CETA Application Guide CAG-008

Certification Matrix for Sterile & Nonsterile USP Compounding Facilities

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Certification Matrix for Sterile Compounding Facilities		

The CETA Board of Directors thanks the Action Committee members that contributed to this Guide.

Daniel R. Velasquez, Chair

Elizabeth P. Battaglia, Vice Chair/Secretary

Josh Buffat

Wayne A. Copeland

Lew Exner

Bernard Guarino

Ralph McBride

David S. Phillips

CAG Administrator: R. Vijayakumar

CAG Administration Committee Chair: Tony Caughron

CETA Board Approval

Committee	Title	Signature	Name	Version	Date
Executive	President	Kimberly Coughlin	Kimberly Coughlin	03:2022	March 2022

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Foreword

The Controlled Environment Testing Association (CETA) is an international organization. One of CETA's objectives is to promote quality assurance through the review of existing standards and the development of new methodologies. One of the main vehicles for obtaining this goal is our CETA Application Guides. The CETA Application Guides have proven to be an immeasurably valuable tool to a wide variety of professionals in our industry. They have been used by many safety professionals, industrial hygienists, facility engineers and quality control personnel.

The standards and other documents normatively referenced, in whole or in part, in this CETA Application Guide are indispensable for its use and application. The content of this CAG has its origin in material found in these reference documents. Preparation and development of these guides are the outcome of work completed by technical committees that are formed by the CETA Board of Directors.

Abstract

The need to have Sterile Compounding Facilities certified on a semi-annual basis has been dictated by current USP Guidelines. This Application Guide will serve as the baseline to have a Sterile Compounding Facility and its Primary Engineering Controls successfully certified in accordance with current ISO, USP, NSF and IEST standards. The requirements are laid out, test methods specified, acceptance criteria listed, and equipment needed to test described secondary engineering controls. Consideration should be taken to choose which testing to use based on Secondary and Primary Engineering Control Type.

Certification Matrix for Sterile Compounding Facilities

1 Introduction

The United States Pharmacopeia (USP) is supporting an environment of enhanced patient care and staff protection by revising chapters <795> and <797> and publishing new chapters <800> and <825>. Although these chapters address significantly varied topics, each shares the requirements for effective secondary and primary engineering controls testing.

The Controlled Environment Testing Association (CETA) has published this application guide (CAG-008) for the purposes of educating the users of certification reports and testing technicians on what tests are required for varied environments and what data must be contained in a compliant certification report. This guide's purpose does not include how the various tests are performed as this information is included in other CETA Application Guides.

Other guidelines applicable to these procedures include CAG-003, CAG-009 and all other CAGs.

2 Scope

The following provides an overview for reviewing the certification of primary and secondary engineering controls in compounding facilities to comply with USP chapter 2019 <795>, proposed 2021 <797>, proposed 2019 <800>, and 2020 <825>.

2.1 Limitations

This review does not include viable environmental monitoring (See CAG-009 for guidance on environmental monitoring). It is limited to the engineering control performance verification (certification) procedures covered in the CETA/CAG document as referenced in chapters <795>, <797>, <800>, and <825>.

Temperature, relative humidity (RH), and lighting are not covered in this document.

Review room design separately.

Primary Engineering Controls and Robotic Enclosures are not fully covered and should be evaluated on a per unit basis taking into account the references provided, manufacturing design, and placement in the facility.

3 Target Audience

Designated Person as defined in USP chapters, Pharmacist-in-charge/Supervising Pharmacist, certifiers and providers of certification services.

4 References

For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

4.1 Reference Documents

CETA CAG-003: CETA Certification Guide for Sterile Compounding Facilities to USP (2022). Controlled Environment Testing Association (CETA), Raleigh, NC, US.

IEST-RP-CC002.4: Unidirectional Flow Clean-Air Devices (2016). Institute for Environmental Standards and Technology (IEST), Schaumburg, IL, US.

NEBB Procedural Standard for Certified Testing of Cleanrooms (2009). National Environmental Balancing Bureau, Gaithersburg, MD, US.

4.2 Cited Bibliography

The following documents are cited in the guide. They may be obtained from the source of the publication.

CETA CAG-002: Compounding Isolator Testing Guide (2008). Controlled Environment Testing Association (CETA), Raleigh, NC, US.

CETA CAG-014: Airflow Visualization Study (2022). Controlled Environment Testing Association (CETA), Raleigh, NC, US.

IEST-RP-CC034.4: HEPA and ULPA Filter Leak Tests (2016). Institute for Environmental Standards and Technology (IEST), Schaumburg, IL, US.

ISO 14644-1: Cleanrooms and associated environments - Part 1: Classification of air cleanliness by particle concentration (2015). International Organization for Standardization (ISO), Geneva, Switzerland.

NSF/ANSI 49 Biosafety Cabinetry: Design, Construction, Performance and Field Certification (2016). NSF International (NSF), Ann Arbor, MI, US.

U.S. Department of Health and Human Services, Food and Drug Administration (CDER,CBER,ORA): Guidance for Industry - Sterile Drug Products Produced by Aseptic Processing - Current Good Manufacturing Practice (2004). Food and Drug Administration, Rockville, MD, US.

USP General Chapter <797>: Pharmaceutical Compounding - Sterile Preparations (2021). United States Pharmacopeia, Rockville, MD, US.

USP General Chapter <800>: Hazardous Drugs - Handling in Healthcare Settings (2019). United States Pharmacopeia, Rockville, MD, US.

USP General Chapter <825>: Radiopharmaceuticals - Preparation, Compounding, Dispensing and Repackaging (2019). United States Pharmacopeia, Rockville, MD, US.

USP 42 NF <795>, <797>, <800>, and <825> (2022). United States Pharmacopeia, Rockville, MD, US.

5 Nomenclature

Airflow Capture Hood - See Capture Hood.

Airflow Visualization Study - Generic term for airflow pattern smoke testing which can be conducted under dynamic or static conditions on PECs or rooms (SECs).

Ante-room - A room with fixed walls and doors where personnel hand hygiene, garbing procedures, and other activities that generate high particulate levels may be performed. The ante-room is the transition room between the unclassified area of the facility and the buffer room. When the ante-room connects to a negative pressure room used in sterile compounding (e.g., hazardous drug compounding room), the ante-room must be an ISO Class 7 or cleaner room. When the ante-room is connected only to a positive pressure compounding room used for sterile compounding, the ante-room must be an ISO Class 8 or cleaner room. It is also a transition area that provides assurance that pressure relationships are constantly maintained so that air flows from clean to less-clean areas, and certain activities may be restricted to areas within the ante-room with a line of demarcation.

BSC - Biological Safety Cabinet, Class II - A ventilated cabinet with an open front and inward and downward unidirectional HEPA-filtered airflow and HEPA-filtered exhaust, providing both personal and preparation protection. A BSC used to prepare a Compounded Sterile Preparation (CSP) must be capable of providing an ISO Class 5 or better environment for preparation of the CSPs. BSCs used for hazardous drug preparation must be externally vented or, in the case of compounded non sterile preparations, may be double HEPA filtered.

Buffer Area: Radiopharmaceutical - An ISO Class 8 or cleaner area with fixed walls and doors within a nuclear pharmacy where PEC(s) that generate and maintain an ISO Class 5 environment are physically located. The buffer area may only be accessed through the ante-room.

Buffer Room: Non-Radiopharmaceutical - ISO Class 7 or cleaner room with fixed walls and doors where PEC(s) that generate and maintain an ISO Class 5 environment for preparation of sterile compounds are physically located. The buffer room may only be accessed through the ante-room or pass through/airlock.

C-PEC - See Containment Primary Engineering Control.

C-SCA - See Containment Segregated Compounding Area.

C-SEC - See Containment Secondary Engineering Control.

CAI - See Compounding Aseptic Isolator.

Capture Hood - Also referred to as Digital Direct Reading Hood (NEBB) or Air Flow Capture Hood that captures and measures a volume of air flowing from a supply or exhaust register into or out of the ventilation system. Note: A capture hood may also be used for inflow on a biological safety cabinet.

CFM – Cubic Feet per Minute. A measure of airflow rate.

Classified Area - A controlled area that maintains an air quality classification based on the ISO14644-1 standard. (USP 797 Glossary Page 33, 2019; USP 825 Glossary Page 26, 2019).

Cleanroom Suite - A classified area that consists of at least one ante-room and one buffer room.

Compounding Aseptic Containment Isolator (CACI) - A type of restricted-access barrier system (RABS) that uses HEPA filtration to provide an ISO Class 5 unidirectional air environment designed for the compounding of sterile HDs.

Compounding Aseptic Isolator (CAI) - A type of RABS that uses HEPA filtration to provide an ISO Class 5 unidirectional air environment designed for preparing CSPs. May not be used for compounding of sterile HDs or volatile radiopharmaceuticals.

Compounded Sterile Preparation (CSP) - A preparation intended to be sterile that is created by combining, admixing, diluting, pooling, reconstituting, repackaging, or otherwise altering a drug product or bulk drug substance. (USP 797 Glossary Page 33, 2019).

Containment Primary Engineering Control (C-PEC) - A ventilated device designed and operated to minimize worker and environmental exposures to HDs by controlling emissions of airborne contaminants through the following:

- The full or partial enclosure of a potential contaminant source
- The use of airflow capture velocities to trap and remove airborne contaminants near their point of generation
- The use of air pressure relationships that define the direction of airflow into the cabinet
- The use of HEPA filtration on all potentially contaminated exhaust streams

Containment Secondary Engineering Control (C-SEC) - The room with fixed walls in which the C-PEC is placed. It incorporates specific design and operational parameters required to contain the potential hazard within the compounding room.

Containment Segregated Compounding Area (C-SCA) - A type of C-SEC with nominal requirements for airflow and room pressurization as they pertain to HD compounding. Nothing more than a category 1 CSP may be prepared in this room. (USP 800 Glossary Page 13, 2019).

Containment Ventilated Enclosure (CVE) - A full or partial enclosure for nonsterile compounds that uses ventilation principles to capture, contain, and remove airborne contaminants through HEPA filtration and prevent their release into the work environment.

CSP - See Compounded Sterile Preparation

CVE - See Containment Ventilated Enclosure

DCA - See Direct Compounding Area

Designated Person(s) - One or more individuals assigned to be responsible and accountable to regulatory authorities for the performance and operation of the compounding facility and personnel in the preparation of CSPs, CNSPs, and radiopharmaceuticals.

Direct Compounding Area (DCA) - A critical area within an ISO Class 5 PEC where critical sites are exposed to unidirectional HEPA-filtered air, also known as first air.

Direct Processing Area (DPA) - An area within an ISO Class 5 PEC used in preparing nuclear radiopharmaceuticals where critical sites are exposed to unidirectional vertical HEPA-filtered air, also known as first air.

DPA - See Direct Processing Area

Dynamic Airflow Smoke Pattern Test - A PEC test in which a visible source of smoke, which is neutrally buoyant, is used to observe air patterns within the unidirectional space (i.e., the DCA) under dynamic operating conditions (see Dynamic operating conditions). This test is not appropriate for ISO Class 7 or ISO Class 8 cleanrooms (SECs) that do not have unidirectional airflow (see visual smoke study).

Dynamic Operating Conditions - Conditions in the SRPA or classified area in which operating personnel are present and performing actual or simulated activities. The PECs within the areas should contain equipment and materials regularly used and the conditions should reflect the largest number of personnel and highest complexity of compounding expected during routine operations as determined by the designated person(s).

Effective Filter Area - The portion of the HEPA filter through which air flows.

Feet Per Minute (FPM) – A unit of measurement used to measure airflow velocity.

Hazardous Drug (HD) - Any drug identified by NIOSH or appropriate regulatory authorities with at least one of the following criteria:

- Carcinogenicity, teratogenicity, or developmental toxicity
- Reproductive toxicity in humans
- Organ toxicity at low dose in humans or animals
- Genotoxicity or new drugs that mimic existing HDs in structure or toxicity

HD - See Hazardous Drug

HD Storage Room - An externally ventilated, negative-pressure room with at least 12 air changes per hour (ACPH).

Hot-cell - A device used for the shielding and containment of radioactive materials. The shielding material(s) (e.g., lead) is generally incorporated into the structure of the unit itself. Radiopharmaceutical personnel carry out the majority of the tasks within the hot-cell from the exterior of the unit. This is accomplished by the use of remote manipulation systems (e.g., manipulator arms, automated dispensing system) of various designs. Numerous air quality configurations of the hot-cell may exist, including integrated HEPA filtration systems to render all or a specified portion of the direct processing area (DPA) of the device capable of certifying to a controlled ISO Class 5 environment. In other situations, the hot-cell offers only radiation protection and a laminar flow PEC, capable of achieving an ISO Class 5 environment, is placed within the enclosure to allow for safe aseptic manipulations. A hot-cell may also be referred to by other designations (e.g., shielded isolator with laminar flow, PET (Positron Emission Tomography) dispensing station, manipulator hot-cell, shielded isolators for dispensing, radiopharmaceutical dispensing isolator).

Inches Water Gauge - A measurement of differential pressure.

Integrated Vertical Laminar Flow Zone (IVLFZ) - A designated ISO Class 5 area serving as the PEC within ISO Class 7 non radiological buffer room. In the IVLFZ, unidirectional airflow is created within the buffer room by placing HEPA filters over the entire surface of the work tables and effective placement of air returns.

ISO Class - An air-quality classification according to ISO 14644-1 based on levels of airborne particulates from the International Organization for Standardization.

IVLFZ - See Integrated Vertical Laminar Flow Zone

K Factor - A factor correlating the volumetric flow as measured with a capture hood to the flow calculated by multiplying the average thermal anemometer measured air velocity by the effective area for the filter or diffuser being used.

LAFS - See Laminar Airflow System

LAFW - See Laminar Airflow Workbench

Laminar Airflow System (LAFS) - Provides an ISO Class 5 or better air quality environment for sterile compounding. The device provides a unidirectional HEPA-filtered airflow. Examples of LAFS include Laminar airflow workbench (LAFW), biosafety cabinets (BSCs), and Integrated Vertical Laminar Flow Zone (IVLFZ).

Laminar Airflow Workbench (LAFW) - A device that is a type of LAFS that provides an ISO Class 5 or better air quality environment for sterile compounding. The device provides an unidirectional HEPA-filtered airflow. Note: Nuclear Pharmacy requires LAFW be vertical unidirectional.

Liters per Second (L/S) - A measure of airflow rate.

Meters Per Second (m/s) - A unit of measurement used to measure airflow velocity

Pascals (Pa) – a measurement of differential pressure

PEC - See Primary Engineering Control

Pharmaceutical Isolator - An enclosure that provides HEPA-filtered ISO Class 5 unidirectional air operated at a continuously higher pressure than its surrounding environment and is decontaminated using an automated system. It is not a CAI or CACI because it uses only decontaminated interfaces or rapid transfer ports for materials transfer.

Primary Engineering Control (PEC) - A unidirectional airflow ISO class 5 device such as Laminar Air Flow Workstation (LAFW), Biological Safety Cabinet (BSC), Compounding Aseptic Isolators (CAI), and Compounding Aseptic Containment Isolators (CACI) used to prepare sterile preparations.

RABS - See Restricted Access Barrier System

Radiolabeled Blood Components Area - An ISO Class 5 BSC located in an ISO Class 7 buffer area with an ISO Class 8 ante area. This is specific to nuclear pharmacy.

Radioactive Materials (RAM) License - A document(s) issued by the US NRC or an Agreement State agency that authorizes various activities involving the use of radioactive materials that may include ventilation and pressurization requirements that take priority over USP. These uses can include possession, research and development, distribution, medical use, and other purposes not included in this list. Only those activities specifically authorized are allowed.

RAM - See Radioactive Materials (RAM) license

Restricted Access Barrier System (RABS) - An enclosure that provides HEPA-filtered ISO Class 5 unidirectional air that allows for the ingress and/or egress of materials through defined openings that have been designed and validated to preclude the transfer of contamination, and that are generally not to be opened during operations.

Restricted Area - Any area to which access is controlled for the protection of individuals from exposures to radiation and radioactive materials per USP 825.

SCA - See Segregated Compounding Area

SEC - See Secondary Engineering Control

Secondary Engineering Control (SEC) - The facilities used to house the primary engineering control(s) and support the sterile compounding operation; the buffer room and the ante-room.

Segregated Compounding Area (SCA) - A designated, unclassified space, area, or room with a defined perimeter that contains a PEC and is suitable for preparation of Category 1 CSPs only.

Segregated Radiopharmaceutical Processing Area (SRPA) - A designated, classified space, area, or room with a defined (by facility procedures) perimeter with or without a PEC. An SRPA is only suitable for radiopharmaceutical preparation (with and without minor deviations), dispensing,

and repackaging. If the SRPA is used to elute radionuclide generators it must have ISO Class 8 non-viable particle count air quality.

SRPA - See Segregated Radiopharmaceutical Processing Area

Static Airflow Smoke Pattern Test - A PEC test in which a visible source of smoke, which is neutrally buoyant, is used to observe at rest air patterns within the unidirectional space (i.e., the DCA) of the PEC to affirm the PEC is placed correctly in the SEC.

Sterile Hazardous Compounding Room - Also known as a buffer room for sterile hazardous drug compounding: A type of C-SEC under negative pressure that meets ISO Class 7 or better air quality where the C-PEC that generates and maintains an ISO Class 5 environment is physically located. Activities that occur in this area are limited to the preparation and staging of components and supplies used when compounding HDs.

Sterile Non-hazardous Compounding Room - Also known as a buffer room for non-hazardous sterile compounding: A SEC that maintains ISO Class 7 or cleaner air quality with fixed walls and doors where PEC(s) that generate and maintain an ISO Class 5 environment are physically located. The buffer room may only be accessed through the ante-room.

Thermal Anemometer - An air velocity measurement device that uses a heated probe element that is inserted into an airstream. Air speed can then be inferred from the heating power necessary to maintain the probe at a temperature elevation.

Unidirectional Airflow - Airflow moving within a PEC in a single direction in a robust and uniform manner and at sufficient speed to sweep particles away from the DCA/DPA.

Water Column (w.c.) - The unit of measurement used to measure static pressure.

Visual Smoke Study - A test, used in ISO Class 7 and ISO Class 8 rooms that do not have unidirectional airflow, in which a visible source of smoke, which is neutrally buoyant, is used to verify an absence of stagnant airflow where particulates can accumulate. This test does not need to be performed under dynamic operating conditions and is not appropriate for PECs. Note: Section 4.3 of USP<797> states “Air returns in the cleanroom suite must be low on the wall unless a visual smoke study demonstrates an absence of stagnant airflow where particulate will accumulate.”

6 Materials and Equipment

See individual sections for specific listings.

7 Precautions/Safety

Does not apply.

8 Theory of Operation

The following table summarizes requirements for the primary and secondary engineering controls, and refers to the section that describes the required tests.

Table 1: Requirements for Certifying Sterile Compounding Facilities (CETA, 2021)

Room Type	ISO (minimum)	Total ACPH (minimum)	Differential Pressure	Comments
Sterile Non-Hazardous Buffer Room ☑ 〈797〉 ☐ 〈800〉 ☐ 〈825〉	ISO Class 7 (8.1.3)	30 (8.2.3)	≥0.020" w.c. (≥5 Pa) (8.4.3)	Room HEPA filter integrity testing required. Rooms where air return/exhaust are not low on the wall require a visual smoke study.
Radio Pharmaceutical Sterile Compounding ISO Class 7[1]* ☐ 〈797〉 ☐ 〈800〉 ☑ 〈825〉	ISO Class 7 (8.1.4)	30 (8.2.4)	≥0.020" w.c. (≥5 Pa) (8.4.4)	Room HEPA filter integrity testing required. Rooms where air return/exhaust are not low on the wall require a visual smoke study. Additional requirements per RAM license.
Radio Pharmaceutical Labeled Blood Component ISO Class 7[2]* ☐ 〈797〉 ☐ 〈800〉 ☑ 〈825〉	ISO Class 7 (8.1.5)	30 (8.2.5)	≥0.020" w.c. (≥5 Pa) (8.4.5)	Room HEPA filter integrity testing required. Rooms where air return/exhaust are not low on the wall require a visual smoke study. Additional requirements per RAM license.
Radio Pharmaceutical Sterile Processing ISO Class 8[3]* ☐ 〈797〉 ☐ 〈800〉 ☑ 〈825〉	ISO Class 8 (8.1.6)	20 (8.2.6)	≥0.020" w.c. (≥5 Pa) (8.4.6)	Room HEPA filter integrity testing required. Rooms where air return/exhaust are not low on the wall require a visual smoke study. Additional requirements per RAM license.

[1] Radio Pharmaceutical Sterile Compounding ISO Class 7: USP <825> requires this room to be ISO Class 7 with an ISO Class 8 or better ante-room.
[2] Radio Pharmaceutical Labeled Blood Component ISO Class 7: USP <825> requires this room to be ISO Class 7 with an ISO Class 8 or better ante-room.
[3] Radio Pharmaceutical Sterile Processing ISO Class 8: USP <825> requires this room to be ISO Class 8 or better. This room does require an ante-room.

Certification Matrix for Sterile Compounding Facilities

Room Type	ISO (minimum)	Total ACPH (minimum)	Differential Pressure	Comments
Sterile Hazardous Buffer Room ☐ 〈797〉 ☑ 〈800〉 ☐ 〈825〉	ISO Class 7 (8.1.7)	30 (8.2.7)	-0.010 to -0.030" w.c. (- 2.5 to - 7.5 Pa) (8.4.7)	Room HEPA filter integrity testing required. Rooms where air return/exhaust are not low on the wall require a visual smoke study.
Ante-room ISO Class 7 ☑ 〈797〉 ☑ 〈800〉 ☑ 〈825〉	ISO Class 7 (8.1.8)	30 (8.2.8)	≥0.020" w.c. (≥5 Pa) (8.4.8)	Room HEPA filter integrity testing required. Rooms where air return/exhaust are not low on the wall require a visual smoke study.
Ante-room ISO Class 8 ☑ 〈797〉 ☐ 〈800〉 ☑ 〈825〉	ISO Class 8 (8.1.9)	20 (8.2.9)	≥0.020" w.c. (≥5 Pa) (8.4.9)	Room HEPA filter integrity testing required. Rooms where air return/exhaust are not low on the wall require a visual smoke study.
Segregated Radiopharmaceutical Processing Area (SRPA)*- Classified[4] ☐ 〈797〉 ☐ 〈800〉 ☑ 〈825〉	ISO Class 8 (8.1.10)	20 (8.2.10)	Positive (8.4.10)	Room HEPA filter integrity testing required. Rooms where air return/exhaust are not low on the wall require a visual smoke study. Additional requirements per RAM license.
Containment Segregated Compounding Area (C-SCA) ☐ 〈797〉 ☑ 〈800〉 ☐ 〈825〉	N/A (8.1.11)	12 (8.2.11)	-0.010 to -0.030" w.c. (- 2.5 to - 7.5 Pa) (8.4.11)	
Segregated Compounding Area (SCA) ☑ 〈797〉 ☐ 〈800〉 ☐ 〈825〉	N/A (8.1.11)	N/A (8.2.11)	N/A (8.4.12)	
Nuclear Nonsterile Processing (negative pressure) "Restricted Area"[5]* ☐ 〈797〉 ☐ 〈800〉 ☑ 〈825〉	N/A (8.1.12)	N/A (8.2.12)	N/A (8.4.13)	Additional requirements per RAM license.

[4] Segregated Radiopharmaceutical Processing Area (SRPA) - Classified: USP <825> requires this room to be ISO Class 8. This room does not require an ante-room.

[5] Nuclear Nonsterile Processing (negative pressure) "Restricted Area": USP <825> requires this room to be under negative pressure, but does not require an ISO air cleanliness classification and does not require an ante-room.

Room Type	ISO (minimum)	Total ACPH (minimum)	Differential Pressure	Comments
Nonsterile Hazardous Compounding Room ☐ 〈797〉 ☑ 〈800〉 ☐ 〈825〉	N/A (8.1.13)	12 (8.2.13)	-0.010 to -0.030” w.c. (- 2.5 to - 7.5 Pa) (8.4.14)	
Hazardous Drug Storage Room ☐ 〈797〉 ☑ 〈800〉 ☐ 〈825〉	N/A (8.1.14)	12 (8.2.14)	Negative (8.4.15)	

*for facilities with a RAM license, requirements for air cleanliness, air exchanges and pressure may differ and will supersede the USP requirements

8.1 Total Airborne Particle Sampling

8.1.1 Total Airborne Particle Sampling Test Equipment

Calibrated discrete particle counter capable of detecting 0.5 micrometer size particles. Maximum recommended calibration interval is 12 months.

8.1.2 Total Airborne Particle Sampling Procedures and Minimum Reported Values

The minimum number of sampling locations shall be derived from ISO 14644-1:2015, Table A.1.

Minimum sample requirements are 2 liters for volume, 1 minute for time.

Document the number of personnel present in each PEC and SEC during total particle count tests.

Note: The number of people present during dynamic testing is the maximum number of people allowed in the room during operating conditions. Number of people includes the certifier.

Report all individual concentration readings by location. A layout diagram to illustrate the location of each reading shall be displayed.

The permitted concentration of airborne particles and applicable classification for the space shall be listed. (e.g. ISO Class 7 or ISO Class 8).

An airborne optical particle counter is used to sample particle levels at working height within the buffer and ante areas. Sampling for the PEC will be conducted in the plane of the work activity in the area where there is greatest risk to the exposed CSPs.

Sampling shall be for particles equal to or greater than 0.5 micrometer in size. Sampling shall be done with rooms in dynamic operating condition. A statement of pass or fail should be clearly made for every classified area.

8.1.3 Particle Count Acceptance Criteria - Sterile Non-Hazardous Buffer Room

A buffer room must meet at least ISO Class 7 air quality.[6]

8.1.4 Particle Count Acceptance Criteria - Radio Pharmaceutical Sterile Processing ISO Class 7

A buffer room used to prepare sterile radiopharmaceuticals must meet at least ISO Class 7 air quality.[7]

[6] USP General Chapter ⟨797⟩ Reprinted from USP 42-NF 37 (2021) p. 8
[7] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 18

8.1.5 Particle Count Acceptance Criteria - Radio Labeled Blood Component ISO Class 7

A buffer room used to prepare sterile radiopharmaceuticals must meet at least ISO Class 7 air quality.[8]

8.1.6 Particle Count Acceptance Criteria - Radio Pharmaceutical Processing ISO Class 8

This buffer room must meet at least ISO Class 8 air quality.[9]

8.1.7 Particle Count Acceptance Criteria - Sterile Hazardous Buffer Room

A buffer room used for sterile HD compounding must meet at least ISO Class 7 air quality.[10]

8.1.8 Particle Count Acceptance Criteria - Ante-room ISO Class 7

A buffer room used for sterile HD compounding must have an ante-room meeting at least ISO Class 7 air quality.[11]

8.1.9 Particle Count Acceptance Criteria - Ante-room ISO Class 8

A buffer room used for sterile non HD compounding must have an ante-room meeting at least ISO Class 8 air quality.[12] [13]

8.1.10 Particle Count Acceptance Criteria - Segregated Radiopharmaceutical Processing Area - Classified

An SRPA meeting requirements for the use and storage of non-direct infusion radionuclide generators must meet at least ISO Class 8 air quality.[14]

8.1.11 Particle Count Acceptance Criteria - Containment Segregated Compounding Area

This area does not have an air cleanliness requirement.[15]

8.1.12 Particle Count Acceptance Criteria – Segregated Compounding Area

This area does not have an air cleanliness requirement.

[8] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 21
[9] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 11
[10] USP General Chapter ⟨800⟩ Reprinted from USP 42-NF 37 (2019) p. 5
[11] USP General Chapter ⟨800⟩ Reprinted from USP 42-NF 37 (2019) p. 5
[12] USP General Chapter ⟨797⟩ Reprinted from USP 42-NF 37 (2021) p. 8
[13] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 26
[14] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 7
[15] USP General Chapter ⟨800⟩ Reprinted from USP 42-NF 37 (2019) p. 4

8.1.13 Particle Count Acceptance Criteria - Nuclear Nonsterile Processing (negative pressure) “Restricted Area”

This area does not have an air cleanliness requirement.

8.1.14 Particle Count Acceptance Criteria - Nonsterile Hazardous Compounding Room

This area does not have an air cleanliness requirement.

8.1.15 Particle Count Acceptance Criteria - Hazardous Drug Storage Room

This area does not have an air cleanliness requirement.

8.1.16 Primary Engineering Controls

All PECs shall be certified to ISO class 5.

8.2 Airflow

8.2.1 Airflow Test Equipment

The preferred test equipment is the airflow capture hood used to measure directly in airflow volume (CFM or L/s). In some rare cases, a capture hood will not fit in the given space and a thermal anemometer or multipoint tube array will be needed to measure in velocity (FPM or m/s).

Note: When using a thermal anemometer or multipoint tube array, a K factor must be applied to correlate the volumetric flow as measured with a capture hood to the flow calculated by multiplying the average measured air velocity by the effective area for the filter or diffuser being used.

Maximum initial recommended calibration interval as specified by test equipment manufacturer or IEST-RP-CC013.3.

8.2.2 Airflow Procedures and Minimum Reported Values

Identify whether total supply air or total exhaust air will be used to calculate ACPH.

Note: The traditional method of determining ACPH is to calculate using air supplied to the room through HEPA filters or the ventilation system. However, for rooms like the Hazardous Drug Storage Area that are required to be negatively pressurized, there may be no significant volume of air supplied to the room. In these cases, a more meaningful measure of ACPH may use the volume of air exhausted from the room including BSCs that are externally exhausted.

- Air volume through each supply HEPA filter or register or exhaust in CFM
- Total air volume supplied to or exhausted from the room in CFM
- Where applicable, recirculated air from PECs

- Room volume in ft^3/m^3
- A statement of pass or fail should be clearly made for the room air exchange rate within each room tested.

$$ACPH = \frac{Total\ air\ volume\ supplied\ or\ exhausted\ \left(ft^3/_{min}\right) \times 60\ min/_{hr}}{Room\ volume\ (ft^3)}$$

Note: Formula for room Air Changes Per Hour (ACPH)

8.2.3 Airflow Acceptance Criteria - Sterile Non-Hazardous Buffer Room

The total HEPA filtered ACPH must be adequate to maintain ISO Class 7 under dynamic conditions.[16]

At least 15 ACPH of the total air change rate in a room must come from the HVAC through HEPA filters located in the ceiling.[17]

The HEPA-filtered air from the PEC(s), when added to the HVAC-supplied HEPA-filtered air, increases the total HEPA filtered ACPH to at least 30 ACPH.[18]

If the PEC is used to meet the minimum total ACPH requirements, the PEC must not be turned off except for maintenance.[19]

The ACPH from HVAC, ACPH contributed from PECs, and total ACPH must be documented on certification reports.[20]

8.2.4 Airflow Acceptance Criteria - Radio Pharmaceutical Sterile Processing - ISO Class 7

The total HEPA filtered ACPH must be adequate to maintain ISO Class 7 under dynamic conditions.[21]

At least 15 ACPH of the total air change rate in a room must come from the HVAC through HEPA filters located in the ceiling.[22]

[16] USP General Chapter ⟨797⟩ Reprinted from USP 42-NF 37 (2021) p. 11
[17] USP General Chapter ⟨797⟩ Reprinted from USP 42-NF 37 (2021) p. 11
[18] USP General Chapter ⟨797⟩ Reprinted from USP 42-NF 37 (2021) p. 11
[19] USP General Chapter ⟨797⟩ Reprinted from USP 42-NF 37 (2021) p. 11
[20] USP General Chapter ⟨797⟩ Reprinted from USP 42-NF 37 (2021) p. 11
[21] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 8
[22] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 8

The HEPA-filtered air from the PEC, when added to the HVAC-supplied HEPA-filtered air, increases the total HEPA filtered ACPH to at least 30 ACPH.[23]

If the PEC is used to meet the minimum total ACPH requirements, the PEC must not be turned off except for maintenance.[24]

The ACPH from HVAC, ACPH contributed from PECs, and total ACPH must be documented on certification reports.[25]

8.2.5 Airflow Acceptance Criteria - Radio Labeled Blood Component - ISO Class 7

The total HEPA filtered ACPH must be adequate to maintain ISO Class 7 under dynamic conditions.[26]

At least 15 ACPH of the total air change rate in a room must come from the HVAC through HEPA filters located in the ceiling.[27]

The HEPA-filtered air from the PEC, when added to the HVAC-supplied HEPA-filtered air, increases the total HEPA filtered ACPH to at least 30 ACPH.[28]

If the PEC is used to meet the minimum total ACPH requirements, the PEC must not be turned off except for maintenance.[29]

The ACPH from HVAC, ACPH contributed from PECs, and total ACPH must be documented on certification reports.[30]

8.2.6 Airflow Acceptance Criteria - Radio Pharmaceutical Processing - ISO Class 8

The total HEPA filtered ACPH must be adequate to maintain ISO Class 8 under dynamic conditions.[31]

At least 15 ACPH of the total air change rate in a room must come from the HVAC through HEPA filters located in the ceiling.[32] The total ACPH must be 20.

The total ACPH must be documented on certification reports.[33]

[23] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 8
[24] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 8
[25] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 9
[26] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 8
[27] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 8
[28] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 8
[29] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 8
[30] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 9
[31] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 9
[32] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 9
[33] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 9

8.2.7 Airflow Acceptance Criteria - Sterile Hazardous Buffer Room

For an ISO Class 7 buffer room with an ISO Class 7 ante-room configuration, C-SEC must be externally vented and have minimum of 30 ACPH.[34]

The total HEPA filtered ACPH must be adequate to maintain ISO Class 7 under dynamic conditions.

For an Unclassified C-SCA, C-SEC must be externally vented and have minimum of 12 ACPH.[35]

8.2.8 Airflow Acceptance Criteria - Ante-room ISO Class 7

The total HEPA filtered ACPH must be adequate to maintain ISO Class 7 under dynamic conditions.[36]

At least 15 ACPH of the total air change rate in a room must come from the HVAC through HEPA filters located in the ceiling.[37]

The HEPA-filtered air from the PEC, when added to the HVAC-supplied HEPA-filtered air, increases the total HEPA filtered ACPH to at least 30 ACPH.[38]

If the PEC is used to meet the minimum total ACPH requirements, the PEC must not be turned off except for maintenance.[39]

The ACPH from HVAC, ACPH contributed from PECs, and total ACPH must be documented on certification reports.[40]

8.2.9 Airflow Acceptance Criteria - Ante-room ISO Class 8

The total HEPA filtered ACPH must be adequate to maintain ISO Class 8 under dynamic conditions.[41]

At least 15 ACPH of the total air change rate in a room must come from the HVAC through HEPA filters located in the ceiling.[42]

[34] USP General Chapter ⟨800⟩ Reprinted from USP 42-NF 37 (2019) p. 5
[35] USP General Chapter ⟨800⟩ Reprinted from USP 42-NF 37 (2019) p. 5
[36] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 8
[37] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 8
[38] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 8
[39] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 8
[40] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 9
[41] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 9
[42] USP General Chapter ⟨797⟩ Reprinted from USP 42-NF 37 (2021) p. 11, USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 9

A minimum of 20 total HEPA-filtered ACPH must be supplied to ISO Class 8 rooms.[43]

The total ACPH must be documented on certification reports.[44]

8.2.10 Airflow Acceptance Criteria - Segregated Radiopharmaceutical Processing Area (SRPA) - Classified

The total HEPA filtered ACPH must be adequate to maintain ISO Class 8 under dynamic conditions.[45]

At least 15 ACPH of the total air change rate in a room must come from the HVAC through HEPA filters located in the ceiling.[46]

The total ACPH must be documented on certification reports.[47]

8.2.11 Airflow Acceptance Criteria- Containment Segregated Compounding Area (C-SCA)

Externally vented negative pressure room with at least 12 air changes per hour (ACPH).[48]

8.2.12 Airflow Acceptance Criteria- Nuclear Nonsterile Processing (negative pressure) “Restricted Area”

This area does not have an ACPH requirement.

8.2.13 Airflow Acceptance Criteria- Nonsterile Hazardous Compounding Room

Externally vented negative pressure room with at least 12 air changes per hour (ACPH).[49]

8.2.14 Airflow Acceptance Criteria- Hazardous Drug Storage Room

Negative pressure room with at least 12 air changes per hour (ACPH).[50]

[43] USP General Chapter ⟨797⟩ Reprinted from USP 42-NF 37 (2021) p. 11,USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 9
[44] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 9
[45] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 9
[46] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 9
[47] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 9
[48] USP General Chapter ⟨800⟩ Reprinted from USP 42-NF 37 (2019) p. 5
[49] USP General Chapter ⟨800⟩ Reprinted from USP 42-NF 37 (2019) p. 4
[50] USP General Chapter ⟨800⟩ Reprinted from USP 42-NF 37 (2019) p. 3

8.3 HEPA Filter Integrity

8.3.1 HEPA Filter Integrity Test Equipment

An aerosol photometer with a linear readout that is capable of measuring aerosol concentrations of up to 100 µg/L with a threshold sensitivity capable of measuring 0.0001 µg/L. The device should have a detection limit of at least 0.1 x the designated leak. The device should have a volumetric flow rate of 28.3L/min (1.0 CFM) (IEST - RP- CC034 6.1.1, 2016). A scanning probe with an inlet opening of square or rectangle configuration that provides an inlet airflow velocity within -10% to +20% of the average exit airflow velocity of the filter(s) being scanned when operating at the sample flow rate of the aerosol photometer (IEST-RP-CC034 section 6.1.7, 2016).

Maximum recommended calibration interval-12 months (NSF 49 Annex A.2.2.1, 2016; IEST-RP-CC013, 2013).

8.3.2 HEPA Filter Integrity Procedures and Minimum Reported Values

All HEPA filters located in ISO classified environments must be leak tested after installation and at every certification using an aerosol photometer and an appropriate aerosol challenge.

A challenge aerosol is introduced into the air handling system or each individual duct that feeds a HEPA filter, as far upstream of the HEPA filters as needed to produce a properly mixed aerosol.

The upstream aerosol concentration for each HEPA filter is compared to the downstream aerosol concentration to determine if there are any leaks in excess of the maximum allowed.

Aerosol introduction location and method.

Upstream measurement location.

Measured or calculated upstream aerosol concentration in micrograms per liter at each filter under test.

A diagram of the filter, along with an indication of all leaks found and patches made, if any.

Report the percent penetration for each filter leak and provide a statement that no leaks in excess of the maximum allowable 0.010% were detected for each HEPA filter.

A statement of pass or fail should be clearly made for every HEPA filter.

Note: In some installations, an upstream concentration cannot be measured. In those cases, an upstream aerosol concentration can be calculated and reported as such. If a calculated challenge is used, the specific injection method used and all of the calculations should be reported along with a reason that a challenge was not measured and how uniform distribution to each HEPA was verified. A calculated concentration is acceptable when one return supplies one HEPA filter.

8.3.3 HEPA Filter Integrity Acceptance Criteria

The maximum allowable leakage is 0.010% of the upstream aerosol concentration.

8.4 Measuring Pressure Differentials

8.4.1 Pressure Differentials Test Equipment

The preferred equipment is an electronic manometer with a resolution to at least thousandths of an inch water column.

Maximum recommended calibration interval of the test instrument must be less than 12 months.

8.4.2 Establishing and Maintaining Pressure Differentials Procedures and Minimum Reported Values

Differential pressure at every door from each designated room to every adjacent space in inches water column.

A room layout diagram clearly identifying which direction the pressure is flowing.

8.4.3 Pressure Differential Acceptance Criteria - Sterile Non-Hazardous Buffer Room

The pressure differential between the buffer room and an ante-room must not be less than +0.020 inches water column (5 Pa).[51]

8.4.4 Pressure Differential Acceptance Criteria - Radio Pharmaceutical Sterile Processing - ISO Class 7

The pressure differential between the buffer room and an ante-room must not be less than +0.020 inches water column (5 Pa).[52]

[51] USP General Chapter ⟨797⟩ Reprinted from USP 42-NF 37 (2021) p. 12
[52] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 10

8.4.5 Pressure Differential Acceptance Criteria - Radio Labeled Blood Component - ISO Class 7

The pressure differential between the room and an ante-room must not be less than +0.020 inches water column (5 Pa).[53]

Note: As specified in USP 825, section 10.3, there must be a complete physical separation where blood products are handled. Therefore, this requirement applies to fixed and non-fixed walls.

8.4.6 Pressure Differential Acceptance Criteria - Radio Pharmaceutical Processing - ISO Class 8

The pressure differential between the room and an ante-room must not be less than +0.020 inches water column (5 Pa).[54]

8.4.7 Pressure Differential Acceptance Criteria - Sterile Hazardous Buffer Room

The pressure differential between the buffer room and an ante-room must be between -0.010 and -0.030 inches water column (-2.5 to -7.5 Pa).[55]

8.4.8 Pressure Differential Acceptance Criteria - Ante-room ISO Class 7

The pressure differential between the ante-room and unclassified areas must not be less than +0.020 inches water column (5 Pa).[56]

8.4.9 Pressure Differential Acceptance Criteria - Ante-room ISO Class 8

The pressure differential between the ante-room and unclassified areas must not be less than +0.020 inches water column (5 Pa).[57]

8.4.10 Pressure Differential Acceptance Criteria - Segregated Radiopharmaceutical Processing Area (SRPA) - Classified

The SRPA must be negatively pressurized compared to unrestricted areas in the presence of volatile or airborne radiopharmaceuticals.[58]

[53] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 10
[54] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 10
[55] USP General Chapter ⟨800⟩ Reprinted from USP 42-NF 37 (2019) p. 5
[56] USP General Chapter ⟨797⟩ Reprinted from USP 42-NF 37 (2021) p. 12, USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 11
[57] USP General Chapter ⟨797⟩ Reprinted from USP 42-NF 37 (2021) p. 12, USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 11
[58] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 10

8.4.11 Pressure Differential Acceptance Criteria - Containment Segregated Compounding Area (C-SCA)

The pressure differential between the C-SCA and adjacent area must be between -0.010 and -0.030 inches water column (-2.5 to -7.5 Pa).[59]

8.4.12 Pressure Differential Acceptance Criteria- Nuclear Nonsterile Processing (negative pressure) "Restricted Area"

A restricted area must be negatively pressurized compared to unrestricted areas in the presence of volatile or airborne radiopharmaceuticals.[60]

8.4.13 Pressure Differential Acceptance Criteria - Nonsterile Hazardous Compounding Room

The pressure differential between the Nonsterile Hazardous Compounding Room and adjacent area must be between -0.010 and -0.030 inches water column (-2.5 to -7.5 Pa) or RAM license for Nuclear.[61]

8.4.14 Pressure Differential Acceptance Criteria - Hazardous Drug Storage Room

The Hazardous Drug Storage Area must be negatively pressurized compared to adjacent areas.[62]

8.5 Dynamic Airflow Smoke Pattern Test for PECs & SECs

See CETA Application Guide 014 for Airflow Visualization Studies procedures and acceptance criteria.

8.6 Primary Engineering Controls

Listed below are the Primary Engineering Controls (PECs) that may be used in the secondary engineering controls specified by the USP chapters. For each PEC, the references for the test equipment, test procedures and minimum reported values are provided.

8.6.1 Biological Safety Cabinet (BSC)

Biological Safety Cabinet Test Equipment

- Reference: NSF/ANSI Standard 49, Annex N5 (formerly Annex F)

[59] USP General Chapter ⟨800⟩ Reprinted from USP 42-NF 37 (2019) p. 5
[60] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 10
[61] USP General Chapter ⟨800⟩ Reprinted from USP 42-NF 37 (2019) p. 4
[62] USP General Chapter ⟨825⟩ Reprinted from USP 42-NF 37 (2019) p. 3

Biological Safety Cabinet Minimum Reported Values

- Reference: NSF/ANSI Standard 49, Annex N5 (formerly Annex F)
- Reference: ISO-14644-1 [2015] section 5.4 (Test Report)

8.6.2 Compounding Aseptic Isolator (CAI) and Compounding Aseptic Containment Isolator (CACI)

Compounding Aseptic Isolator (CAI) and Compounding Aseptic Containment Isolator (CACI) Test Equipment

- Reference: CETA CAG-002 (latest revision)

Compounding Aseptic Isolator (CAI) and Compounding Aseptic Containment Isolator (CACI) Minimum Reported Values

- Reference: CETA CAG-002 (latest revision)
- Reference: ISO 14644-1 [2015] section 5.4 (Test Report)

8.6.3 Laminar Air Flow Workstation (LAFW)

Laminar Air Flow Workstation (LAFW) Test Equipment

- Reference: IEST-RP-CC-002.4 / IEST-RP-CC034.4 Section 6.1.1 and 6.1.4.

Laminar Air Flow Workstation (LAFW) Minimum Reported Values

- Reference: CAG-003, ISO 14644-1 [2015] section 5.4 (Test Report)

8.6.4 Integrated Vertical Laminar Flow Zone (IVLFZ)

- Refer to manufacturer provided references for test equipment, procedures, minimum reported values and requirements.

Note: Dynamic airflow pattern tests have shown it is difficult to achieve this type of design and also achieve and maintain unidirectional airflow under dynamic airflow conditions.[63]

8.6.5 Robotic Enclosures

Refer to manufacturer provided references for test equipment, procedures, minimum reported values and requirements. Dynamic smoke studies must be conducted very 6 months.

[63] USP General Chapter ⟨797⟩ Reprinted from USP 42-NF 37 (2021) p. 10

9 Addresses and Contacts

Controlled Environment Test Association (CETA)
701 Exposition Place, Suite 206, Raleigh, NC 27615 US
Phone: 919-792-6339
Email:info@cetainternational.org
Website: www.cetainternational.org

ANSI
1899 L Street, NW, 11th Floor, Washington, DC 20036 US
Phone: 202-293-8020
Email: info@ansi.org
Website: www.ansi.org

Department of Health and Human Services
Food and Drug Administration (FDA)
10903 New Hampshire Avenue, Silver Spring, MD 20993-0002
Phone: 1 888-463-6332
Website: www.fda.gov

Institute of Environmental Sciences and Technology (IEST)
1827 Walden Office Square, Suite 400, Schaumburg, IL 60173 US
Phone: (847) 981-0100
Email: information@iest.org
Website: www.iest.org

International Organization For Standardization (ISO)
Chemin de Blandonnet 8, CP 401
1214 Vernier, Geneva, CH
Phone: +41-22-7490111
E-mail: central@iso.org

NSF INTERNATIONAL
P.O. Box 130140
789 N. Dixboro Road, Ann Arbor, MI 48105, US
Phone: 734-769-8010
Email: info@nsf.org
Website: www.nsf.org

United States Pharmacopeia (USP)
12601 Twinbrook Parkway, Rockville, MD 20852 US
Phone: 800-227-8772
Email: compoundingsl@usp.org
Website: www.usp.org

ANNEX A: TABULAR CROSS REFERENCE OF ROOM TYPE, APPLICATION AND USE

Table 2: Tabular Cross Reference of Room Type, Application and Use (CETA, 2021)

Typical User	Room Description	Typical Use of Room	Summary of Requirements
Alternate Site Infusion	Containment Segregated Compounding Area (C-SCA)	Sterile Compounding of Hazardous Drugs (Category 1 only)	Adjoining Ante-room not required, ISO Class not required, 12 ACPH, HEPA filters not required, Visual smoke study not required, Pressurization -0.010 to -0.030" (2.5 to 7.5 Pa) w.c.
Home Infusion Pharmacy or Nuclear Pharmacy	Ante-room ISO Class 7	Where personnel hand hygiene, garbing procedures, and other activities that generate high particulate levels may be performed.	Adjoining Ante-room not required, ISO Class 7, 30 ACPH, HEPA filter test required, Visual smoke study required, Pressurization +0.020" (5 Pa) w.c. or greater
	Ante-room ISO Class 8	Where personnel hand hygiene, garbing procedures, and other activities that generate high particulate levels may be performed.	Adjoining Ante-room not required, ISO Class 8, 20 ACPH, HEPA filter test required, Visual smoke study required, Pressurization +0.020" (5 Pa) w.c. or greater
Home Infusion Provider	Sterile Non-Hazardous Buffer Room	Sterile Compounding of Non-Hazardous Drugs (Category 1 and 2)	Adjoining ISO Class 8 Ante-room required, ISO Class 7, 30 ACPH, HEPA filter test required, Visual smoke study required, Pressurization +0.020" (5 Pa) w.c. or greater
	Sterile Hazardous Buffer Room	Sterile Compounding of Hazardous Drugs (Category 1 and 2)	Adjoining ISO Class 7 Ante-room required, ISO Class 7, 30 ACPH, HEPA filter test required, Visual smoke study required, Pressurization -0.010 to -0.030" (2.5 to 7.5 Pa) w.c.
Home Infusion Provider Or Nonsterile Compounding Pharmacy	Hazardous Drug Storage Room	Storage of Hazardous Drugs	Adjoining Ante-room not required, ISO Class not required, 12 ACPH, HEPA filters not required, Visual smoke study not required, Negative pressurization required
Nonsterile Compounding Pharmacy	Nonsterile Hazardous Compounding Room	Nonsterile Compounding	Adjoining Ante-room not required, ISO Class not required, 12 ACPH, HEPA filters not required, Visual smoke study not required, Pressurization -0.010 to -0.030" (2.5 to 7.5 Pa) w.c.

Certification Matrix for Sterile Compounding Facilities

Typical User	Room Description	Typical Use of Room	Summary of Requirements
Nuclear Pharmacy	Radio Pharmaceutical Sterile Processing (ISO Class 7)	Sterile Compounding from sterile or nonsterile ingredients (Category 1 and 2) Preparation with minor deviations [USP 825 Section 10.2] Dispensing, Repackaging, Preparation	Adjoining ISO Class 8 Ante-room required, ISO Class 7, 30 ACPH, HEPA filter test required, Visual smoke study required, Pressurization +0.020” (5 Pa) w.c. or greater
	Radio Labeled Blood Component (ISO Class 7)	Preparation of radiolabeled blood components (e.g., radiolabeled leukocytes)	Adjoining ISO Class 8 Ante-room required, ISO Class 7, 30 ACPH, HEPA filter test required, Visual smoke study required, Pressurization +0.020” (5 Pa) w.c. or greater
	Radio Pharmaceutical Processing (ISO Class 8)	Preparation with minor deviations [USP 825 Section 10.2] Dispensing, Repackaging, Preparation Store and elute non-direct infusion radionuclide generators (e.g., TC-99m or Ga-68)	Adjoining ISO Class 8 Ante-room required, ISO Class 8, 20 ACPH, HEPA filter test required, Visual smoke study required, Pressurization +0.020” (5 Pa) w.c. or greater
	Segregated Radiopharmaceutical Processing Area (SRPA) - Classified	Preparation with minor deviations [USP 825 Section 10.2] Dispensing, Repackaging, Preparation Store and elute non-direct infusion radionuclide generators (e.g., TC-99m or Ga-68)	Adjoining Ante-room not required, ISO Class 8, 20 ACPH, HEPA filter test required, Visual smoke study required, Pressurization must be negative, Additional requirements per RAM license.
	Nuclear Nonsterile Processing (negative pressure) "Restricted Area"	Nonsterile Compounding in the presence of volatile or airborne radiopharmaceuticals	Adjoining Ante-room not required, ISO Class not required, ACPH not required, HEPA filters not required, Visual smoke study not required, Pressurization not required, Additional requirements per RAM license.