BC Cancer Agency
CARE & RESEARCH

Hazardous Drug Cleanroom Standards

Module 3

Table of Contents

Section A

A.1 International Standards Organization (ISO) Classifications

As the need for international cleanroom classifications and standards grew, the International Standards Organization established a technical committee and several working groups to delineate a set of standards. (http://www.terrauniversal.com/cleanrooms/iso-classification-cleanroom-standards.php) The International Standards Organization (ISO) classification standards for particulate matter in room air are rated according to the number of particles per cubic meter at a specified particle size (e.g., 0.5 *u*m and larger).[1]

ISO Classification of Particulate Matter in Room Air (limits are in particles of 0.5 µm and larger per cubic meter [current ISO] and cubic feet [former Federal Standard No. 209E, FS 209E].[1]

Class Name		Particle Count	
ISO Class	**U.S. FS 209E**	**ISO, m^3**	**FS 209E, ft^3**
3	Class 1	35.2	1
4	Class 10	352	10
5	Class 100	3,520	100
6	Class 1,000	35,200	1,000
7	Class 10,000	352,000	10,000
8	Class 100,000	3,520,000	100,000

A.2 Hazardous Drug Cleanroom and Anteroom

All parenteral cytotoxic/hazardous drug admixtures must be prepared in a minimum Class II Type B Biological Safety Cabinet (BSC) that maintains an ISO Class 5 environment.[1]

- **The cleanroom or buffer room housing the BSC must be an ISO Class 7 environment physically separated from an adjacent ISO Class 7 or better ante-area[1,2]** However, in facilities that prepare a low volume of hazardous drugs, the use of two tiers of containment (example: closed-system vial-transfer device within a BSC or CACI that is located in a non-negative pressure room) is acceptable[1]
- **A differential of at least 0.01 inch water column (negative pressure) must be maintained between the cleanroom and the pharmacy (anteroom).[1]** This will provide inward airflow to the cleanroom to contain any airborne hazardous drug (HD) particulate[1]
- A pressure indicator should be installed that can readily monitor room pressurization[1]
- Water sources should be kept to a minimum within the cleanroom. Drains should be avoided. If present, they should be designed to minimize the risks of microbial or foreign material contamination
- **Floors, walls, ceilings and all exposed surfaces must be nonporous and washable[1,2]**
- **Cleaning must take place in the cleanroom at a time when no aseptic operations are in progress[1,2]**
- All new cleanrooms should be equipped with floors that do not require waxing as dried worn wax can contribute to airborne particulates. If an existing cleanroom is equipped with a floor that requires waxing to ensure a nonporous surface, waxing should not take place at a time when cytotoxic/hazardous drug admixtures are being prepared
- **Essential furniture in buffer rooms and cleanrooms must be nonporous, smooth, non-shedding, impermeable, cleanable, and resistant to disinfectants[1,3]**
- Shelves and supplies should be kept to a minimum in the cleanroom to decrease the number of airborne particulates

- **Access to the cleanroom must be limited to authorized personnel who are assigned to work there.**[1-7] All other personnel should go no further than the anteroom
- **A warning sign must clearly identify the hazard and state that access to the cleanroom is controlled and limited to authorized personnel only**[2,8]
- **Doors must not be left open**[7]
- The door opening into the cleanroom and the door leading to the anteroom should not be opened at the same time in order to maintain pressure differential between the two rooms[2]
- Consideration should be given to include a public address (PA) speaker in the cleanroom to alert workers in the case of an emergency
- During parenteral admixture preparation, activities that will disrupt airflow in the vicinity of the BSC or transport contaminants into or out of the cleanroom and/or the BSC such as opening boxes and opening and closing nearby doors should be minimized[7]
- Telephones or hands-free intercoms should be used for communication with the staff in the cleanroom
- **Appropriate personal protective equipment (PPE) must be donned by all personnel prior to entering the cleanroom to minimize the spread of skin particles that may shed**[1]
- **Lab coats must not be worn in the cleanroom in place of chemotherapy gowns**[1]
- **No shipping or other external cartons may be taken into the cleanroom or the compounding area**[1,2]
- The anteroom may be used for switching of supplies, loading and unloading of carts, setting up of orders, donning personal protective equipment, and preparation for entry into the cleanroom.
- Supplies for the cleanroom should be removed from boxes in the anteroom. Corrugated cardboard should not be stored in the anteroom
- **Hazardous drugs must be stored separately from other inventory in a manner that prevents HD contamination and personnel exposure.**[1-6,9] Many HDs have sufficient vapour pressures that allow volatilization at room temperature, therefore should be stored within a contained negative pressure room with sufficient general exhaust ventilation, at least 12 air exchanges per hour to dilute and remove any airborne contaminants[1-4]
- Cytotoxic spill kits should be available near the storage area[2]

A.2.1 Location of Biological Safety Cabinets

It is recommended that the BSC be located in a cleanroom that has minimal microbial and particulate contamination. An adjacent support area or anteroom also helps to minimize the particulate burden. The Class II BSC shall be placed in an area that is physically separated from non-hazardous drug preparation areas.[1]

A BSC used for HD compounding must be located away from doorways, traffic corridors, and air conditioning and heating vents[1,3,10,11] **inside a restricted access negative pressure ISO Class 7 cleanroom.**[1]

Summary of USP <797> Engineering Control Requirements for Hazardous Drug Sterile Product Preparation and Storage Areas

	Cleanliness classification	HVAC (Heating Ventilation and Air Conditioning)					
		Temperature and humidity	Min Total Air Changes per Hour (ACPH)	Relative pressurization to adjacent area	Pressure monitoring device installed and monitored	Area exhaust ventilation	HEPA filtered supply air
HD Cleanroom (Buffer room)	ISO Class 7 [1,12] (under dynamic conditions)	20° or cooler[1] 25-50% relative humidity*[13] *appropriate controls present	≥ 30 ACPH[1]	**Negative[1]** (not less than 0.01-inch water column negative pressure to adjacent positive pressure ISO Class 7 or better ante-areas[1]	Required[1]	Required[1]	Required[1,12]
Anteroom (adjacent to HD cleanroom)	ISO Class 7 [1,12] (under dynamic conditions)		≥ 12 ACPH[14]	**Positive[1]**	Required[1] (between anteroom and the general environment		Required[1]
HD Storage Area(s) (may include HD Clinical Trials area and HD receiving area if HDs are stored in area)			≥ 12 ACPH[1]	Negative* *preferred[1]		Required[1]	

Section B

B.1 Cleaning

Environmental contact is a major source of microbial contamination of compounded sterile products, and HD contamination on surfaces is a potential source of personal exposure for healthcare workers. Consequently, scrupulous attention to cleaning, disinfection and decontamination in the hazardous drug cleanroom and anteroom where staff work to prepare sterile products is required.[1]

Staff must be instructed on how to safely carry out their cleaning responsibilities within the cleanroom, the anteroom and in the vicinity of the BSC in order to minimize HD exposure to themselves and the environment.[1,2]

B.1.1 Pharmacy Responsibilities

Daily

- Clean interior of the BSC
- Clean HD checking and set-up counter(s)
- Clean the pass through windows, walls and shelves
- HD garbage
  - ✓ Tie the bag and/or seal the container before removing
  - ✓ Do not compress contents as it may generate airborne HD particles
  - ✓ Do not store new garbage bags in the bottom of the HD waste container

Weekly

- Decontaminate the interior and clean the exterior of the BSC[15]
- Clean IV admixture dispensing trays
- Clean transfer carts

Monthly

- Clean refrigerator shelves
- Clean storage shelves
- Clean non-transfer carts
- Clean hazardous drug and supply bins

B.1.2 Housekeeping Responsibilities

Daily

- Clean sinks
- Clean stools/chairs
- Clean floors

Monthly

- Clean walls
- Clean ceilings
- Clean window blinds (if present)

Section C

C.1 Documentation

Documentation records of routine BSC, cleanroom and anteroom cleaning must be completed and maintained.[2] Both refrigeration[2] and freezer temperature logs should be maintained on a daily basis. Follow-up action taken as a result of temperature variation should also be documented.[2]

The following are suggestions for regular documentation logs.

C.1.1 Daily Procedures:

Pharmacy

Record fridge & freezer temperatures
Record BSC gauge readings (downflow and exhaust airflow)
Clean interior of the BSC
Clean HD checking and set up counter(s)
Clean the pass through windows, walls and shelves
Remove HD garbage

Month_____ (Fridge Temperature) **Year**_____

1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

Month_____(BSC Gauge Readings)

1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

Month_____(Cleaning completed – Initial below)

1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

Housekeeping

Clean floors
Clean sinks
Clean stools/chairs

Month_____(Cleaning completed - Initial below) **Year** _____

1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

C.1.2 Weekly Procedures:

Pharmacy

Clean transfer carts
Clean IV admixture dispensing trays
Decontaminate the interior and clean the exterior of the BSC

Week (Cleaning completed - Initial below) **Month** _____ **Year**_____

1	2	3	4	5

C.1.3 Monthly Procedures:

Pharmacy

Clean non-transfer carts
Clean storage shelves
Clean HD and supply bins
Clean refrigerator shelves
Turn on mounted eye wash station and run for several minutes
Turn on safety shower

Year _____ (Once completed - Initial below)

January		February		March		April	
May		June		July		August	
September		October		November		December	

Housekeeping

Clean walls
Clean ceilings
Clean window blinds (if present)

Year _____ (Cleaning completed - Initial below)

January		February		March		April	
May		June		July		August	
September		October		November		December	

C.1.4 Quarterly Procedures

Pharmacy

Change portable eye wash station solution – check expiry date

Year _____(Once completed - Initial below)

January		April		July		October	
February		May		August		November	
March		June		September		December	

C.1.5 Miscellaneous Procedures

Certify the BSC and complete particulate counts in the clean room every 6 months.

(Initial below and attach a copy of current certification report to BSC)

References

1. United States Pharmacopeia. United States Pharmacopeia (USP) <797> Pharmaceutical Compounding - Sterile Preparations. 2008.

2. International Society of Oncology Pharmacy Practitioners Standards Committee. ISOPP Standards of Practice. Safe Handling of Cytotoxics. J.Oncol.Pharm.Pract. 2007;13 Suppl:1-81. DOI: 10.1177/1078155207082350.

3. ASHP Council on Professional Affairs. ASHP Guidelines on Handling Hazardous Drugs. American Journal of Health-System Pharmacy 2006 15 Jun;63(12):1172-1191. DOI: http://dx.doi.org/10.2146/ajhp050529.

4. National Institute for Occupational Safety and Health (NIOSH). NIOSH Alert Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings. 2004 September;2004-165.

5. American Society of Health-System Pharmacists. Basics of Aseptic Compounding Technique - Video Training Program. Bethesda, MD: ASHP; 2006.

6. Power L, Jorgenson J. Safe Handling of Hazardous Drugs - Video Training Program. Bethesda, MD: ASHP; 2006.

7. Chow L, Moore M, BCCA Division of Pharmacy. Aseptic and Safe Preparation of Cytotoxic Drugs - Procedures and Checklists. Vancouver, BC: BC Cancer Agency; 1995.

8. WorkSafe BC Publications. OHS Regulation Part 6 Substance Specific Requirements - Cytotoxic Drugs. 2006; Available at: http://www2.worksafebc.com/publications/OHSRegulation/Part6.asp#top. Accessed Oct. 9, 2007.

9. CAPhO. Standards of Practice for Oncology Pharmacy in Canada Version 2. November 2009; Available at: http://www.capho.org/docs/StandardsofPractice/StandardsofPracticeFORWEBV2B.htm. Accessed March 4, 2010.

10. CSHP. Guidelines for Handling and Disposal of Hazardous Pharmaceuticals (Including Cytotoxic Drugs). : CSHP; 2003-4. p. 31-42.

11. Use of Biological Safety Cabinets. 2006; Available at: http://www.uiowa.edu/~hpo/biosafety/BSC.htm. Accessed April 16, 2008.

12. Samuelson A. College of Pharmacists of British Columbia Hospital Summary Site Visit Inspection Report. 2011 April 7.

13. Kastango E, DeMarco S. Pharmacy Cleanroom Project Management Considerations: An Experience-Based Perspective. IJPC 2011 May/June;5(3):221-225.

14. Controlled Environment Testing Association. CETA Flowchart of Engineering Control Requirements for Hazardous Drugs. Available at: http://www.clinicaliq.com/content/CETAHazFlowChart.pdf. Accessed December 12, 2011.

15. American Society of Health-System Pharmacists. ASHP Technical Assistance Bulletin on Handling Cytotoxic and Hazardous Drugs. Am.J.Hosp.Pharm. 1990 May;47(5):1033-1049.