms unidirectional flow under actual conditions
Smooth, impervious, cleanable surfaces in SRPA	Sec. 5.2	BSC interior surfaces are smooth, impermeable, and designed for regular disinfection
PEC walls, torso shield, and exposed surfaces cleaned prior to each day of use; check for RAM contamination before cleaning	Sec. 7.3 — Table 5	Integrated shielding surfaces are part of the validated PEC enclosure subject to the same cleaning schedule — no separate external shields to survey independently
Blood component radiolabeling requires ISO Class 5 BSC in ISO Class 7 buffer area	Sec. 10.3	Shielded BSC (Class II BSC) meets the BSC requirement; integrated shielding protects operator during RAM blood radiolabeling

## 6. The Risk-Based Case: Two Frameworks, One Device

### 6.1 The Regulatory Gap USP <825> Does Not Fill

USP <825> mandates an ISO Class 5 PEC. It acknowledges shielding as required within the PEC. It does not mandate that the shielding be integrated into the BSC cabinet itself. That integration requirement comes from the facility's RAM License and ALARA obligations. The gap is closed by engineering judgment and an integrated Shielded BSC closes it most effectively.

### 6.2 Why Integrated Shielding Is Preferable: A Direct Comparison

Criterion	Shielded BSC (Esco Radiopharmacy Hood)	Unshielded BSC + External Lead Shields
USP <825> PEC compliance (Sec. 5.1)	Yes, Class II BSC	Yes, Class II BSC
ISO Class 5 capable	Yes	Yes
Integrated radiation shielding (Sec. 2.3)	Yes, built into cabinet body and sash	No, external L-blocks required separately
Shielding gap risk during syringe handling	Minimal, enclosed enclosure design	Gaps at operator access zones expose extremities
PEC cleaning compliance (Table 5, Sec. 7.3)	Single validated surface, shielding is part of PEC enclosure	External shields must be surveyed and decontaminated separately from PEC protocol

<b>RAM contamination control (Sec. 2.4)</b>	Contained work zone; integrated shielding reduces secondary exposure from spills	External shields can trap RAM contamination; harder to survey and decontaminate
<b>Airflow integrity (Sec. 5.1)</b>	Designed as complete system; smoke study at certification confirms airflow under shielding	External shields may disrupt airflow; not part of certified PEC design
<b>Regulatory defensibility</b>	Single certified device satisfies USP <825> PEC + RAM license ALARA in one validation	Two separate systems; external shields not part of PEC certification

### 6.3 IAEA Operational Level 2A Alignment

The IAEA Operational Guidance on Hospital Radiopharmacy (2008) reinforces the integrated approach. For Operational Level 2A: Tc-99m generator use and cold kit reconstitution, the most common hospital activity, IAEA states that Class II LAF cabinets or isolators “should be equipped with appropriate lead shielding to protect the operator.” The Esco Radiopharmacy Hood is the direct engineering embodiment of this specification.

## 7. USP <825> FAQs: Practical Implications for Shielded BSC Selection

### 7.1 Tc-99m/Mo-99 Generator Elution in an SRPA

USP <825> Section 5.1 permits generator storage and elution in an SRPA meeting ISO Class 8 total airborne particle counts. Section 5.3 requires the sink to be at least 1 m from the PEC and generators. Table 7 caps BUD at 12 hours. A Shielded BSC as the ISO Class 5 PEC within a compliant SRPA fully supports this pathway, the standard hospital Tc-99m operational setup.

### 7.2 Ga-68 Generator Handling and the 511 keV Challenge

Elution of Ge-68/Ga-68 generators may occur in an ISO Class 8 SEC. All container/tubing connections and downstream manipulations must be performed within an ISO Class 5 PEC. Ga-68 emits 511 keV positron annihilation photons, higher energy than Tc-99m (140 keV), requiring meaningful lead attenuation. The Shielded BSC provides the required ISO Class 5 PEC with integrated shielding designed for the higher photon energy.

### 7.3 Fume Hood vs. BSC The USP <825> Position

USP <825> FAQ is explicit: a fume hood is not a PEC and cannot be retrofitted into ISO Class 5. Facilities using a fume hood as their primary sterile preparation environment are non-compliant. A Shielded BSC with HEPA filtration is the compliant replacement that simultaneously addresses product sterility and RAM license radiation protection requirements.

## 8. Esco Radiopharmacy Hood: Engineered for Dual Compliance

The Esco Radiopharmacy Hood (Lead-Shielded Biological Safety Cabinet) is purpose-built for radiopharmaceutical dispensing of generator-produced radioisotopes and dose calibration of all radioisotopes. As a Class II BSC, it is an approved PEC type under USP <825> Section 5.1.

Feature	USP <825> Compliance and Benefit
<b>Class II BSC classification</b>	Approved PEC type under Section 5.1 for all sterile radiopharmaceutical preparation
<b>HEPA-filtered downward unidirectional airflow</b>	Maintains ISO Class 5 in the Direct Processing Area (DPA) as required by Section 5.1
<b>HEPA-filtered exhaust</b>	Environmental protection; consistent with contamination control requirements
<b>Integrated lead shielding (body, sash, viewing window)</b>	Addresses Section 2.3 shielding requirement and RAM license ALARA obligations in a single device; no external shields required
<b>Smooth, impermeable interior surfaces</b>	Meets Section 5.2 cleanability requirements; supports Table 5 daily cleaning schedule
<b>Shielded sash and viewing window</b>	Provides torso protection during dispensing without obstructing aseptic access to the DPA
<b>Applications</b>	Tc-99m dispensing, Ga-68/PET preparation, cold kit reconstitution, blood component radiolabeling, dose calibration, QC testing

## 9. Conclusion

USP <825> requires an ISO Class 5 PEC for all sterile radiopharmaceutical preparation, and Class II BSC is an approved PEC type. Section 2.3 states that shielding is “usually required” within the ISO Class 5 PEC. The RAM license mandates ALARA. Together, these create a dual compliance obligation that cannot be decoupled.

An integrated Shielded BSC addresses both obligations in a single validated device. Facilities that use external L-blocks around an unshielded BSC must manage shielding gaps, separate decontamination of non-PEC surfaces, potential disruption of airflow from poorly positioned shields, and documentation of two separate systems serving two separate regulatory obligations.

The Esco Radiopharmacy Hood significantly reduces these challenges: integrated lead shielding, HEPA-filtered ISO Class 5 airflow, smooth decontaminable surfaces, and a design that USP <825> Section 5.1 explicitly accommodates a Class II BSC with shielding as a known and expected design feature of the radiopharmaceutical processing environment.

The Shielded BSC satisfies a regulatory requirement (ISO Class 5 PEC under USP <825>) and is the risk-based engineering solution for the shielding obligation (RAM License / ALARA). It is not one or the other. It is the only device that is both.

## Reference

*United States Pharmacopeia. USP <825> Radiopharmaceuticals — Preparation, Compounding, Dispensing, and Repackaging. Revision Bulletin Official December 1, 2019. Compendially applicable November 1, 2023.*

*United States Pharmacopeia. USP <825> Postponement Notice (Revision Bulletin, November 22, 2019).*

*International Atomic Energy Agency (IAEA). Operational Guidance on Hospital Radiopharmacy: A Safe and Effective Approach. Vienna: IAEA; 2008.*

*Nuclear Regulatory Commission (NRC). Title 10 CFR Parts 20 and 35. Radiation Protection Standards and Medical Use of Byproduct Material.*

*NSF/ANSI 49: Biosafety Cabinetry — Design, Construction, Performance, and Field Certification.*

## Disclaimer

*This white paper is intended for informational purposes and represents a general review and understanding of comparisons in aseptic barrier systems from different regulatory framework. It does not constitute regulatory guidance, engineering advice, or a product specification. Specific regulatory requirements, process characteristics, and facility constraints will influence the application of this framework to individual program. Manufacturers should engage qualified regulatory, engineering, and quality consultants in developing facility-specific contamination control strategies.*