

# ONCOLOGY PRACTICE MANAGEMENT

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## LEARNING OBJECTIVES

At the end of the presentation and after reviewing the accompanying reading materials, the participant should be able to:

1. Describe the breadth and scope of oncology pharmacy services across the continuum of inpatient and outpatient care.
2. Articulate an understanding of compliance standards related to facilities for drug preparation and dispensing, practice standards for sterile products processing, safe handling and disposal of cytotoxic drugs.
3. Explain the application of automated dispensing technology and electronic health records with their resultant impact on the practice of oncology pharmacy.
4. Apply quality improvement standards to practice of oncology pharmacy.
5. Explain the multi-faceted approach to ordering, procuring, and dispensing drugs for oncology patients in an era of multi-tiered drug acquisition costs, drug shortages and diminishing healthcare resources.

## Domain 3: Practice Administration and Development

Establish, implement, and monitor systems, policies and procedures to ensure the safe, effective, and appropriate use of medications for patients with cancer. **(16% of the examination)**

### Tasks:

1. Design, implement, evaluate, and modify pharmacy services appropriate to the needs of patients across the cancer-care continuum.
2. Ensure that oncology pharmacy services comply with established regulations and standards.
3. Develop and/or modify institutional drug-use guidelines, policies, and procedures, in collaboration with other providers and/or agencies that are consistent with national clinical practice guidelines and standards.
4. Establish and modify systems (i.e., technology and processes) to ensure the safe use of oncology medications.
5. Perform quality-improvement activities aimed at enhancing the safety and effectiveness of medication-use processes in oncology patient care.
6. Develop and implement a process to optimize drug availability for oncology patients.
7. Justify and document clinical and financial value of oncology pharmacy services.

### Knowledge Statements:

01. Clinical practice guidelines for cancer treatment and supportive care published by organizations such as ASCO, National Comprehensive Cancer Network® (NCCN®), IDSA, and MASCC
02. Methods for developing and evaluating clinical practice guidelines
03. Professional practice standards and guidelines (e.g., ASCO-ONS Standards for Safe Chemotherapy Administration, ASHP Guidelines on Handling Hazardous Drugs)
04. National accreditation and regulatory organizations and requirements (e.g., Joint Commission, CMS, NIOSH, USP 797, OSHA, OBRA, DEA, FDA) and their impact on the care of cancer patients
05. Medication reimbursement and patient assistance programs
06. Quality improvement strategies (e.g., MUE/DUE, failure mode and effects analysis, root cause analysis, ISMP recommendations) to enhance the safety and effectiveness of medication-use processes
07. Methods for handling and disposal of hazardous drugs and related materials
08. Investigational drug management (e.g., protocol review, inventory control, documentation, reconciliation)
09. Capabilities and limitations of electronic health information systems
10. Ethics and patient rights for oncology patients (e.g., informed consent, confidentiality)
11. Metrics for evaluating value of oncology pharmacy services (e.g., patient and caregiver satisfaction, length of stay, medication adherence and errors)

## CLINICAL PRACTICE STANDARDS

You are training a new pharmacy technician at your institution. You administer a pre-test to determine their knowledge of compounding hazardous medications. One of the questions on the test is:

**When compounding a hazardous compounded sterile product (CSP), which of the following is required?**

- a. Prepared in a Laminar Flow Hood (LFA)
- b. Wearing a single pair of chemotherapy gloves
- c. Changing gloves once per 8 hour shift
- d. Wearing 2 pairs of chemotherapy gloves

### I. ASHP Guidelines for Hazardous Drug Handling<sup>1</sup>

#### A. Purpose

1. Provide updates regarding new and continuing concerns for health care workers handling hazardous drugs
2. Provide information on recommendations, including those regarding equipment, for handling and compounding hazardous drugs. These recommendations extend to any areas where hazardous drugs are received, stored, prepared, administered or disposed.

#### B. Background

1. At any point during manufacture, transport, distribution, receipt, storage, preparation, and administration, as well as, waste handling, and equipment maintenance and repair exposure to hazardous drugs could occur for workers.
2. Mutagenic properties of hazardous drugs place workers that have the potential to be exposed at risk for acute and short-term reactions (skin, ocular, flu-like symptoms, and headache), risk of fetal abnormalities or fertility impairment, and secondary cancers. Exposure to cyclophosphamide has been estimated to cause 1.4 to 10 cases per million of cancer annually.
3. Routes of exposure:
  - a. Urine – entry of hazardous drugs through inhalation, ingestion of contaminated food or mouth contact with contaminated hands.
  - b. Skin absorption
4. Hazard Assessment
  - a. Identification – qualitative evaluation of the toxicity of a given drug
  - b. Exposure assessment – the amount of worker contact with the drug

#### C. Hazardous Drugs as Sterile Preparations

1. Aseptic reconstitution and dilution are governed by USP Chapter 797 (see compliance section for summary of USP 797 guidelines)

#### D. Definitions of Hazardous Drugs

1. Federal hazard communications standard (HCS) defines a hazardous drug (NIOSH definition follows below) as any chemical entity that is a physical or health hazard. A

health hazard is defined as a chemical for which there is statistically significant evidence, based on at least one study conducted in accordance with established scientific principles that acute or chronic health effects may occur in exposed employees.

2. Health hazard (per HCS) – chemicals that are carcinogens, toxic or highly toxic agents, reproductive toxins, irritants, corrosives, sensitizers, and agents that produce target organ effects.
3. Facilities are recommended to create their own list of hazardous drugs based on specific criteria.

E. Recommendations

1. Safety Program

- a. Comprehensive program for managing hazardous drugs must apply to all aspects of use throughout the facility and being a product of collaboration between pharmacy, nursing, medical staff, environmental services, transportation, facilities, employee health, risk management, clinical laboratories, and safety/security.

**Comparison of 2014 NIOSH and 1990 ASHP Definitions of Hazardous Drugs<sup>1</sup>**

<b>NIOSH</b>	<b>ASHP</b>
Carcinogenicity	Carcinogenicity in animal models, in the patient population, or both as reported by the International Agency for Research on Cancer.
Teratogenicity*	Teratogenicity in animal studies or in treated patients.
Reproductive toxicity*	Fertility impairment in animal studies or in treated patients.
Organ toxicity at low doses*	Evidence of serious organ or other toxicity at low doses in animal models or treated patients.
Genotoxicity**	Genotoxicity (i.e., mutagenicity and clastogenicity in short-term test systems).
Structure and toxicity profile of new drugs that mimic existing drugs determined hazardous by the above criteria	

\*NIOSH’s definition contains the following explanation: “All drugs have toxic side effects, but some exhibit toxicity at low doses. The level of toxicity reflects a continuum from relatively nontoxic to production of toxic effects in patients at low doses (for example, a few milligrams or less). For example, a daily therapeutic dose of 10 mg / day or a dose of 1 mg / kg / day in laboratory animals that produces serious organ toxicity, developmental toxicity, or reproductive toxicity has been used by the pharmaceutical industry to develop occupational exposure limits (OELs) of less than 10 micrograms/meter<sup>3</sup> after applying appropriate uncertainty factors. OELs in this range are typically established for potent or toxic drugs in the pharmaceutical industry. Under all circumstances, an evaluation of all available data should be conducted to protect health care workers.”

\*\*NIOSH’s definition contains the following explanation: “In evaluating mutagenicity for potentially hazardous drugs, responses from multiple test systems are needed before precautions can be required for handling such agents. The EPA evaluations include the type of cells affected and *in vitro* versus *in vivo* testing.”

- b. Ready access to Material Safety Data Sheets (MSDS) for all staff is imperative. ([www.msdsonline.com](http://www.msdsonline.com)) MSDS sheets define appropriate handling precautions, necessary protective equipment and spill management for individual drugs.
- c. Labels for hazardous drugs should clearly indicate that safe handling precautions are required during transport and use.
- d. Outside of vials for hazardous drugs should be expected to be contaminated – this includes the package inserts and inside of the packing cartons. This impacts any staff member receiving shipping containers and repackaging drug product.
- e. Environmental services workers, patient care/medical assistants and nursing personnel that handle drug waste and patient waste are also at risk and require training for handling hazardous materials.
- f. Manufacturer packing should be labeled with a distinctive identifier that notifies personnel receiving them to wear appropriate personal protective equipment (PPE) while handling.
- g. Standard operating procedures (SOP) should be in place for handling damaged cartons or containers of hazardous drugs, including the use of PPE and an NIOSH-certified respirator (if needed), and procedures for returning the damaged goods to the manufacturer.

2. Labeling and Packaging from Point of Receipt

- a. Drug packages, bins, shelves, and storage areas for hazardous drugs must bear distinctive labels for identifying special handling precautions.
- b. Segregation of hazardous drug stock from other drug inventory should be considered. The area of storage should have sufficient exhaust ventilation to dilute and remove any air-borne contaminants.
- c. Optimize use of storage bins (high fronts, shelving with guards) to minimize chance for breakage.
- d. Consider “look-alike, sound-alike” drugs when organizing stock and label accordingly. This is a significant issue for Joint Commission during inspections.
- e. Staff members should double-glove when stocking and inventorying hazardous drugs.
- f. Hazardous drug packages must be in sealed containers and labeled with a unique identifier.
- g. Carts and transport devices should be designed with guards to protect against falling and breakage of a hazardous drug package.
- h. Individuals transporting hazardous drugs must have safety training that includes spill control and have spill kits readily available.
- i. Workers handling hazardous drugs must be trained to appropriately perform job duties using protocolized safety precautions and use required PPE.

3. Environment

- a. Hazardous drugs should be compounded in a controlled area where access is limited to authorized personnel trained in handling requirements.
- b. Due to the hazardous nature of hazardous drug compounding, a contained environment where air pressure is negative to the surrounding areas or that is protected by airlock or anteroom is preferred. Further addressed in USP 797.
- c. During administration, access to the administration areas should be limited to patient receiving therapy and essential personnel. Eating, drinking, applying makeup and the presence of food should be avoided.
- d. For inpatient units, administering hazardous drugs should be coordinated to avoid exposure of family members visiting a patient and arrival of dietary trays.
- e. For outpatient infusion clinics, care should be taken to minimize environmental contamination and maximize effectiveness of decontamination procedures.
- f. Avoid carpeting and upholstered surfaces and separate break room and kitchen areas away from treatment areas.
- g. Administration of hazardous medications in unique treatment settings such as the operating rooms requires specialized procedures to prevent contamination and provide training to staff. Spill kits, containment bags, and disposal containers must be available in all areas where hazardous drugs are handled.
- h. Techniques and ancillary devices which minimize the risk of open systems should be used when administering hazardous drugs through unusual routes or in nontraditional locations.

4. Ventilation Controls

- a. For CSPs that are hazardous, a Class II or III biologic safety cabinet (BSC) is required. Alternatively, an isolator intended for aseptic preparation may be substituted.
- b. Class II BSC have limitations including risk of vaporization of hazardous drug particles upon vial entry that may reduce effectiveness of high-efficiency particulate air (HEPA) filtration. Studies have documented contamination with hazardous drugs on the floor surface inside the BSC, on gloves of the staff using the BSC, on the final product and in the within the BSC.
- c. Class III BSC are totally enclosed fixed glove access with the internal cabinet maintained under negative pressure. Supply and exhaust air are HEPA filtered. This equipment is typically reserved for highly infectious or toxic material and seldom used for extemporaneous compounding of sterile products because of the high cost.
- d. Glove boxes are most commonly used in the nuclear industry and not compounding hazardous drugs.
- e. Isolators may be considered a ventilated controlled environment that has fixed walls, floor and ceiling. For CSPs, air supply requires HEPA filtration and exhaust air must be HEPA filtered and flow outside of the building and not in the

workroom. Workers access the isolator main chamber through gloves, sleeves, air-locks or pass-throughs. Air flow must achieve an ISO class 5 environment within the isolator. Guidelines for application of isolators to health care facilities are provided by the Controlled Environment Testing Association ([www.cetainternational.org/reference/isolator3.pdf](http://www.cetainternational.org/reference/isolator3.pdf)).

- f. The totally enclosed design of isolators may reduce the escape of contaminants during the compounding process and be less responsive to environmental drafts. Isolators do not prevent generation of contamination within the cabinet workspace and there still exists the risk of drug contamination from the main cabinet to the pass-through.
- g. Isolators that discharge air into the workroom, even through high-efficiency filters present exposure concerns similar to those of unvented Class II BSCs with vaporized hazardous drugs during compounding.
- h. Closed-system transfer devices (CSTD) may prevent the transfer of environmental contaminants into the system and the escape of drug vapor out of the system. Several proprietary CSTD products are on the market and have several years of clinical use. These are multi-component systems with a double-membrane to enclose a specialty cut injection cannula as it moves into a drug vial.
- i. Several studies have documented a reduction in environmental contamination with CSTD; however, the use of CSTD is **not** a substitute for use of a ventilated cabinet.

**A new pharmacy technician in your cancer center is training. He asks you about required personnel protective equipment (PPE). He asks you if any of the following listed below are NOT required:**

- a. Chemotherapy gloves
- b. Wearing impermeable gowns
- c. Shoe and hair covers
- d. Respirator

- 5. Personnel Protective Equipment
  - a. Gloves – Essential for handling hazardous drugs and must be worn at **all** times when handling drug packaging, cartons and vials including while performing inventory control procedures and when gathering hazardous drugs and supplies for compounding a batch or a single dose.
  - b. During compounding in a Class II BSC, gloves and gowns are required to prevent skin surfaces from coming in to contact with hazardous drugs. Both latex and non-latex gloves are effective against penetration and permeation by most hazardous drugs. Gloves made of nitrile; neoprene rubber and polyurethane have been tested successfully against antineoplastic drugs.
  - c. Standards for testing gloves are available from the American Society for Testing and Materials (ASTM). Gloves that prevent permeation with antineoplastic

drugs are designated “chemotherapy gloves”. Gloves selected for use with hazardous agents should meet this ASTM standard.

- d. Under standard working conditions, double-gloving and wearing gloves for no longer than 30 minutes at a time is recommended.
- e. Hands should be washed thoroughly prior to donning gloves and following removal.
- f. Two pair of gloves is recommended while compounding hazardous drugs. After compounding is complete the outer gloves are removed. The inner gloves are then used to affix labels and place the preparation into a sealable containment bag for transport.
- g. One pair of gloves is recommended when using the fixed-glove assembly.
- h. Outer gloves should be changed whenever it is necessary to exit and re-enter the BSC. For aseptic preparation of sterile preparations, the outer gloves must be sanitized with an appropriate disinfectant when reentering the BSC.
- i. Gloves must be changed immediately if torn, punctured, or knowingly contaminated.
- j. When wearing two pairs of gloves in the BSC, one pair is worn under the gown cuff and the second pair placed over the cuff.
- k. When removing gloves, the contaminated glove fingers must only touch the outer surface of the glove, never the inner surface. If the inner gloves become contaminated, then both pairs of gloves must be changed.
- l. When removing any PPE, care must be taken to avoid contaminating the surrounding environment with hazardous drug residue.
- m. Gloves should be placed in a sealable plastic bag for containment within the BSC or isolator pass-through before disposal as hazardous waste.
- n. If an IV set is attached to the final preparation in the BSC or isolator, care must be taken to avoid contaminating the tubing with hazardous drug from the surface of the gloves, BSC or isolator.
- o. Gloves or gauntlets attached to BSCs or isolators should be considered contaminated once used for compounding hazardous drug and sanitized per manufacturer’s recommendations.
- p. All final preparations should be surface decontaminated by staff wearing clean gloves to avoid spreading contamination.
- q. Personal protective gowns are recommended during the handling of hazardous drug preparations to protect the worker from inadvertent exposure to extraneous drug particles on the surfaces or generated during the compounding process. Use of gowns is recommended in compounding in the BSC, drug administration, spill control and waste management.
- r. Gowns should be lint-free, low-permeability fabric with a closed front, long-sleeves, and tight-fitting elastic or knit cuffs.



- s. Only gowns with polyethylene or vinyl coatings prevented drug permeation.
- t. Gowns used for compounding hazardous CSPs must never be worn outside the immediate drug preparation area. They should be removed carefully and discarded as contaminated waste.
- u. Eye and face protection should be worn whenever there is a possibility of exposure from splashing or uncontrolled aerosolization of hazardous drugs.
- v. If a respirator is deemed appropriate, all workers using a respirator must be fit-tested and trained according to the OSHA Respiratory Protection Standard.
- w. Shoe and hair coverings should be worn during the sterile compounding process.

## 6. Work Practices

- a. Compounding Sterile Hazardous Drugs
  - i. Work practices differ from Class II and III BSCs and isolators
  - ii. All activities not requiring a critical environment (e.g. checking labels, dose calculations) should be done outside the BSC/isolator.
  - iii. Two pair of gloves should be worn to gather hazardous drugs and supplies.
  - iv. Fresh gloves should be donned and appropriately sanitized before aseptic manipulation.
  - v. Only supplies and drugs essential to compounding the dose or batch should be placed in the work area of the BSC or main chamber of the isolator.
  - vi. Spiking an IV set containing hazardous drugs or priming an IV set with hazardous drugs in an uncontrolled environment should be avoided. Priming the IV set with the diluent prior to adding the hazardous drug is an acceptable practice.
  - vii. CSTD should achieve a dry connection between the administration set and the hazardous drug's final container. This connection allows for the container to be spiked with a secondary IV set and the set to be primed with backflow from a primary non-hazardous solution. This may be done outside of a BSC or isolator to reduce the potential for surface contamination. A new IV set must be used with each dose of hazardous drug.
  - viii. Transport bags must never be placed in the BSC or isolator work chamber to avoid inadvertent contamination on the outer surface of the bag.
  - ix. Final preparations must be surface decontaminated after compounding is complete.
  - x. In either a BSC or isolator, clean inner gloves must be worn when labeling and placing the final preparation into the transport bag.

- xi. Handling final preparations with contaminated gloves transfers contamination to other workers or potentially patients. Don fresh gloves whenever there is doubt as to the cleanliness of the inner or outer gloves.
  - b. Working in BSCs and Isolators
    - i. Hazardous drug residue may be introduced into the workroom area via pass-through and airlocks.
    - ii. Surface decontamination of the preparation before removal from the main chamber of an isolator is recommended with alcohol, sterile water, peroxide, or sodium hypochlorite solutions provided that the packaging is not permeable to the solution and the labels remain intact.
  - c. BSCs
    - i. BSCs use vertical flow, HEPA-filtered air (ISO class 5) as their controlled aseptic environment.
    - ii. Workers are to wash hands, don chemotherapy gloves and a coated gown followed by a second pair of chemotherapy gloves.
    - iii. The front shield of the cabinet should be lowered to the proper level to protect the face and eyes.
    - iv. All drugs and supplies should be sanitized with 70% sterile alcohol.
    - v. All items should be placed away from the front of the unfiltered air at the front of the cabinet and perform manipulations at least 6 inches away from the sidewalls of the cabinet.
  - d. Isolators
    - i. All drugs and supplies should be sanitized with 70% sterile alcohol.
    - ii. An enclosed tray with drug and supplies may be introduced into the main chamber for compounding use.
    - iii. Contaminated materials are removed using the closed trash system of the isolator.
    - iv. A second sealable bag should be used for transport of the compounded product.
    - v. Additional work practices for cleaning off the gloves or gauntlets and final preparation are recommended.
  - e. Aseptic Technique
    - i. When reconstituting hazardous drugs in vials, it is critical to avoid pressurizing contents of the vial which increases risk of drug aerosolization.
    - ii. Safe handling of hazardous drug solutions and vials or ampules requires the use of a syringe that is no more than 3/4 full when filled

with the solution, to minimize the risk of plunger separating from the syringe barrel.

- iii. The final preparation should be labeled, including an auxiliary warning and the injection port covered with a protective shield.
  - iv. The final container should be placed, using clean gloves, into a sealable bag to contain any leakage.
  - v. Hazardous drugs removed from an ampule should use an appropriate filter needle or filter straw attached to a syringe large enough that it will not be more than 3/4 full.
- f. Training and demonstration of competence
- i. All staff that will compound hazardous drugs require training in aseptic and negative-pressure techniques to prepare sterile products.
  - ii. Competency must be demonstrated by an objective method and assessed on a regular basis.
- g. Preparation and handling of non-injectable hazardous drug dosage forms
- i. Procedures for the preparation and use of equipment (e.g. BSCs, bench-top hoods with HEPA filters) must be developed to avoid release of aerosolized powder or liquid into the environment during manipulation of hazardous drugs.
- h. Decontamination, deactivation, and cleaning
- i. No single process has been found to deactivate all hazardous agents.
  - ii. Decontamination of all BSCs and isolators should follow manufacturer recommendations.
  - iii. Strong oxidizing agents such as sodium hypochlorite are effective deactivators of many hazardous drugs.
  - iv. Cabinets used for aseptic compounding must be disinfected at the beginning of the workday and each successive shift.
  - v. Appropriate preparation of materials used in compounding before introduction into the Class II BSC or the pass-through of an isolator including spraying or wiping with a 70% alcohol or appropriate disinfectant.
  - vi. The area under the work tray of the BSC should be cleaned at least monthly to reduce contamination levels.
- i. Administration of hazardous drugs
- i. Policies and procedures for administration of hazardous drugs should be developed by pharmacy and nursing for the mutual safety of health care workers.
  - ii. Extensive guidelines for hazardous drug administration have been published by OSHA and the Oncology Nursing Society.<sup>2</sup>

- j. Spill management
    - i. Written procedures defining roles of personnel during spill events and define the size and scope of the spill are recommended.
    - ii. Spill kits should be assembled and readily available in areas where hazardous drugs are administered.
    - iii. Only workers with appropriate PPE and respirators should attempt to manage a hazardous drug spill.
  - k. Worker contamination
    - i. Isotonic eyewash supplies and soap should be readily available in areas where hazardous drugs are handled.
    - ii. Workers who have skin or eye contamination with hazardous drugs require immediate medical attention.
7. Hazardous Waste Containment and Disposal
- a. Trace-contaminated hazardous drug waste
    - i. Resource Conservation and Recovery Act (RCRA) enacted by Congress in 1976 allowed tracking of hazardous waste from generation to disposal which is enforced by the Environmental Protection Agency (EPA).
    - ii. RCRA designates the following as hazardous or “characteristic” waste: epinephrine, nicotine, physostigmine, arsenic trioxide, chlorambucil, cyclophosphamide, daunomycin, diethylstilbestrol, melphalan, mitomycin C, streptozocin, and uracil mustard.
    - iii. Containers that hold less than 3% of characteristic waste are exempt from hazardous waste regulations.
    - iv. General categories of hazardous waste include: trace-contaminated hazardous waste, bulk hazardous waste, hazardous drugs not listed as hazardous waste, and hazardous waste and mixed infectious hazardous waste.
    - v. Trace-contaminated hazardous drug waste may include “RCRA-empty” containers, needles, syringes, trace-contaminated gowns, gloves, pads and empty IV sets which may be incinerated at regulated medical waste incinerator.
  - b. Bulk hazardous waste
    - i. Differentiates containers that held either (1) RCRA-listed or characteristic hazardous waste or (2) any hazardous drugs that are not RCRA empty or any materials from hazardous drugs spill cleanups.
    - ii. These wastes should be managed as hazardous.
  - c. Hazardous drugs not listed as hazardous waste

- i. RCRA regulations have not kept up with drug development and consequently there are over 100 hazardous drugs that are not listed as hazardous waste.
  - ii. Regulations may vary by state – for example, Minnesota listed hormonal agents as hazardous waste.
- d. Hazardous waste and mixed infectious-hazardous waste
- i. Most hazardous waste vendors cannot manage regulated medical waste or infectious waste; therefore they cannot accept used needles or other items contaminated with blood.
  - ii. Properly labeled, leak proof, and spill-proof containers of non-reactive plastic are required for areas where hazardous waste is generated.
  - iii. Hazardous drugs may be in thick, sealable, plastic bags before being placed in approved satellite accumulation containers.
  - iv. Waste contaminated with blood or other body fluids should not be mixed with hazardous waste.
  - v. Transport of hazardous waste containers from satellite accumulation to storage sites must be done by individuals who have completed OSHA mandated hazardous waste awareness training.
  - vi. More information on hazardous waste disposal may be found at [www.hercenter.org](http://www.hercenter.org) . Accessed 4/11/2015.

8. Alternative Duty and Medical Surveillance

- a. A comprehensive management program for preventing hazardous drug exposure to workers includes engineering controls, training, work practices and PPE.
- b. Safety programs should identify at risk individuals and alternative duty should be offered to workers who are pregnant or attempting to conceive.
- c. All workers who handle hazardous drugs should be routinely monitored in a medical surveillance program. The specifics of such a program are not defined in the document.

**II. ASHP Guidelines on Compounding Sterile Preparations – 2014<sup>2</sup>**

- A. Provides guidance to personnel to prepare high-quality CSPs and reduce potential for harm to patients and consequences for compounding personnel.
- B. Summary of regulations for CSPs
- C. Outline Physical Facilities and Equipment including primary engineering controls (PEC), architecture, air supply, surfaces, renovations, pharmacy compounding devices and power requirements.

### Primary Engineering Controls (PEC)

PEC Device	Used to Prepare Non-Hazardous CSPs	Used to Prepare Hazardous CSPs
Conventional	Laminar Airflow workbench (LAFW)	Class II Biologic Safety Cabinet (BSC)
Isolators	Compounding aseptic isolator (CAI)	Compounding aseptic containment isolator (CACI)

### Facilities Features Required for Specific Types of Compounding (Based on USP 797)

	Low-Risk with ≤12 hour BUD (non-hazardous)	Low-Risk (Non-Hazardous)	Medium-Risk (Non-Hazardous)	High-Risk (Non-Hazardous)	Hazardous Drugs
Architectural Style	Segregated	Open or closed	Open or closed	Closed	Closed
Buffer Zone ISO Classification	N/A	ISO Class 7 or better	ISO Class 7 or better	ISO Class 7 or better	ISO Class 7 or better
Ante area ISO classification	N/A	ISO Class 8 (ISO Class 7 if opens into negative pressure area) or better	ISO Class 8 (ISO Class 7 if opens into negative pressure area) or better	ISO Class 8 (ISO Class 7 if opens into negative pressure area) or better	ISO Class 7 or better
Minimum air exchanges for buffer area	N/A	30	30	30	30
Minimum air exchanges for ante area	N/A	20 if ISO 8; 30 if ISO 7	20 if ISO 8; 30 if ISO 7	20 if ISO 8; 30 if ISO 7	30
Pressure	N/A	Positive	Positive	Positive	Negative

\*Clean room (Buffer area) differs from ordinary ventilated room by having:

1. Increased air supply
2. HEPA filtration

3. Room Pressurization

4. A perforated plate or swirl of air diffuser (if an air diffuser is necessary); high-induction supply air diffuser should not be used in buffer areas.

D. Minimum Frequency for Cleaning of Specific Sites

Site	Minimum Frequency
ISO Class 5 PEC	Beginning of each shift; before each batch; every 30 minutes while compounding; after spills; when surface contamination is known or suspected
Counters and easily cleanable work surfaces	Daily
Floors	Daily
Walls	Monthly
Ceilings	Monthly
Storage shelving	Monthly

**Environmental Sampling Frequency**

At commissioning and certification of new facilities and equipment
Every six months during routine certification of equipment and facilities
After any facility or equipment maintenance, including construction or remodeling of adjacent department or work on shared air handlers
At any point when the problems are identified with products, preparations, or employee technique or if a CSP is suspected to be the source of patient infection

### Environmental Monitoring Requirements

Parameter	Monitored By	Frequency
Temperature	Compounding personnel or facilities management staff (if electronic monitoring is centralized)	Documented daily (at minimum)
Pressure differential or velocity across line of demarcation	Compounding personnel	Documented each shift (preferentially), daily (at a minimum)
Nonviable particles	Qualified certifier	At least every 6 months
Surface sampling	Qualified certifier	Periodically, as defined by compounding and infection control personnel, at least every 6 months or after significant changes in procedures or cleaning practices
Electronic device sample of viable particles	Compounding or laboratory personnel	At least every 6 months

### Controlled Temperatures

	Centigrade	Fahrenheit
Room temperature	20 to 25° C	68 to 77° F
Cold temperature (refrigerated)	2 to 8° C	36 to 46° F
Freezer (frozen)	-25 to -10° C	-13 to 14° F



E. CSP risk level with expiration and beyond use dating

Risk Category	Compounding Location	Garbing Required	Aseptic Technique Required	BUD of CSP stored at Room Temperature	BUD of CSP stored at Refrigeration	BUD of CSP stored at Frozen
Low-risk	ISO Class 5 PEC, ISO Class 7 buffer area, ISO Class 8 ante area	Yes	Yes	48 hours	14 days	45 days
Low-risk with < 12 hour BUD	ISO Class 5 PEC segregated from other operations	Yes	Yes	12 hours	12 hours	N/A
Medium-risk	ISO Class 5 PEC, ISO Class 7 buffer area, ISO Class 8 ante area	Yes	Yes	30 days	9 days	45 days
High-risk	ISO Class 5 PEC, ISO Class 7 buffer area, ISO Class 7 ante area	Yes	Yes	24 hours	3 days	45 days
Immediate Use	Medication preparation areas should be clean, uncluttered and functionally separate	No	Yes	1 hour	N/A	N/A

F. Ampules vs. Single-dose vials vs. multi-dose containers

BUD for ampules, single-dose and multiple-dose containers

	Opened and maintained within an ISO Class 5 Environment	Opened outside an ISO 5 environment or taken from ISO Class 5 conditions to less clean air
Ampules	One time use; cannot be stored	One time use; cannot be stored
Single-dose vials	One time use, cannot be stored; contents of unopened vial may be repackaged in times of critical need	One time use; cannot be stored
Pharmacy bulk packages	6 hours	Not intended for use outside ISO 5 environment
Multiple-dose vials	28 days	28 days

III. **USP 797 Pharmaceutical Compounding – Sterile Preparations<sup>3</sup>**

- A. Goal – Describe conditions and practices to prevent harm, including death, to patients that could result from (1) microbial contamination (nonsterility), (2) excessive bacterial endotoxins, (3) variability in the intended strength of correct ingredients that exceeds either monograph limits for official articles or 10% for nonofficial articles, (4) unintended chemical and physical contaminants, and (5) ingredients of inappropriate quality in compounded sterile preparations (CSPs).
- B. Four specific categories of CSPs are described in the USP 797 guidelines (detailed criteria follow below):
  - 1. Low-risk level
  - 2. Medium-risk level
  - 3. High-risk level
  - 4. Immediate use

C. ISO Classification of Particulate Matter in Room Air

Class Name		Particle Count	
ISO Class	US FS 209E*	ISO, m <sup>3</sup>	FS 209E ft <sup>3</sup>
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

\*Adapted from former Federal Standard No. 209E.

D. Responsibility of Compounding Personnel

1. Practices and quality assurances required to prepare, store, and transport CSPs that are sterile and acceptably accurate, pure and stable.

E. CSP Microbial Contamination Risk Levels

1. Proper training and evaluation of personnel, proper cleaning and garbing of personnel, proper cleaning and disinfecting of compounding work environments, and proper maintenance and monitoring of controlled environmental locations (all of which are detailed in their respective sections).

2. Low-Risk Level CSPs:

- a. Aseptic manipulations within an ISO Class 5 environment using three or fewer sterile products and entries into any container.
- b. In absence of passing sterility test, store not more than 48 hours at controlled temperature, 14 days at cold temperature, and 45 days in solid frozen state at -25 to -10°C degrees or colder.
- c. Media fill test at least annually by compounding personnel.

3. Low-Risk Level CSPs with 12 hour or less BUD (Beyond Use Dating):

- a. Fully comply with all four specific criteria.
- b. Sinks should not be located adjacent to the ISO Class 5 engineering control.
- c. Sinks should be separated from the immediate area of the ISO Class 5 primary engineering control device.

4. Medium-Risk Level CSPs

- a. Aseptic manipulations within an ISO 5 environment using prolonged and complex mixing and transfer, more than three sterile products and entries into

any container, and pooling ingredients from multiple sterile products to prepare multiple CSPs.

- b. In the absence of passing sterility test, store not more than 30 hours at controlled room temperature, 9 days at cold temperature, and 45 days in solid frozen state at -25 to -10°C degrees or colder.
- c. Media-fill test at least annually by compounding personnel.

#### 5. High-Risk Level CSPs

- a. Confirmed presence of non-sterile ingredients and devices, or confirmed or suspected exposure of sterile ingredients for more than one hour to air quality inferior to ISO Class 5 before final sterilization.
- b. Sterilization method verified to achieve sterility for the quantity and type of containers.
- c. Meet allowable limits for bacterial endotoxins.
- d. Maintain acceptable strength and purity of ingredients and integrity of containers after sterilization.
- e. In absence of passing sterility test, store not more than 24 hours at controlled room temperature, 3 days at cold temperature, and 45 days in solid frozen state at -25 to -10°C degrees or colder.
- f. Media-fill test at least semiannually by compounding personnel.

#### F. Personnel Training and Evaluation in Aseptic Manipulations

- 1. Pass didactic, practical skill assessment and media-fill testing initially, followed by an annual assessment for a low- and medium-risk level compounding and semi-annual assessment for high-risk level compounding.
- 2. Compounding personnel who fail written tests, or whose media-fill test vials result in gross microbial colonization, shall be instructed and re-evaluated by expert compounding personnel to ensure correction of all aseptic practice deficiencies.

#### G. Immediate-use CSPs

- 1. Fully comply with all six specified criteria:
  - a. Hand hygiene per CDC recommendations
  - b. Aseptic technique is followed
  - c. No hazardous drugs are used

- d. Simple transfer of no more than three sterile, non-hazardous drugs in the manufacturer's original containers are involved in compounding and no more than two entries into any one container occurs
- e. No batching or storage of CSPs occurs
- f. The preparation is labeled with patient identification, names and amounts of all ingredients, name or initials of the preparer and exact 1 hour BUD and time

#### H. Single-Dose and Multiple-Dose containers

- 1. Beyond-use date 28 days, unless specified otherwise by the manufacturer, for closure sealed multiple-dose containers after initial opening or entry.
- 2. Beyond-use time of 6 hours, unless specified otherwise by the manufacturer, for closure sealed multiple-dose containers in ISO Class 5 or cleaner air after initial opening or entry.
- 3. Beyond-use time of 1 hour for closure sealed single-dose containers after being opened or entered in worse than ISO Class 5 air.
- 4. Storage of opened single-dose ampules is not permitted.

#### I. Hazardous Drugs as CSPs

- 1. Appropriate personnel protective equipment.
- 2. Appropriate primary engineering controls (BSCs and CACIs) are used for concurrent personnel protection and exposure of critical sites.
- 3. Hazardous drugs shall be stored separately from other inventory in a manner to prevent contamination and personnel exposure.
- 4. At least 0.01 inch water column negative pressure and 12 air changes per hour in non-cleanrooms in which CACIs are located.
- 5. Hazardous drugs shall be handled with caution at all times using appropriate chemotherapy gloves during receiving, distribution, stocking, inventorying, preparing for administration, and disposal.
- 6. Hazardous drugs shall be prepared in an ISO Class 5 environment with protective engineering controls in place, and following aseptic practices specified for the appropriate contamination risk levels.
- 7. Access to drug preparation areas shall be limited to authorized personnel.
- 8. A pressure indicator shall be installed that can readily monitor room pressurization, which is documented daily.

9. Annual documentation of full training of personnel regarding storage, handling, and disposal of hazardous drugs.
10. Negative-pressure buffer area is not required for low-volume compounding operations when CSTD is used in BSC or CACI.
11. Compounding personnel of reproductive capability shall confirm in writing that they understand the risk of handling hazardous drugs.
12. Disposal of all hazardous drug wastes shall comply with all applicable federal and state regulations.
13. Total external exhaust of primary engineering controls.
14. Assay of surface wipe samples every 6 months.

**IV. Hazardous Drugs – Handling in Healthcare Settings USP 800.<sup>4</sup>**

- A. Note: At the time of this publication, USP has drafted a new proposed chapter on Hazardous Drugs – Handling in Health Care Settings – USP 800. USP posted the first draft of the chapter in April 2014 and published a revised chapter based on the initial comment period on December 1, 2014. USP will accept comments to the current revision until May 31, 2015.
- B. The purpose of the new proposed General Chapter is to provide standards to protect personnel and the environment when handling hazardous drugs (HDs). Each year, approximately 8 million U.S. healthcare workers are potentially exposed to HDs. This chapter identifies requirements for receipt, storage, compounding, dispensing, and administration of HDs to protect the patient, healthcare personnel, and environment. The new proposed General Chapter defines processes intended to provide containment of HDs to as low of a limit as reasonably achievable.
- C. USP 797 and USP 800 will have differences harmonized through an upcoming revision of USP 797 which will include the following:
  1. Elimination of the current allowance in USP 797 for facilities that prepare a low volume of HDs that permits placement of a Biologic Safety Cabinet (BSC) or Compounding Aseptic Containment Isolator (CACI) in a non-negative pressure room. All hazardous drug compounding must be done in a separate area designated for compounding HDs.
  2. Addition of an allowance in USP 800 for a Containment Segregated Compounding Area (C-SCA), a separate, negative pressure room with at least 12 air changes per hour (ACPH) for use when compounding HDs. Low- and medium- compounded sterile preparations (CSP) of HDs may be prepared in a BSC or CACI located in a C-CSA, provided the beyond-use date of the CSP does not exceed 12 hours.
- D. The new proposed General Chapter <800> Hazardous Drugs—Handling in Healthcare Settings addresses:

1. Standards that apply to all personnel who compound hazardous drug preparations and all places where HDs are prepared, stored, transported, and administered
2. Receiving, storing, compounding, dispensing, administering, and disposing of both nonsterile and sterile products and preparations
3. The standards apply to all personnel who compound HDs preparations and all places where HDs are prepared (e.g. pharmacies, hospitals, and other healthcare institutions, patient treatment clinics, physician practice facilities, veterinarians' offices) and other locations and facilities where HDs are stored, transported and administered.
4. Entities that handle HDs must incorporate the standards in the chapter into their occupational safety plan. The entity's health and safety management plan must, at a minimum, include:
  - a. Engineering controls
  - b. Competent personnel
  - c. Safe work practices
  - d. Proper use of appropriate Personal Protective Equipment (PPE)
  - e. Policies for waste segregation and disposal of HDs

E. Chapters:

1. Introduction and Scope – as outlined above
2. List of Hazardous Drugs
  - a. Healthcare entities must maintain a list of HDs, which shall be updated annually.
  - b. The list of HDs may include all items on the current NIOSH Hazardous Drug listing addition to other agents not on the list
  - c. The NIOSH list of antineoplastic and other HDs provide criteria used to identify HDs. These criteria must be used to identify HDs that enter the market after the most recent version of the NIOSH list, or for investigational agents dispensed at an institution. If insufficient information is available, consider the drug hazardous until more information is available.
  - d. Containment Requirements
    - i. Any antineoplastic HD requiring manipulation and HD Active Pharmaceutical Ingredients (API) on the NIOSH list must follow requirements of chapter USP 800.

- ii. Final antineoplastic dosage forms that do not require any further manipulation other than counting final dosage forms may be dispensed without any further requirements for containment unless required by the manufacturer.
  - iii. For dosage forms of other HDs on the NIOSH list, the entity may perform an assessment of risk to determine alternative containment strategies and/or work practices.
- e. Some dosage forms of drugs defined as hazardous may not pose a significant risk of direct occupational exposure because of their dosage formulation (e.g., tablets or capsules – solid, intact medications that are administered to patients without modifying the formulation). However, dust from tablets and capsules may present risk of exposure by skin contact and/or inhalation. An assessment of risk may be performed for these dosage forms to determine alternative containment strategies and/or work practices.
- f. The assessment of risk must, at a minimum contain the following:
- i. Type of HD (e.g. antineoplastic, non-antineoplastic, reproductive risk)
  - ii. Risk of exposure
  - iii. Packaging
  - iv. Manipulation
- g. If an assessment of risk approach is taken, the entity must document what alternative containment strategies and/or work practices are being employed for specific dosage forms to minimize occupational exposure. If used, the assessment of risk must be reviewed at least annually and the review documented.

3. Types of Exposures

- a. Routes of unintentional exposure include dermal and mucosal absorption, inhalation, injection and ingestion (e.g. contaminated foodstuffs, spills, mouth contact with contaminated hands). Both clinical and nonclinical personnel may be exposed to HDs when they handle HDs or touch contaminated surfaces.
- b. Examples of Potential Routes of Exposure Based on Activity

Activity	Potential Route of Exposure
Dispensing	Counting tablets and capsules from bulk containers
Compounding	Crushing tablets or opening capsules



	<p>Pouring oral or topical liquids from one container to another</p> <p>Weighing or mixing components</p> <p>Constituting or reconstituting powdered or lyophilized HDs</p> <p>Withdrawing or diluting injectable HDs from parenteral containers</p> <p>Expelling air or HDs from syringes</p> <p>Contacting HD residue present on PPE or other garments</p> <p>Deactivating, decontaminating, cleaning, and disinfecting areas contaminated with or suspected to be contaminated with HDs</p> <p>Maintenance activities for potentially contaminated equipment and devices</p>
Administration	<p>Generating aerosols during administration of HDs by various routes (e.g. injection, irrigation, oral, inhalation, or topical application)</p> <p>Performing certain specialized procedures (e.g. intraoperative, intraperitoneal injection or bladder instillation)</p> <p>Priming an IV administration set</p>
Patient-Care Activities	<p>Handling body fluids (e.g. urine, feces, sweat, or vomit) or body-fluid-contaminated clothing, dressings, linens, and other materials</p>
Spills	<p>Spill generation, management, and disposal</p>
Receipt	<p>Contacting with HD residues present on drug containers, individual dosage units, outer containers, work surfaces, or floors</p>

Transport	Moving HDs within a healthcare setting
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4. Responsibilities of Personnel Handling Hazardous Drugs
  - a. Each entity must have a designated person who is qualified and trained to be responsible for developing and implementing appropriate procedures, compliance with USP800 and other applicable laws, regulations and standards; ensuring competency of personnel; and ensuring environmental control of the storage and compounding areas. The designated individual must thoroughly understand the rationale for risk-prevention policies, risks to themselves and others, risks of non-compliance that may compromise safety and the responsibility to report potentially hazardous situations to the management team. The designated individual must also be responsible for the continuous monitoring of the facility and maintaining reports of testing/sampling performed in facilities.
  - b. All personnel who handle HDs are responsible for understanding the fundamental practices and precautions and for continually evaluating these procedures and the quality of final HDs to prevent harm to patients, minimize exposure to personnel, and minimize contamination of the work and care environment.
  
5. Facilities
  - a. HDs must be handled under conditions that promote patient safety, worker safety, environmental protection, and infection prevention.
  - b. Areas where compounding of HDs takes place shall be restricted to authorized personnel to protect person not involved in handling of HDs. The location of compounding area shall be away from break rooms or refreshment areas for staff, patient or visitors to reduce risk of exposure. Signs designating the hazard must be prominently displayed before the entrance to the HD handling areas.
  - c. Designated areas shall be available for:
    - i. Receipt and unpacking of antineoplastic HDs or HD API
    - ii. Storage of HDs
    - iii. Nonsterile HD compounding (if performed by the entity)
    - iv. Sterile HD compounding (if performed by the entity)
  - d. Receipt: Antineoplastic HDs and APIs must be unpacked (i.e., removal from external shipping containers) in an area that is neutral/normal or negative

pressure relative to the surrounding areas. HDs must not be unpacked from their shipping containers in sterile compounding areas or in positive pressure areas.

- e. Storage: HDs must be stored in a manner that prevents spillage or breakage if the container falls. Do not store HDs on the floor. In areas prone to specific types of natural disasters (e.g. earthquakes) the manner of storage must meet applicable safety precautions, such as secure shelves with raised front lips.
  - i. Storage of non-antineoplastic reproductive risk only and final dosage forms of HDs may be stored with other inventory. Antineoplastic HDs requiring manipulation other than counting final dosage forms and any HD API must be stored separately from non-HDs in a manner that prevents contamination and personnel exposure. These HDs must be stored in a negative-pressure room with at least 12 ACPH.
  - ii. Sterile and non-sterile HDs may be stored together. Depending on facility design, HDs may be stored within a negative pressure buffer room with at least 12 ACPH. However, only HDs used for sterile compounding may be stored in the negative pressure buffer room.
  - iii. Refrigerated antineoplastic HDs must be stored in a dedicated refrigerator in a negative pressure area with at least 12 ACPH (e.g. storage room, buffer room, or containment segregated compounding area (C-SCA)). If a refrigerator is placed in a negative pressure buffer room, an exhaust located adjacent to the refrigerator's compressor and behind the refrigerator should be considered.
- f. Compounding: Engineering controls are required to protect the preparation from cross-contamination and microbial contamination (if preparation is intended to be sterile) during all phases of the compounding process. Engineering controls for containment are divided into three categories representing primary, secondary, and supplementary levels of control. A containment primary engineering control (C-PEC) is a ventilated device designed to minimize worker and environmental HD exposure when directly handling HDs. Containment secondary engineering controls (C-SEC) is the room in which the C-PEC is placed. Supplemental engineering controls (e.g. closed-system transfer device –CSTD) are adjunct controls to offer additional levels of protection. Appendix B provides examples of designs of HD compounding areas.
- g. Sterile and nonsterile HDs must be compounded within a C-PEC located in a C-SEC. The C-SEC used for sterile and nonsterile compounding must:
  - i. Be externally vented through high-efficiency particulate air (HEPA) filtration

- ii. Be physically separated (i.e., a different room from other preparation areas)
  - iii. Have a negative pressure between 0.01 and 0.03 inches of water column
- h. C-PEC shall operate continuously if used for sterile compounding or if the CPEC supplies the negative pressure. Activities occurring in the C-PEC must be suspended for a loss of power, repair or moving of the unit. If necessary, protect the unit by covering it appropriately per the manufacturer's recommendations. Once the C-PEC can be powered on, decontaminate, clean and disinfect (if used for sterile compounding) all interior surfaces and wait the manufacturer-specified recovery time before resuming compounding.
- i. A sink must be available for hand washing as well as emergency access to water for removal of hazardous substances from eyes and skin. An eyewash station and/or other emergency or safety precautions that meet applicable laws and regulations must be readily available. However, care must be taken to locate them in areas where their presence will not interfere with required ISO classifications.
- j. For entities that compound both nonsterile and sterile HDs, the respective C-PEC's must be placed in segregated rooms separate from each other, unless those C-PECs used for nonsterile compounding are sufficiently effective that the room can continuously maintain ISO 7 classification throughout the nonsterile compounding activity. If the C-PECs used for sterile and nonsterile compounding are placed in the same room, they must be placed at least 1 meter apart and particle-generating activity must not be performed when sterile compounding is in process.
- k. Non-sterile compounding – must follow standards in USP 795.
  - i. A C-PEC is not required if manipulations are limited to handling of final dosage forms (e.g. tablets and capsules) that do not produce particles, aerosols, or gasses.
  - ii. The C-PECs used for manipulation of nonsterile HDs must be either externally vented (preferred) or redundant-HEPA filtered in series. Nonsterile HD compounding must be performed in a C-PEC that provides personnel and environmental protection, such as a Class I Biologic Safety Cabinet (BSC) or Containment Ventilated Enclosure (CVE). A Class II BSC or a CACI may also be used. For occasional nonsterile HD compounding, a C-PEC used for sterile compounding (e.g., Class II BSC or CACI) may be used but must be decontaminated, cleaned, and disinfected before resuming sterile compounding in that C-PEC. A C-PEC used only for nonsterile compounding does not need to have unidirectional airflow because the critical environment does not need to be ISO classified.

- iii. The C-PEC must be placed in a C-SEC that has at least 12 ACPH. Due to the difficulty cleaning HD contamination from surfaces, the architectural finish requirements (e.g. smooth, seamless, impervious surfaces) described in USP 797 also apply to nonsterile compounding areas.

C-PEC	C-SEC Requirements
Externally vented (preferred) or redundant-HEPA filtered in series  Examples: CVE, Class I or II BSC, CACI	12 ACPH  Externally vented  Negative pressure between 0.01 and 0.03 inches of water column

- I. Sterile HDs compounding – applicable compounding standards in USP 797 must be followed.
  - i. All C-PECs used for manipulation of sterile HDs must be externally vented. Sterile HD compounding must be performed in a C-PEC that provides a Class 5 or better air quality, such as Class II or III BSC or CACI. Class II BSC types A2, B1 and B2 are all acceptable. For most known HDs type A2 cabinets offer a simple and reliable integration with the ventilation and pressurization requirements of the C-SEC. Class II type B2 BSCs are typically reserved for use with volatile components.
  - ii. A laminar airflow workbench (LAFW) or compounding aseptic isolator (CAI) must not be used for compounding of an antineoplastic HD. A BSC or CACI used for preparation of HDs must not be used for the preparation of non-HDs unless the non-HD preparation is placed into a protective outer wrapper during removal from the C-PEC and is labeled to require PPE handling precautions.
  - iii. The C-PEC must be located in a C-SEC, which may be either an ISO Class 7 buffer room (preferred) or an unclassified containment segregated compounding area (C-SCA). If the C-PEC is placed in a C-SCA, the beyond-use date (BUD) of all CSPs prepared must be limited as defined in USP 797 for CSPs prepared in a segregated compounding area.
  - iv. Engineering Controls for Sterile HD Compounding

Configuration	C-PEC	C-SEC	Maximum BUD
ISO Class 7 Buffer Room	Externally vented, examples: Class II BSC or CACI	30 ACPH Externally vented Negative pressure between 0.01 and 0.03 inches of water column	As described in USP 797
C-SCA	Externally vented, examples: Class II BSC or CACI	12 ACPH Externally vented Negative pressure between 0.01 and 0.03 inches of water column	As described in USP 797 for segregated compounding area

- m. ISO Class 7 buffer room: The C-PEC may be placed in an ISO Class 7 buffer room that has a negative pressure between 0.01 and 0.03 inches of water column and has a minimum of 30 ACPH of HEPA-filtered supply air.
- n. Anteroom requirements
- i. ISO Class 7 or better
  - ii. Anteroom shall be maintained at a minimum positive pressure of 0.02 inches of water column relative to all adjacent unclassified spaces
  - iii. Minimum of 30 ACPH of HEPA-filtered supply air
  - iv. The anteroom shall be maintained at a minimum positive pressure of at least 0.01 inches of water column relative to the HD buffer room
  - v. A hand washing sink shall be placed within the anteroom at least 1 meter from the entrance of the buffer room to avoid contamination migration into the negative pressure HD buffer room.
  - vi. Although not a recommended facility design, if the negative pressure buffer area is entered through the positive-pressure non-HD buffer room the following is required:
    - i. A line of demarcation must be defined within the negative pressure area for garbing and degarbing

- ii. A method to transport HDs, CSPs and waste into and out of the negative pressure buffer room to minimize the spread of HD contamination. This may be accomplished by use of a pass-through between the negative pressure buffer area and adjacent space. The pass through must be included in the facility's certification to ensure that particles are not compromising the air quality of the negative pressure buffer room. Do not use a refrigerator pass through. Other methods of containment (such as sealed containers) may be used if the entity can demonstrate HD containment and appropriate environmental control.
- o. Containment segregated compounding areas (C-SCA)
  - i. The C-PEC may be placed in an unclassified C-SCA that has a negative pressure between 0.01 and 0.03 inches of water column relative to all adjacent spaces and has a minimum of 12 ACPH of HEPA-filtered air supply. A hand-washing sink must be placed at least 1 meter from C-PEC. Only low- and medium-risk HD CSPs may be prepared in a C-SCA. HD CSPs prepared in the C-SCA must not exceed the BUDs described in USP 797 for CSPs prepared in a segregated compounding area.
- p. Containment Supplemental Engineering Controls
  - i. Some CSTDs have been shown to limit the potential for generating aerosols during compounding; however, there is no certainty that all CSTDs will perform adequately. Since there is no published universal performance standard by which all CSTDs are evaluated for containment, users should carefully evaluate the performance claims associated with available CSTDs based on independent studies and demonstrated containment reduction. A CSTD must not be used as a substitute for a C-PEC when compounding. CSTDs should be used when compounding HDs when the dosage form allows. CSTDs must be used when administering HDs when the dosage form allows.

## 6. Environmental Quality and Control

- a. Environmental wipe studies for HDs should be performed routinely at least every 6 months. Surface wipes sampling should include:
  - i. Interior of the C-PEC and equipment contained in it
  - ii. Staging or work areas near the C-PEC
  - iii. Areas adjacent to CPECs (e.g. floors directly under staging and dispensing areas)
  - iv. Patient administration areas

- b. There are currently no studies demonstrating the effectiveness of a specific number or size of wipe samples in determining levels of HD contamination. Wipe sampling kits should be verified before use to ensure the method and reagent used have been tested to recover a specific percentage of known marker drugs from various surface types found in the sampled area. There are currently no certifying agencies for vendors of wipe sample kits.
- c. There is currently no standard for acceptable limits for HD surface contamination. Common markers include cyclophosphamide, ifosfamide, methotrexate, fluorouracil, and platinum drugs. An example of measureable contamination (e.g. cyclophosphamide >1.00ng/cm<sup>2</sup>), which were shown in some studies to result in uptake of the drug in exposed workers. IF any measurable contamination is found, the compounding supervisor must identify, document and contain the cause of the contamination. Such action may include reevaluating work practices, re-training personnel, performing thorough deactivation/decontamination and cleaning, and improving engineering controls. Repeat the wipe sampling to validate that deactivation/decontamination and cleaning steps have been effective.

7. Personnel Protective Equipment (PPE)

- a. PPE provides worker protection to reduce exposure to HDs aerosolization and drug residue. When performing a task where C-PECs are not generally available, such as cleaning a spill, additional PPE may be required. The NIOSH list of antineoplastic and other HDs provides some general guidance on PPE for possible scenarios that may be encountered in healthcare settings.
- b. Gowns, gloves, head, hair, and shoe covers are required for compounding sterile and nonsterile HDs. Gloves are required for administering antineoplastic HDs. Gowns are required when administering injectable antineoplastic HDs. For all other activities, the entity’s SOP must describe the appropriate PPE to be worn based on its occupational safety plan and assessment of risk (if used). The entity must develop SOPs for PPE based on the risk of exposure (see Types of Exposure) and activities performed.
- c. Appropriate PPE must be worn when handling HDs including during:

Receipt
Storage
Transport
Compounding
Administration
Deactivation/Decontamination, Cleaning, and Disinfecting
Spill Control



- d. Gloves
  - i. When required, gloves must be tested as American Society for Testing and Materials (ASTM) standard D6978 (or its successor). Chemotherapy gloves must be powder-free because powder can contaminate the work area and can absorb and retain HDs. Gloves must be inspected for physical defects before use. Do not use gloves with pin holes or weak spots.
  - ii. Chemotherapy gloves must be changed every 30 minutes or when torn, punctured, or contaminated.
  
- e. Gowns
  - i. When required, disposable gowns must be tested and shown to resist permeability by HDs. Gowns must be selected based on the HDs handled.
  - ii. Disposable gowns made of polyethylene-coated polypropylene and other laminate materials offer better protection than those made of noncoated materials.
  - iii. Gowns must close in the back (i.e., no open front), be long sleeved, and closed cuffs that are elastic or knit.
  - iv. Gowns must not have seams or closures that could allow HDs to pass through.
  - v. Cloth laboratory coats, surgical scrubs, isolation gowns or other absorbent materials are not appropriate outer wear when handling HDs because they permit the permeation of HDs and can hold spilled drugs against the skin, thereby increasing exposure.
  - vi. Clothing may also retain HD residue from contact, and may transfer to other healthcare workers or various surfaces. Washing of non-disposable clothing contaminated with HD residue may transfer drug residue to other clothing.
  - vii. Gowns must be changed per the manufacturer's information for permeation of the gown. If no permeation information is available for the gowns used, change them every 2-3 hours or immediately after a spill or splash. Gowns worn in HD handling areas must not be worn to other areas in order to avoid spreading HD contamination and exposing other healthcare workers.
  
- f. Head/hair/shoe/sleeve covers
  - i. Head and hair (including beards/moustaches) and shoe covers provide protection from contact with HD residue on surfaces and floors.

When compounding sterile HDs, a second pair of shoe covers must be donned before entering the buffer room and removed when exiting the buffer room. Shoe covers worn in HD handling areas must not be worn to other areas to avoid spreading HD contamination and exposing other healthcare workers.

- ii. Disposable sleeve covers constructed of coated materials may be used to protect for the areas of the arms that may come in contact with HDs. If used, sleeve covers must be carefully removed and properly disposed of after the task is completed.

g. Eye and face protection

- i. Many HDs are irritating to the eyes and mucous membranes. Appropriate eye and face protection shall be worn when handling HDs when there is a risk for spills or splashes of HDs or HD waste materials when working outside of a C-PEC (e.g., administration in the surgical suite, working at or above eye level, or cleaning a spill). A full-facepiece respirator provides eye and face protection. Goggles must be used when eye protection is needed. Eye glasses alone or safety glasses with side shields do not protect the eyes adequately from splashes to the face and eyes. Face shields alone do not provide full eye and face protection.

h. Respiratory protection

- i. For most activities requiring respiratory protection, a fit-tested NIOSH certified N95 mask is sufficient to protect against airborne particles.
- ii. N95 masks offer no protection against gases and vapors and little protection from direct liquid splashes.
- iii. Surgical masks do not provide respiratory protection against drug exposure. A surgical N95 respirator provides the respiratory protection of an N95 respirator, and like a surgical mask, provides a barrier to splashes, droplets and sprays around the nose and mouth.
- iv. Personnel unpacking HDs that are not contained in plastic should wear an elastomeric half-mask with multi-gas cartridge and P100-filter. If the type of drug can be better defined, then a more targeted cartridge can be used.
- v. Fit test the respirator and train workers to use respiratory protection. Follow all requirements in the Occupational Safety Health Administration (OSHA) respiratory protection standard. An appropriate full-facepiece, chemical cartridge-type respirator must be worn when attending to HD spills larger than what can contained with

a spill kit, or when there is a known or suspected airborne exposure to powders or vapors.

i. Disposal of used PPE

- i. Consider all PPE worn when handling HDs as being contaminated, at a minimum, with trace HDs.
- ii. PPE must be placed in an appropriate waste container and further disposed of per local, state, and federal regulations.
- iii. PPE used during compounding should be disposed of in the proper waste container before leaving the C-SEC.
- iv. Chemotherapy gloves worn during compounding must be carefully removed and discarded immediately in an approved HD waste container inside the C-PEC or contained in a sealable bag for discarding outside the C-PEC. Potentially contaminated clothing must not be taken home under any circumstances.

8. Hazard Communication Program

- a. Entities are required to establish policies and procedures that ensure worker safety during all aspects of HD handling. The entity must develop SOPs to ensure effective training regarding proper labeling, transport, and storage of the HDs and use of Safety Data Sheets (SDS), based on the Globally Harmonized System of Classification and Labeling of Chemicals (GHS).
- b. Elements of the plan include:
  - i. A written plan that describes how the standard will be implemented
  - ii. All containers of hazardous chemicals shall be labeled, tagged, or marked with the identity of the material and appropriate hazard warnings.
  - iii. Entities must have an SDS for each hazardous chemical they use.
  - iv. Entities must ensure that the SDSs for each hazardous chemical used are readily accessible to personnel during each work shift and when they are in their work areas.
  - v. Personnel who may be exposed to hazardous chemicals when working shall be provided information and training before initial assignment to work with a hazardous chemical or whenever the hazard changes.

9. Personnel Training

- a. All personnel who handle HDs shall be fully trained on their job function (e.g., in the receipt, storage, handling, compounding, dispensing, and disposal of HDs).
- b. Training must occur before the employee independently handles HDs.
- c. The effectiveness of training for HD handling competencies must be demonstrated by each employee. Personnel competency must be reassessed at least every 12 months and when a new HD or new equipment is used or a new or significant change in process or SOP occurs. All training and competency assessment must be documented.
- d. Training must include at least the following:
  - i. Overview of the entity’s list of HDs and their risks
  - ii. Review of the entity’s SOPs related to the handling of HDs
  - iii. Proper use of PPE
  - iv. Proper use of equipment and devices (e.g., engineering controls)
  - v. Spill management
  - vi. Response to known or suspected HD exposure

10. Receiving

- a. The entity must establish SOPs for receiving HDs. HDs should be received from the supplier sealed in impervious plastic to segregate them from other drugs and to improve safety in the receiving and internal transfer process. HDs must be delivered to the HD storage area immediately upon arrival.
- b. PPE, including ASTM-tested, powder-free chemotherapy gloves, must be worn when unpacking HDs.
- c. A spill kit shall be accessible in the receiving area.
- d. The entity must enforce policies that include a tiered approach, starting with visual examination of the shipping container for signs of damage or breakage (e.g., visible stains from leakage, sounds of broken glass containers). The table below summarizes the steps for receiving and handling of damaged shipping containers.

If the shipping container appears damaged	Seal container without opening and contact the supplier for instructions  If the unopened package is to be returned to the supplier, enclose the package in an
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	<p>impervious container and label the outer container "Hazardous"</p> <p>If the supplier declines return, dispose of properly</p>
<p>If a damaged shipping container must be opened</p>	<p>Seal the container in plastic or an impervious container</p> <p>Transport it to a C-PEC and place on a plastic-backed preparation mat</p> <p>Open the package and remove usable items</p> <p>Wipe the outside of the usable items with a disposable wipe</p> <p>Enclose the damaged item(s) in an impervious container and label the outer container "Hazardous"</p> <p>If the supplier declines the return, dispose of properly</p> <p>Decontaminate/deactivate and clean the C-PEC and discard the mat and cleaning disposables as hazardous waste</p>

- e. When opening damaged shipping containers, they should preferably be transported to a C-PEC designated for nonsterile compounding. If a C-PEC designated for sterile compounding is the only one available, it must be thoroughly disinfected after the decontamination/deactivation and cleaning step before returning to any sterile compounding activity.
- f. Damaged packages or shipping cartons must be considered spills that must be reported to the designated person and managed according to the entity's SOPs. Clean-up must comply with established SOPs.

11. Labeling, Packing and Transport

- a. The entity must establish SOPs for the labeling, handling, packaging, and transport of HDs. The SOPs must address prevention of accidental exposures or spills, personnel training on response to exposure, and use of a spill kit. Examples of special exposure-reducing strategies include small-bore connectors (such as Luer Lock) and syringes, syringe caps, CSTDs, the capping of

container ports, sealed impervious plastic bags, impact-resistant and/or water-tight containers, and cautionary labeling.

- b. Labeling: HDs identified by the entity as requiring special HD handling precautions must be clearly labeled at all times during their transport.
- c. Packaging: Compounding personnel must select and use packaging containers and materials that will maintain physical integrity, stability, and sterility (if needed) of the HDs during transport. Packaging materials must protect the HD from damage, leakage, contamination, and degradation, while protecting healthcare workers who transport HDs. The entity must have written SOPs to describe appropriate shipping containers and insulating materials, based on information from product specifications, vendors, mode of transport, and experience of the compounding personnel.
- d. Transport: HDs that need to be transported must be labeled, stored, and handled in accordance with applicable federal, state and local regulations. HDs must be transported in containers that minimize the risk of breakage or leakage. Pneumatic tubes must not be used to transport any liquid or antineoplastic HDs because of the potential for breakage and contamination. When shipping HDs to locations outside the entity, the entity must consult the Transport Information on the SDS. The entity must ensure that labels and accessory labeling for the HDs include storage instructions, disposal instructions, and HD category information in a format that is consistent with the courier's policies.

## 12. Dispensing Final Dosage Forms

- a. HDs that do not require further manipulation before delivery to the patient may be dispensed without further requirements unless specified by the manufacturer or visual indicators of HD exposure hazards (e.g., HD dust or leakage) are present.
- b. Counting of HDs should be done carefully. Clean equipment should be dedicated for use with these drugs. Tablet and capsule forms of HDs must not be placed in automatic counting or packing machines, which subject them to stress and may introduce powdered contaminants into the work area.

## 13. Compounding

- a. Entities and personnel involved in compounding HDs must be compliant with the appropriate USP standards for compounding including Chapters 795 and 797. Compounding must be done in proper engineering controls as described in Compounding. When compounding nonsterile and sterile HD preparations in a C-PEC, a plastic-backed preparation mat must be placed on the work surface of the C-PEC. The mat should be changed immediately if a spill occurs and regularly during use, and should be discarded at the end of the daily compounding activity. Disposable or clean equipment for compounding (such

as mortars and pestles, and spatulas) must be dedicated for use with HDs. Compounding personnel must ensure that the labeling processes for compounded preparations do not introduce contamination into non-HD handling areas.

- b. When compounding nonsterile HD preparations, use commercially available products as starting ingredients whenever possible. Liquid formulations are preferred over crushing tablets or opening capsules. APIs should only be used when there are no other options. When compounding sterile HD preparations, APIs should be avoided if a suitable manufactured product is available and appropriate for use (e.g., use an injectable product rather than API).
- c. Bulk containers of liquid and API HD must be handled carefully to avoid spills. If used, APIs should be handled in a C-PEC to protect against occupational exposure, especially during particle generating activities (such as crushing tablets, opening capsules and weighing powder).

#### 14. Administering

- a. HDs must be administered safely by using protective medical devices and techniques. Examples of protective techniques include the spiking or priming of IV tubing in a C-PEC and crushing tablets in plastic sleeves.
- b. Appropriate PPE must be worn when administering HDs. After use, PPE must be removed and disposed of in an approved HD waste container at the site of drug administration. Equipment (such as tubing and needles) and packaging materials must be disposed of properly, such as HD waste containers after administration.
- c. CSTDs must be used for administration when the dosage form allows. Techniques and ancillary devices that minimize the risk posed by open systems must be used when administering HDs through certain routes. Administration into certain organs or body cavities (e.g., the bladder, eye, peritoneal cavity, or chest cavity) often requires equipment for which locking connections may not be readily available or possible.
- d. Healthcare personnel should avoid manipulating HDs such as crushing tablets or opening capsules if possible. Liquid formulations are preferred if solid oral dosage forms are not appropriate for the patient. If HD dosage forms do require manipulation such as crushing tablets(s) or opening capsule(s) for a single dose, personnel must don appropriate PPE and use a plastic sleeve to contain any dust or particles generated.
- e. The Oncology Nursing Society (ONS) Safe Handling of Hazardous Drugs publication contains additional information on handling HDs for administration.

#### 15. Deactivation/Decontamination, Cleaning, and Disinfection

- a. All areas where HDs are handled (e.g. such as during receiving, compounding, transport, administering, and disposal) and all reusable equipment and devices (e.g. C-PEC, carts and trays) must be routinely deactivated/decontaminated and cleaned. Additionally, sterile compounding areas and devices must be routinely disinfected.
- b. All healthcare personnel who perform deactivation/decontamination, cleaning and disinfection activities in HD handling areas must be trained in appropriate procedures to protect themselves and the environment from contamination. All personnel performing these activities must wear appropriate PPE resistant to the cleaning agents used, including two pairs of ASTM-tested chemotherapy gloves and impermeable disposable gowns. Consult manufacturer or supplier information for compatibility with clean agents used. Additionally, eye protection and face shields must be used if splashing is possible. Respiratory protection must be used if warranted by the activity.
- c. The entity must establish written procedures for decontamination, deactivation, cleaning, and disinfection (for sterile compounding areas). Cleaning of nonsterile and sterile compounding areas must also comply with USP 795 and USP 797 chapters. Written procedures for cleaning must include procedures, agents used, dilutions used, frequency, and documentation requirements.
- d. The deactivating, decontaminating, cleaning, and disinfecting agents selected must be appropriate for the type of HD contaminants, location, and surface materials. The products used must not contaminate the surfaces with substances that are toxic, volatile, corrosive, or otherwise harmful to surface material. Perform cleaning in areas that are sufficiently ventilated to prevent accumulation of hazardous airborne drug concentrations and decontamination agents.

Cleaning Step	Purpose	Agents
Deactivation	Render compound inert or inactive	As listed in the HD labeling or if no specific information is available, sodium hypochlorite, or other Environmental Protection Agency (EPA)- registered oxidizer
Decontamination	Remove inactivated residue	Sterile alcohol, sterile water, peroxide or sodium hypochlorite
Cleaning	Remove organic or	Germicidal detergent



	inorganic material	and sterile water
Disinfection	Destroy microorganisms	Sterile alcohol or other EPA-registered disinfectant appropriate for use

- e. Deactivation/decontamination: Deactivation renders a compound inert or inactive. Decontamination occurs by physically removing HD residue from non-disposable surfaces and transferring it to absorbent, disposable materials (e.g., wipes, pads, or towels) appropriate to the area being cleaned. All disposable materials must be discarded as contaminated HD waste.
- i. Chemical deactivation of HD residue is preferred, but no single process has been found to deactivate all currently available HDs. Studies have examined oxidizing agents such as potassium permanganate, hydrogen peroxide, and sodium hypochlorite; vaporized hydrogen peroxide and detergents; and high- and low-pH solutions, all with varying results. Some potential deactivators have produced byproducts that are as hazardous as the original drug. Other deactivators have respiratory effects or result in caustic damage to surfaces. Note that sodium hypochlorite is corrosive to stainless steel surfaces if left untreated; therefore, sodium hypochlorite must be neutralized with sodium thiosulfate or followed by use of a germicidal detergent.
  - ii. A multi-component deactivation system is theoretically more efficient than a single agent system because of the diverse nature of HDs. One commercially available product provides a system for decontamination and deactivation using sodium hypochlorite, surfactant, and thiosulfate neutralizer. This combination product, followed by rinsing, has been shown to be effective for cleaning HD-contaminated surfaces. Other products use combinations of deactivating agents and/or cleaning agents, followed by rinsing and disinfecting. Because of the growing number of assays available for HDs, additional surface wipe sampling is now possible and should be done to document the effectiveness of any agent used for decontamination of HD residue from work surfaces.
- f. Cleaning and Disinfection: Cleaning is a process that results in the removal of contaminants (e.g., soil, microbial contamination, HD residue) from objects and surfaces using water, detergents, surfactants, solvents and/or other chemicals. Disinfection is a process of destroying microorganisms. Disinfection must be done for areas intended to be sterile including the sterile compounding areas.

- g. Cleaning and the Compounding Area: The Cleaning and Disinfecting the Compounding Area section in USP 797 applies to both sterile and nonsterile HD compounding areas. Cleaning agents used on compounding equipment should not introduce microbial contamination.
- i. All C-PEC used for either nonsterile or sterile compounding must be decontaminated between compounding of different HDs, any time a spill occurs, before and after certification, any time voluntary interruption occurs, and if the ventilation toll is moved. No cleaning step may be performed when compounding activities are occurring.
  - ii. The amount of HD contamination introduced into the C-PEC may be reduced by surface decontamination (i.e., wiping down) of HD containers. Although no wipe-down procedures have been studied, the use of disposable material moistened with alcohol, sterile water, peroxide, or sodium hypochlorite solutions may be effective. To avoid spreading HD residue, spray the wiper, not the HD container. The solution used for wiping HD packaging must not alter the product label.
  - iii. C-PECs may have areas under the work tray where contamination can build up. These areas must be cleaned at least monthly to reduce the contamination level in the C-PEC. Accessing this area may be difficult. Clean as much as possible of the C-PEC surfaces before accessing the area under the work tray. When cleaning the area under the work tray of a C-PEC, the containment airflows are compromised by opening the cabinets. To provide protection to the worker performing this task, respiratory protection may be required. A NIOSH-approved respirator worn by a worker who has been fit tested and cleared to use a respirator would be appropriate.

#### 16. Spill Control

- a. All personnel who may be required to clean-up a spill of HDs must receive proper training in spill management and the use of PPE and NIOSH-certified respirators. Spills must be contained and cleaned immediately only by qualified personnel with appropriate PPE. Qualified personnel must be available at all times in entities handling HDs. Signs must be available for restricting access to the spill area. Spill kits containing all of the materials needed to clean HD spills must be readily available in all areas where HDs are routinely handled. If HDs are being prepared or administered in a non-routine healthcare area, a spill kit and respirator must be available. All spill materials must be disposed of as hazardous waste.
- b. The circumstances and management of spills must be documented. Personnel who are potentially exposed during the spill or spill clean-up or who have direct skin and eye contact with HDs require immediate evaluation. Non-employees

exposed to an HD spill should report to the designated emergency service for initial evaluation and also complete an incident report or exposure form.

- c. SOPs must be developed to prevent spills and to direct the clean-up of HD spills. SOPs must address the size and scope of the spill and specify who is responsible for spill management and the type of PPE required. The management of the spill (e.g., decontamination, deactivation, and cleaning) may be dependent on the size and type of spill. The SOP must address the location of spill kits and clean-up materials as well as the capacity of the spill kit. Written procedures should address use of appropriate full-facepiece, chemical cartridge-type respirators if the capacity of the spill kit is exceeded or if there is known or suspected airborne exposure to vapors or gases.
17. Disposal: Disposal of all HD waste (including used and unusable HDs) must comply with all applicable federal, state and local regulations. All personnel who perform routine custodial waste removal and cleaning activities in HD handling areas must be trained in appropriate procedures to protect themselves and the environment to prevent HD contamination.
  18. Documentation and Standard Operating Procedures:
    - a. Activities that must be documented include, but are not limited to, the acquisition, preparation, and dispensing of an HD; personnel training; and the use and maintenance of equipment and supplies. These records must be available for review. Personnel who transport, compound, or administer HDs must document their training according to OSHA standards and other applicable laws and regulations.
    - b. The entity must maintain SOPs for the safe handling of HDs for all situations in which these HDs are used throughout a facility. The SOPs must be reviewed at least annually by the designated responsible individual, and the review must be documented. Revision in forms or records must be made as needed and communicated to all personnel handling HDs.
    - c. The SOPs for handling of HDs should include:
      - i. Hazard communication program
      - ii. Occupational safety program
      - iii. Labeling of HDs
      - iv. Procurement of HDs
      - v. Use of proper engineering controls (e.g., C-PECs, C-SECs)
      - vi. Use of PPE based on activity (e.g., receipt, transport, compounding, administration, spill and disposal)

- vii. Decontamination/deactivation, cleaning and disinfection
- viii. Transport
- ix. Environmental monitoring
- x. Spill control
- xi. Medical surveillance

#### 19. Medical Surveillance

- a. Medical surveillance is part of a comprehensive exposure control program complementing engineering controls, safe work practices, and the use of PPE. Entities should ensure that healthcare workers who handle HDs as a regular part of their job assignment are enrolled in a medical surveillance program. The general purpose of a medical surveillance program is to minimize adverse health effects in personnel potentially exposed to HDs. Medical surveillance programs involve assessment and documentation of symptom complaints, physical findings, and laboratory values (such as blood count) to determine whether there is a deviation from the expected norms.
- b. Medical surveillance can also be viewed as a secondary prevention tool that may provide a means of early detection if a health problem develops. Tracking personnel through medical surveillance allows the comparison on of health variables over time in individual workers, which may facilitate early detection of a change in a laboratory value or health condition. Medical surveillance programs also look for trends in populations of workers. Examining grouped data compared with data from unexposed workers may reveal a small alteration or increase in the frequency of a health effect that would be obscured if individual workers' results alone were considered.
- c. Medical surveillance evaluates the protection afforded by engineering controls, other administrative controls, safe work processes, PPE, and worker education about the hazards of the materials they work with within the course of their duties. The data-gathering elements of a medical surveillance program are used to establish a baseline of workers' health then to monitor their future health for any changes that may result from exposure to HDs.
- d. Elements of a medical surveillance program should be consistent with the entity's Human Resources policies and should include:

Development of an organized approach to identify workers who are potentially exposed to HDs on the basis of their job duties.

Use of an entity-based or contracted employee health service to perform the medical surveillance while protecting the confidentiality of the employees' personal medical information.

Initial baseline assessment (pre-placement) of a worker's health status and medical history. Data elements collected include a medical (including a reproductive) history and work history to assess exposure to HDs, physical examination, and laboratory testing. Methods used to assess exposure history include a review of:

- Records of HDs handled, with quantities and dosage forms
- Number of HD preparations/administrations per week
- Estimates of hours spent handling HDs per week and/or per month
- Performance of a physical assessment and laboratory studies linked to target organs of commonly used HDs, such as baseline complete blood count. Note that biological monitoring to determine blood and urine levels of specific HDs is not currently recommended in surveillance protocols, but may have a role in the follow-up of acute spills with a specific agent.

Medical records of surveillance should be maintained according to OSHA regulation concerning access to employee exposure and medical records.

Monitoring workers health prospectively through periodic surveillance using the elements of data gathering described above (updated health and exposure history), physical assessment and laboratory measures, if appropriate

Monitoring of the data to identify prevention failures leading to health effects; this monitoring may occur in collaboration with employee health services

Development of a follow-up plan for workers who have shown health changes suggesting toxicity or who have experienced an acute exposure. This follow-up should include evaluation of current engineering and administrative controls and equipment to ensure that all systems are appropriately and accurately implemented.

Completion of an exit examination when a worker's employment at the entity ends, to document the information on the employee's medical, reproductive, and exposure histories. Examination and laboratory evaluation should be guided by the individual's history of exposures and follow the outline of the periodic evaluation.

- e. Follow-up plan: The occurrence of exposure-related health changes should prompt immediate re-evaluation of primary preventative measures (e.g., administrative and engineering controls, PPE, and others). In this manner, medical surveillance acts as a check on the effectiveness of controls already in use. The entity should take the following actions:

- i. Perform a post-exposure examination tailored to the type of exposure (e.g., spills or needle sticks from syringes containing HDs). An assessment of the extent of exposure should be conducted and included in a confidential database and in an incident report. The physical examination should focus on the involved area as well as other organ systems commonly affected (i.e., the skin and mucous membranes for direct contact or inhalation; the pulmonary system for aerosolized HDs). Treatment and laboratory studies will follow as indicated and be guided by emergency protocols.
- ii. Compare performance of controls with recommended standards; conduct environmental sampling when analytical methods are available.
- iii. Verify and document that all controls are in proper operating condition.
- iv. Verify and document that the worker complied with existing policies. Review policies for the use of PPE and employee compliance with PPE use and policies.
- v. Develop and document a plan of action that will prevent additional exposure of workers.
- vi. Ensure confidential, two-way communication between the worker and the employee health unit(s) regarding notification, discussions about a change in health condition, or detection of an adverse health event.
- vii. Provide and document a follow-up medical survey to demonstrate that the plan implemented is effective.
- viii. Ensure that any exposed worker receives confidential notification of any adverse health effect. Offer alternate duty or temporary reassignment.
- ix. Provide ongoing medical surveillance of all workers at risk for exposure to HDs to determine whether the plan implemented is effective.

## 20. Examples of Designs for Hazardous Drug Compounding Areas (Appendix B) – USP800

Use	Optimal Primary and Secondary Control	Minimum ACPH	Limitations Primary and Secondary Control	Minimum ACPH	Notes for limitations	
Nonsterile HD compounding		12				
Sterile HD compounding		30		12	Maximum BUD as described in <797> for segregated compounding area.	
	OR			30	If this design is in place, measures must be taken to avoid contamination of the positive-pressure buffer room.	
	OR		<p>This design is not recommended</p>	30	Maximum BUD as described in <797>.	
Both sterile HD and nonsterile HD compounding	A separate room for sterile and nonsterile compounding is recommended			30	For rooms used for both sterile and nonsterile compounding, particle-generating activity must not be performed when sterile compounding is in process. C-PECs must be at least 1 meter apart.	
			OR		12	Maximum BUD as described in <797> for segregated compounding area.
			OR		12	Maximum BUD as described in <797> for segregated compounding area.

\* The arrows indicate direction of airflow.

**V. Ensuring Healthcare Worker Safety When Handling Hazardous Drugs: The Joint Position Statement from the Oncology Nursing Society, the American Society of Clinical Oncology and the Hematology/Oncology Pharmacy Association<sup>5</sup>**

- A. Organizations in which hazardous drugs (HDs) are present will establish evidence-based policies and procedures for safe handling that comply with regulatory requirements.
- B. Organizations in which HDs are prepared and administered will provide and maintain primary engineering controls and evaluate the utility of supplemental engineering controls such as closed-system transfer devices to reduce worker exposure.
- C. Organizations in which HDs are present will ensure that appropriate personal protective equipment (PPE) is available to all staff to minimize exposure.
- D. Organizations in which HDs are present will provide education and training specific to each worker's role for staff that are potentially exposed. Education and training will include the risks of exposure, including the reproductive and developmental effects, the recommended precautions for specific handling activities, safe handling of contaminated patient excreta, and proper disposal of contaminated waste and how to handle acute exposure.
- E. Organizations in which HDs are present will protect the right of staff who are trying to conceive, pregnant or breast feeding to engage in alternate duty that does not require HD handling.
- F. Organizations in which HDs are present will ensure that patients who receive these drugs and their caregivers receive education about safe handling to minimize unintended exposure.
- G. Organizations will ensure that HD waste is disposed of according to regulatory guidelines and in a manner that protects staff and the environment.
- H. ONS, ASCO and HOPA will continue to explore evidence-based strategies for mitigation of risk associated with handling HDs and share recommendations with our respective members.

**VI. NIOSH: Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in the Health Care Settings<sup>6</sup>**

- A. NIOSH Warning: Working with or near hazardous drugs in health care settings may cause skin rashes, infertility, miscarriage, birth defects, and possibly leukemia or other cancers.
- B. Adherence to guidelines for handling hazardous drugs is sporadic and measurable concentrations of some hazardous drugs have been found in the urine of health care workers.
- C. Potential for Worker Exposure
  - 1. Exposure may occur from manufacture to transport/distribution to use in health care
  - 2. The number of workers exposed to hazardous drugs in the US is approximately 5.5 million. These include shipping and receiving personnel, pharmacists, pharmacy technicians, nursing personnel, physicians, operating room personnel, environmental services personnel and workers in veterinary practices.



#### D. Conditions for Exposure

1. Both clinical and non-clinical workers may be exposed to hazardous drugs when they create aerosols, generate dust, clean up spills or touch contaminated surfaces during the preparation, administration, or disposal of hazardous drugs.
2. The following list of activities may result in exposures through inhalation, skin contact, ingestion, or injection:
  - a. Reconstituting powdered or lyophilized drugs and further diluting either the reconstituted powder or concentrated liquid forms of hazardous drugs
  - b. Expelling air from syringes filled with hazardous drugs
  - c. Administering hazardous drugs by intramuscular, subcutaneous, or intravenous routes
  - d. Counting out individual, uncoated oral doses and tablets from multidose bottles
  - e. Unit-dosing uncoated tablets in a unit-dose machine
  - f. Crushing tablets to make oral liquids doses
  - g. Compounding potent powders into custom-dosage capsules
  - h. Contacting measurable concentrations of drugs present on drug vial exteriors, work surfaces, floors, and final drug products (bottles, bags, cassettes, and syringes)
  - i. Generating aerosols during administration of drugs, either by direct IV push or by IV infusion
  - j. Priming the IV set with a drug-containing solution at the patient bedside (this procedure should be done in the pharmacy)
  - k. Handling contaminated wastes generated at any step of the preparation or administration process
  - l. Performing certain specialized procedures (such as intraoperative chemotherapy) in the operating room
  - m. Handling unused hazardous drug or hazardous-drug-contaminated waste
  - n. Decontaminating and cleaning drug preparation or clinical areas
  - o. Transporting infectious, chemical or hazardous waste containers
  - p. Removing and disposing of PPE after handling hazardous drugs or waste

## E. Exposure Routes

1. Exposure to hazardous drugs may occur through inhalation, skin contact, skin absorption, ingestion, or injection.
2. Detectable concentrations of hazardous drugs have been found on BSCs, floors, counter tops, storage areas, tables and chairs in patient treatment areas and locations adjacent to drug-handling areas.

## F. Evidence for Worker Exposure

1. Evidence indicates that workers are being exposed to hazardous drugs and are experiencing serious health consequences despite current work practice guidelines.
2. Factors that affect worker exposure include:
  - a. Drug handling circumstances (preparation, administration, or disposal)
  - b. Amount of drug prepared
  - c. Frequency and duration of drug handling
  - d. Potential for absorption
  - e. Use of ventilated cabinets
  - f. PPE
  - g. Work practices
3. CSTD usage for 6 months reduced both the concentration of cyclophosphamide and ifosfamide in the urine of exposed health care workers and the percentage of samples containing these drugs.

## G. Evidence for Health Effects in Workers

1. Mutagenicity
  - a. Multiple studies document that antineoplastic drugs may cause increased genotoxic effects in pharmacists and nurses exposed in the workplace.
2. Developmental and Reproductive Effects
  - a. Antineoplastic drugs have reproductive effects such as increased fetal loss, congenital malformations, low birth weight, congenital abnormalities and infertility.
3. Cancers

- a. An increased risk of leukemia has been reported in oncology nurses from a Danish cancer registry from 1943-87.

H. Current Standards and Recommendations – there is no recommended exposure limit for hazardous drugs.

1. OSHA<sup>7</sup>

- a. Publishes the OSHA Hazard Communication Standard.
- b. Publishes the Occupational exposure to hazardous chemicals in laboratories standard.
- c. Published the OSHA Technical Manual which includes:
  - i. Categorization of drugs as hazardous
  - ii. Hazardous drugs as occupational risks
  - iii. Work area
  - iv. Prevention of employee exposure
  - v. Medical surveillance
  - vi. Hazard communication
  - vii. Training and information dissemination
  - viii. Record keeping

2. EPA<sup>8</sup>

- a. EPA/RCRA regulations require that hazardous waste be managed according to strict regulatory requirements.
- b. Hazardous drug waste includes partially filled vials, undispersed products, unused IVs, needles and syringes, gloves, gowns, underpads, contaminated materials, from spill cleanups, and containers such as IV bags or drug vials that contain more than trace amounts of drug.
- c. Published EPA guidelines:<sup>9</sup>
  - i. US Environmental Protection Agency (EPA) Managing Hazardous Waste: A Guide for Small Businesses (2001).
  - ii. US Environmental Protection Agency (EPA) RCRA Hazardous Waste Regulations.

I. Recommendations

1. Assess the hazards of the workplace
2. Evaluate the workplace to identify and assess hazardous before anyone begins work with hazardous drugs. This evaluation should include:
  - a. Total working environment
  - b. Equipment (i.e., ventilated cabinets, close-system drug transfer devices, glove, bags, needleless systems, and PPE)
  - c. Physical layout of work areas
  - d. Types of drugs being handled
  - e. Volume, frequency, and form of drugs handled (tablets, coated versus uncoated, powder versus liquid)
  - f. Equipment maintenance
  - g. Decontamination and cleaning
  - h. Waste handling
  - i. Potential exposure during work, including hazardous drugs, bloodborne pathogens, and chemical used to deactivate hazardous drugs or clean drug-contaminated surfaces
  - j. Routine operations
  - k. Spill response
  - l. Waste segregation, containment, and disposal
3. Regularly review the current inventory of hazardous drugs, equipment, and practices, seeking input from affected workers.
4. Conduct regular training reviews with all potentially exposed workers in workplaces where hazardous drugs are used.
5. Handle drugs safely
6. Establish policies and procedures that define:
  - a. Presence of hazardous drugs
  - b. Labeling
  - c. Storage
  - d. Personnel issues (e.g. exposure of pregnant workers)

- e. Spill control
7. Implement a program from safely handling hazardous drugs at work and review this program annually on the basis of workplace evaluation.
  8. Establish procedures and provide training for handling hazardous drugs safely, cleaning up spills and using all equipment and PPE properly.
  9. Establish work practices related to drug manipulation techniques and to general hygiene practices – such as not permitting eating or drinking in areas where drugs are handling (the pharmacy or clinic).
  10. Use and maintain equipment properly – develop workplace procedures for using and maintaining all equipment that functions to reduce exposure – such as ventilated cabinets, closed-system transfer devices, needle-less systems and PPE.

J. Detailed Recommendations:

1. Receiving and Storage
2. Drug Preparation and Administration
  - a. Initial Steps
  - b. Preparing Hazardous Drugs
3. Administering Hazardous Drugs
4. Ventilated Cabinets
5. Routine Cleaning, Decontamination, Housekeeping and Waste Disposal
6. Spill Control
7. Medical Surveillance

**VII. NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2014<sup>10</sup>**

- A. History – First NIOSH Alert (Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings) originally published in September 2004 (<http://cdc.gov/niosh/docs/2004-165/>). Appendix A listed a sample list of major hazardous drugs, which was updated in 2010 and 2012. The 2014 update adds 27 drugs and includes a review of the 2004 list resulting in the removal of 12 drugs that did not meet the NIOSH criteria for hazardous drugs.
- B. New Format for Listing of Hazardous Drugs per NIOSH
  1. Group 1: Antineoplastic drugs (AHFS classification 10:00) – Many of these drugs pose a reproductive risk for susceptible populations.

2. Group 2: Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a hazardous drug. Some of these drugs may pose reproductive risks for susceptible populations.

3. Group 3: Drugs that primarily pose a reproductive risk to men and women who are actively trying to conceive and women who are pregnant or breast feeding, because some of the drugs may be present in breast milk.

C. Antineoplastic drugs considered hazardous (Group 1)

Abiraterone*	Goserelin*
Ado-trastuzumab emstansine	Hydroxyurea
Altretamine	Idarubicin
Amsacrine	Ifosfamide
Anastrozole	Imatinib
Arsenic trioxide	Irinotecan
Azacitidine	Ixabepilone
Bacillus calmette Guerin (BCG)	Letrozole*
Bendamustine	Leuprolide
Bexarotene	Lomustine
Bicalutimide*	Mechlorethamine
Bleomycin	Megesterol*
Bortezomib	Melphalan
Brentuximab vedotin	Mercaptopurine
Busulfan	Methotrexate
Cabazitaxel	Mitomycin
Capecitabine	Mitotane
Carboplatin	Mitoxantrone
Carmustine	Nelarabine
Chlorambucil	Nilotinib*

Cisplatin	Omacetaxine
Cladribine	Paclitaxel
Clofaribine	Pazopanib*
Crizotinib*	Pemetrexed
Cyclophosphamide	Pentostatin
Cytarabine	Pralatrexate
Dacarbazine	Procarbazine
Dactinomycin	Romidepsin
Dasatinib	Sorafenib
Daunorubicin	Streptozocin
Decitabine	Sunitinib*
Degarelix*	Tamoxifen*
Docetaxel	Temozolomide
Doxorubicin	Temsirolimus
Epirubicin	Teniposide
Eribulin	Thioguanine
Erlotinib*	Thiotepa
Estramustine	Topotecan
Etoposide	Toremifene*
Everolimus	Trimetrexate
Exemestane*	Triptorelin*
Floxuridine	Valrubicin
Fludarabine	Vandetanib
Fluorouracil	Vemurafenib*
Flutamide*	Vinblastine

Fulvestrant	Vincristine
Gemcitabine	Vinorelbine
Gemtuzumab ozogamicin	Vorinostat

\*Drugs that are not listed as hazardous per Manufacturer Safe Handling Guidelines

- D. Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a hazardous drug including those with manufacturers' safe handling guidelines (Group 2)

Abacavir	Lenalidomide*
Alefacept	Liraglutide recombinant
Apomorphine	Medroxyprogesterone acetate
Azathioprine*	Mycophenolate mofetil
Carbamazepine	Mycophenolic acid
Chloramphenicol	Nevirapine
Cidofovir*	Oxcarbazepine
Cyclosporine	Palifermin
Deferiprone	Phenoxybenzamine
Dexrazoxane*	Phenytoin
Diethylstilbesterol	Pipobroman
Divalproex	Progesterone
Enticavir*	Progestins
Estradiol	Prophylthiouracil
Estrogen/progesterone combinations	Raloxifene
Estrogens, conjugated	Rasagiline
Estrogen, esterified	Risperidone
Estropipate	Sirolimus
Fingolimod	Spironolactone



Fluoxymesterone	Tacrolimus
Fosphenytoin	Thalidomide*
Ganciclovir*	Uracil mustard*
Leflunomide	Valganciclovir*
Lenalidomide	Zidovudine

\*Drugs listed as hazardous per Manufactures' Safe Handling Guidelines

E. Non-antineoplastic drugs that primarily have adverse reproductive effects (Group 3)

Acitretin	Mifepristone
Alitretinoin	Misoprostol
Ambrisentan	Nafarelin
Bosentan	Oxytocin
Cabergoline	Paroxetine
Cetrorelix	Pentetate calcium trisodium
Choriogonadotropin	Plerixafor
Clonazepam	Ribavirin
Colchicine	Telavancin
Dinoprostone	Testosterone
Dronedarone	Topiramate
Dutasteride	Tretinoin
Ergonovine/methylegonovine	Ulipristal
Finasteride	Valproate/valproic acid
Fluconazole	Vigabatrin
Ganirelix	Voriconazole
Gonadotropin, chorionic	Warfarin

Icatibant	Ziprasidone
Mentropins	Zoledronic acid
Methyltestosterone	Zonisamide

### VIII. Other Regulatory Agencies of Interest to Oncology Practitioners

- A. FDA – Food and Drug Administration<sup>11</sup> – The Food and Drug Administration (FDA) is an agency within the U.S. Department of Health and Human Services. It consists of the Office of the Commissioner and four directorates overseeing the core functions of the agency: Medical Products and Tobacco, Foods and Veterinary Medicine, Global Regulatory Operations and Policy, and Operations.
1. Website houses information on drug approvals links to product labeling, deliberations of advisory committee meetings and drug shortages.
  2. Drug Quality and Security Act of 2013 expands FDA’s authority to regulate compounding such that a compounding outsourcing facility must comply with current good manufacturing practices, be subject to inspection by the FDA, and report information about compounded products including adverse events.<sup>12</sup>
  3. Other regulated items include medical devices, radiation-emitting products, vaccines, veterinary medications, cosmetics and tobacco products.
- B. State Boards of Pharmacy
1. Oversee licensure for individual states for pharmacists and pharmacy techs
  2. Set regulations for controlled substance prescribing within a state
  3. Outline standards for physical pharmacy space – retail and institutional
- C. Drug Enforcement Agency (DEA)<sup>13</sup>
1. Section of the United States Department of Justice
  2. Enforcement agency for controlled substance act
  3. Provides registration for providers to prescribe, procure and dispense controlled substances
- D. Joint Commission<sup>14</sup>
1. Accredits and certifies more than 20,000 health care organizations and programs in the US.

2. Establishes standards for hospitals and other health care organizations to adhere to for regulatory compliance
3. Publishes an annual report on Quality and Safety
4. Sets National Patient Safety Goals annually for ambulatory health care, behavioral health care, critical access hospitals, home care, hospitals, laboratory, nursing, long-term care facilities and office-based surgery
5. 2014 Hospital National Patient Safety Goals<sup>15</sup>

<p>NPSG.01.01: Identify patients correctly: Two patient identifiers (name and date of birth).</p> <p>NPSG.01.03.01: Eliminate transfusion errors related to patient misidentification</p> <p>NPSG.02.03.01: Improve effectiveness of communication among caregivers: Report critical test results and diagnostic procedures on a timely basis.</p> <p>NPSG.03.04.01: Label all medications, medication containers and other solutions on and off the sterile field in perioperative and other procedural settings.</p> <p>NPSG.03.05.01: Reduce the likelihood of harm associated with the use of anticoagulant therapy – this applies to hospitals that provide anticoagulant therapy and/or long-term anticoagulant prophylaxis (for example, atrial fibrillation) where the clinical expectation is that the patient’s laboratory values for coagulation will remain outside of normal values.</p> <p>NPSG.03.06.01: Maintain and communicate accurate patient medication information.</p> <p>NPSG.06.01.01: Reduce the harm associated with clinical alarm systems.</p> <p>NPSG. 07.01.01: Comply with either the current Center for Disease Control and Prevention (CDC) hand hygiene guidelines or the current World Health Organization (WHO) hand hygiene guidelines.</p> <p>NPSG.07.03.01: Implement evidence-based practices to prevent health care-associated infections due to multi-drug resistant organisms in acute care hospitals. (e.g. MRSA, C. difficile, VRE and multi-drug resistant gram negative bacteria)</p> <p>NPSG.07.04.01: Implement evidence-based practices to prevent central line-associated bloodstream infections. This requirement covers short- and long-term central venous catheters and peripherally inserted central catheters (PICC).</p> <p>NPSG.07.05.01: Implement evidence-based practices for preventing surgical site infections.</p> <p>NPSG.07.06.01: Implement evidence based practices to prevent indwelling catheter-associated urinary tract infections (CAUTI).</p> <p>NPSG.15.01.01: Identify patients at risk for suicide. This requirement applies only to psychiatric hospitals and patients being treated for emotional or behavioral disorders in general hospitals.</p>
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UP.01.01: Conduct a preprocedure verification process to establish a universal protocol for preventing wrong site, wrong procedure events.

UP.01.01.01: Mark the procedure site.

UP.01.03.01: A time-out performed before the procedure.

E. OBRA – Omnibus Reconciliation Act: Provides federal appropriations and sets out standards for Medicare benefits

1. 1986 – Established hospice as a permanent paid benefit of Medicare

2. 1989 – Increases hospice reimbursement by 20% and ties future increases to hospital market basket

**IX. ASCO/ONS Chemotherapy Administration Safety Standards<sup>16, 17</sup>**

A. American Society of Clinical Oncology and the Oncology Nursing Society initiated a collaborative project in 2008 (and updated in 2013) to develop standards for safe chemotherapy administration to adult cancer patients in the outpatient setting. The scope of the project was limited to patient safety and included both parenteral and oral chemotherapy regimens.

B. Safety standards (NEW standards are **bolded**)

Standard	
1.	The practice/institution has policies, procedures, and/or guidelines for verification of training and continuing education for clinical staff:
A.	Orders for parenteral and oral chemotherapy are written and signed by licensed independent practitioners who are determined to be qualified by the practice/institution according to the practice's/institution's policies, procedures, and/or guidelines.
B.	Chemotherapy drugs (oral or parenteral) are prepared by a pharmacist, pharmacy technician, or nurse determined to be qualified according to the practice's policies, procedures, and/or guidelines.
C.	Only qualified physicians, physician assistants, advanced practice nurses, or registered nurses administer chemotherapy.
D.	The practice/institution has a comprehensive educational program for new staff administering chemotherapy, including a competency assessment, <i>or</i> the practice/institution uses an off-site educational program regarding chemotherapy administration that ends in competency assessment. Chemotherapy administration education must include all routes of administration used in the practice/institution site (e.g., parenteral, oral, intrathecal, intraperitoneal, intravesicular). <i>An example of an off-site educational program is the ONS Chemotherapy and</i>

*Biotherapy Course.*

- E. The practice/institution has a standard mechanism for monitoring chemotherapy administration competency at specified intervals.  
Annual competency reassessment is recommended.
- F. All clinical staff maintains current certification in basic life support.  
Certification should be from a **nationally accredited course**. *Clinical Staff includes all staff involved in patient care; RNs, MDs, NPs, etc.*

- 2. Prior to the first administration of a new chemotherapy regimen, chart documentation available to the practice/institution includes:
  - A. Pathologic confirmation or verification of initial diagnosis. If original pathology report is unobtainable, note of explanation is in chart or a reference to primary source pathology. *This standard does not imply the need to rebiopsy if not clinically necessary.*
  - B. Initial cancer stage or current cancer status. Cancer stage is defined at diagnosis. Cancer status includes a current description of the patient's disease since diagnosis/staging, if relevant (e.g., recurrence, metastases).
  - C. Complete medical history and physical examination that includes, at minimum, height, weight, and assessment of organ-specific function as appropriate for the planned regimen. Example of assessment of organ-specific function as appropriate for the planned regimen: patient plan for cisplatin requires pre-treatment assessment of kidney function.
  - D. Presence or absence of allergies and history of other hypersensitivity reactions.
  - E. Documentation of patient's comprehension regarding chemotherapy regimens (and associated medications), including information regarding disease.
  - F. Assessment regarding psychosocial concerns and need for support, with action taken when indicated.  
Documentation of psychosocial concerns may include: copy of distress, depression, or anxiety screening form in the chart; patient self-report of distress, depression, or anxiety; or chart documentation regarding patient coping, adjustment, depression, distress, anxiety, emotional status, family support and care giving, coping style, cultural background, and socioeconomic status.
  - G. The chemotherapy treatment plan, including, at minimum, chemotherapy drugs, doses, anticipated duration, and goals of therapy.
  - H. For oral chemotherapy, the frequency of office visits and monitoring that is appropriate for the individual and the antineoplastic agent and is defined in the treatment plan.
  - I. Before initiation of an oral chemotherapy regimen, assessment of a patient's ability to obtain the drug and administer it according to the treatment plan is documented, along with a plan to

	address any identified issues.
3.	<p>The practice/institution:</p> <p>A. Defines standard chemotherapy regimens by diagnosis with references readily available, and/or</p> <p>B. Identifies source(s) for chemotherapy regimens, including local or centralized Institutional Review Board [IRB] approved clinical research protocols or guidelines.</p>
4.	<p>For orders that vary from standard chemotherapy regimens, practitioners provide a supporting reference. Reasons for dose modification or exception orders are documented.</p> <p><i>Exception orders may include notation that standard treatment is contraindicated as a result of pre-existing comorbidity, organ dysfunction or prior therapy.</i></p>
5.	<p>The practice/institution maintains written statements that determine the appropriate time interval for regimen-specific laboratory tests that are:</p> <p>A. Evidence-based when national guidelines exist e.g., American Society of Clinical Oncology or National Cancer Care Network guidelines, or</p> <p>B. Determined by practitioners at the site <i>Documentation of regimen-specific laboratory tests may be part of standardized regimen orders</i></p>
6.	<p>The practice/institution maintains a policy for how informed consent is obtained and documented for chemotherapy.</p> <p>The practice/institution may provide options for consent (e.g., use of chart documentation of patient consent or a signed patient consent form) that allow for variation among practitioners in the practice/institution.</p>
7.	<p>If the practice/institution administers chemotherapy that is prepared (mixed) off site, the practice/institution maintains a policy for quality control of that chemotherapy.</p>
8.	<p>If practice/institution manages its own pharmacy, the practice/institution has a policy regarding storage of chemotherapy (including separation of look-a-like products, sound-a-like products, and agents available in multiple strengths). Chemotherapy is stored in a designated area according to regulatory guidelines. (NEW)</p>
9.	<p>The practice/institution does not allow verbal orders except to hold or stop chemotherapy administration. New orders or changes to orders must be made in writing. Fax and e-mail orders are considered written orders.</p>
10.	<p>The practice/institution maintains and uses standardized, regimen-level, preprinted or electronic forms for parental chemotherapy prescription writing.</p> <p>Standardized forms may be incorporated into e-prescribing software or electronic health records.</p>

11. Order forms inclusively list all chemotherapy agents in the regimen and their individual dosing parameters. All medications within the order set are listed using full generic names and follow Joint Commission standards regarding abbreviations.

*Brand names should be included in orders only where there are multiple products or when including the brand name otherwise assists in identifying a unique drug formulation.*

Complete orders must include:

- A. Patient's full name and a second patient identifier (e.g., medical record number, DOB)
- B. Date
- C. Diagnosis
- D. Regimen name and cycle number
- E. Protocol name and number (if applicable)
- F. Appropriate criteria to treat (e.g., based on relevant laboratory results and toxicities)
- G. Allergies
- H. Reference to the methodology of the dose calculation or standard practice equations (e.g., calculation of creatinine clearance)
- I. Height, weight, and any other variables used to calculate the dose
- J. Dosage
- K. Doses do not include trailing zeros; use a leading zero for doses <1 mg.
- L. Route and rate (if applicable) of administration
- M. Length of infusion (if applicable)
- N. Supportive care treatments appropriate for the regimen (including pre-medications, hydration, growth factors, and hypersensitivity medications)
- O. Sequence of drug administration (if applicable)

Practices/institutions are not expected to be in full compliance with this standard if they currently have electronic ordering systems that prevent compliance. Appropriate changes should be implemented as soon as possible to ensure that electronic ordering systems integrate all of these elements. If the information cannot be captured in the electronic system, it should be documented within the patient record.

**NEW!**

12. **Complete prescriptions for oral chemotherapy include:**

- A. Patient's full name and second patient identifier (e.g. medical record number and DOB).**
- B. Drug name**
- C. Date**
- D. Reference to the methodology of the dose calculation (e.g., height, weight, and other variables, as applicable)**
- E. Dosage**
- F. Quantity to be dispensed**
- G. Doses may be rounded to the nearest table size or specify alternate doses each day to obtain the correct overall dosage. Doses do not include trailing zeros; use a leading zero for doses <1mg.**
- H. Route and frequency of administration**
- I. Duration of therapy number of days of treatment (if the medication is not to be taken**

	<p><b>continuously)</b></p> <p><b>J. Number of refills (including none)</b></p> <p><i>Practices/institutions are not expected to be in full compliance with this standard if they currently have electronic ordering systems that prevent compliance. Appropriate changes should be implemented as soon as possible to ensure that electronic ordering systems integrate all of these elements. If the information cannot be captured in the electronic system, it should be documented within the patient record.</i></p>
13.	Orders for parenteral/oral chemotherapy should be written with a time limitation to ensure appropriate evaluation at predetermined intervals.
<b>NEW!</b>	
14.	<b>The practice/institution maintains procedures for communicating discontinuation of oral chemotherapy, including patient education regarding time to stop treatment and disposal of remaining medication. (NEW)</b>
15.	<p>A second person (a practitioner or other personnel approved by the practice/institution to prepare or administer chemotherapy) independently verifies each order for chemotherapy before preparation, including confirming:</p> <ul style="list-style-type: none"> <li>A. Two patient identifiers</li> <li>B. Drug names</li> <li>C. Drug dose</li> <li>D. Drug volume</li> <li>E. Rate of administration</li> <li>F. Route of administration</li> <li>G. The calculation for dosing (including the variables used in this calculation)</li> <li>H. Treatment cycle and day of cycle</li> </ul>

16.	<p>Chemotherapy drugs are labeled immediately upon preparation, including, at minimum:</p> <ul style="list-style-type: none"> <li>A. Patient's full name and a second patient identifier (e.g., medical record number, DOB)</li> <li>B. Full generic drug name</li> <li>C. Drug administration route</li> <li>D. Total dose to be given</li> <li>E. Total volume required to administer this dosage</li> <li>F. Date of administration</li> <li>G. Date and time of preparation</li> <li>H. Date and time of expiration when not for immediate use*</li> </ul> <p><b>NEW ITEMS:</b></p> <ul style="list-style-type: none"> <li><b>I. Special handling instructions as appropriate</b></li> <li><b>J. Administration instructions (oral agents)</b></li> </ul>
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<p><b>K. Number of refills (oral agents)</b></p> <p><b>L. Prescriber name (oral agents)</b></p> <p>*Immediate use must be defined by institutional policy, state, and federal regulations (e.g. use within 2 hours).</p> <p><i>Practices/institutions are not expected to be in full compliance with this standard if they currently have electronic systems that are unable to meet these labeling requirements. Appropriate changes should be implemented as soon as possible to ensure that electronic labels integrate all of these elements.</i></p>
<p>17. Practices/institutions that administer intrathecal medication maintain policies specifying that intrathecal medication will:</p> <p>A. Not be prepared during preparation of any other agents.</p> <p>B. Be stored, once prepared, in an isolated container or location with a uniquely identifiable intrathecal medication label.</p> <p>C. Be delivered to the patient only with other medication intended for administration into the CNS.</p>
<p>18. Before initiation of a chemotherapy regimen, each patient is given written documentation, including, at minimum:</p> <p>A. Information regarding his/her diagnosis</p> <p>B. Goals of therapy</p> <p>C. Planned duration of chemotherapy, drugs, and schedule</p> <p>D. Information on possible short- and long-term adverse effects</p> <p>E. Regimen- or drug-specific risks or symptoms that require notification and emergency contact information, including:</p> <ul style="list-style-type: none"> <li>o How to contact the practice or organization;</li> <li>o Symptoms that should trigger a call;</li> <li>o Who should be called in specific circumstances (oncologist or other provider)</li> </ul> <p>F. Plan for monitoring and follow-up</p> <p>G. Patient education materials should be appropriate for the patient’s reading level / literacy and patient/caregiver understanding.</p>
<p>19. Informed consent for chemotherapy must be documented prior to initiation of a chemotherapy regimen.</p> <p>The consent process should follow appropriate professional and legal guidelines. (For more information and sample forms, see <a href="http://www.asco.org/consent">http://www.asco.org/consent</a>.)</p>
<p>20. All patients who are prescribed oral chemotherapy are provided written or electronic patient education materials about the oral chemotherapy before or at the time of prescription.</p> <p>A. Patient education includes: the preparation, administration, and disposal of oral chemotherapy; <b>concurrent cancer treatment and supportive care medications/measures (when applicable); possible drug/drug and drug/food interactions; the plan for missed doses. (NEW)</b></p> <p>B. The education plan includes family, caregivers, or others based on the patient’s ability to assume</p>

	<p>responsibility for managing therapy.</p> <p>C. Patient education materials should be appropriate for the patient's reading level/literacy and patient/caregiver understanding.</p>
21.	<p>Before chemotherapy administration:</p> <p>Confirm with the patient his/her planned treatment prior to each cycle;</p> <p>At least two practitioners or personnel approved by the practice/institution to prepare or administer chemotherapy, verify the accuracy of:</p> <ul style="list-style-type: none"> <li>A. Drug name</li> <li>B. Drug dose</li> <li>C. Drug volume</li> <li>D. Rate of administration</li> <li>E. Route of administration</li> <li>F. Expiration dates/times; if applicable: [expiration date/time is not required if for immediate use*]</li> <li>G. Appearance and physical integrity of the drugs</li> <li>H. Rate set on the pump, when utilized</li> <li>I. Document to indicate verification was done and;</li> <li>J. At least two individuals, in the presence of patient, verify the patient identification using at least two identifiers (e.g., medical record number, DOB)</li> </ul> <p>* Immediate use must be defined by institutional policy, state, and federal regulations (e.g. use within 2 hours).</p>
22.	<p>Extravasation management procedures are defined and align with current literature and guidelines; antidote order sets and antidotes are accessible.</p>
23.	<p>A licensed independent practitioner is on site and immediately available during all chemotherapy administration <b>in licensed infusion centers and acute care settings. (NEW)</b></p> <p>A licensed practitioner must be on site for the administration of first doses of parenteral chemotherapy and should remain available throughout the administration unless the patient is transitioned to a home care or nonacute facility.</p> <p>***Patients/caregivers are educated in procedures for unplanned events and circumstances when subsequent doses are administered in either a home care or nonacute facility.</p>
24.	<p>The practice/institution maintains protocols for response to life threatening emergencies, including escalation of patient support beyond basic life support.</p> <p>It is recommended that emergency protocols are reviewed annually.</p>

**NEW!**

25. The practice/institution maintains a written policy and/or procedure to complete an initial assessment of patients' adherence to oral chemotherapy. The policy must include a plan for clinical staff to address any issues identified within a time frame appropriate to the patient and regimen.

Examples of assessments for adherence to an oral chemotherapy treatment plan include:

- A. Confirmation that the patient filled the prescription as written
- B. Inquiry regarding concerns about treatment costs
- C. Verification that the patient understands how to take the prescribed oral chemotherapy (e.g., frequency, with/without food, whole or crushed, etc)
- D. Verification that the patient understands what to do in the case of missed doses
- E. Assessment for potential toxicity

26. On each clinical visit or day of treatment during chemotherapy administration, staff:

- A. Assess and document clinical status and/or performance status
- B. Document vital signs and weight
- C. Verify allergies, previous reactions, and treatment-related toxicities
- D. Assess and document psychosocial concerns and need for support; taking action when indicated.

This standard applies to all clinical encounters (including each inpatient day, practitioner visits and chemotherapy administration visits, but not laboratory or administrative visits).

27. At each clinical encounter, staff reviews the patient's current medications including over the counter medications and complementary and alternative therapies. **Any changes in the patient's medications prompt a review for drug-drug interactions. (NEW)**

*This standard applies to all clinical encounters (including each inpatient day practitioner visit and chemotherapy administration visits but not laboratory or administrative visits).*

28. The practice/institution maintains referral resources for psychosocial and other supportive care services

29. The practice/institution establishes a procedure for documentation and follow-up for patients who miss office visits and/or scheduled chemotherapy treatments.

30. The practice/institution evaluates and documents treatment-related toxicities using standard definitions or criteria selected by that practice/institution.

*Examples include NCI Common Toxicity Criteria and WHO Toxicity Criteria.*

31. The practice/institution has policies and procedures that identify:

- A. A process to provide 24/7 triage to a practitioner (e.g., on-call practitioner, emergency department) for care of toxicities.
- B. Consistent documentation and communication of toxicities, modifications of dose or schedule, or discontinuation of treatment, within the practice/institution.

**NEW!**

32. **Each practice/institution has a system in place to promote a safe handoff between all sites of care, including evaluation and communicating appropriateness of, and schedule for, chemotherapy administration in another setting.**

33. Toxicity assessment documentation is available for planning subsequent treatment cycles.

34. The practice/institution has a process to track cumulative doses of chemotherapy agents associated with a risk of cumulative toxicity.

**NEW!**

35. **The practice/institution maintains a plan for ongoing and regimen-specific assessment of each patient's oral chemotherapy adherence and toxicity. The policy includes, at a minimum, patient assessment for adherence and toxicity at each clinical encounter at the practice/institution, as well as a plan for clinical staff to address any issues identified.**

36. The practice/institution uses standard, disease-specific processes to monitor treatment response (e.g., use of evaluations, laboratory results, or scans/imaging) that are based on published literature/guidelines or are determined by the practice/institution.

37. The practice/institution encourages the reporting of errors and near misses and has a formal reporting process for evaluating the data. Error and near-miss reporting are reviewed and evaluated at least semi-annually.

## QUALITY

### I. Quality Oncology Practice Initiative (QOPI)

- A. QOPI<sup>®</sup> is a quality measurement tool developed by the American Society of Clinical Oncology to benchmark clinical practices against accepted standards of practice. Certified practices are evaluated against a comprehensive set of Quality measures and standards.<sup>18</sup>
- B. For details on the requirements to achieve QOPI Certification please review the materials below. QOPI Certification Program measures, performance thresholds, and site standards are publicly available. Standards and measures are continually re-assessed to maintain rigor. Practices are encouraged to review the measures and standards, and implement any needed improvements prior to entering the QOPI Certification Program. All standards and measures are dated.
- C. QOPI Safety Standards are based on the ASCO/ONS Standards for Safe Chemotherapy

Term	Definition
<b>Chemotherapy</b>	All antineoplastic agents used to treat cancer, given through oral and parenteral routes or other routes as specified in the standard. Types include targeted agents, alkylating agents, antimetabolites, plant alkaloids and terpenoids, topoisomerase inhibitors, antitumor antibiotics, monoclonal antibodies, and biologics and related agents. Hormonal therapies are not included in the definition of chemotherapy for the standards.
<b>Chemotherapy Regimen</b>	One or more chemotherapeutic agents used alone or in combination in a well-defined protocol, generally administered cyclically.
<b>Practitioner</b>	Licensed independent practitioner, including physicians, advanced practice nurses (nurse practitioner or clinical nurse specialist), and/or physician assistants, as determined by state law.
<b>Chemotherapy Setting (site)</b>	All chemotherapy treatment settings (inpatient and outpatient).
<b>Adherence</b>	The degree or extent of conformity to the provider's recommendations about day-to-day treatment with respect to timing, dosing, and frequency.
<b>Clinical Encounter</b>	Clinical encounters include each inpatient day, practitioner visits and chemotherapy administration visits, but not laboratory or administrative visits.

### ASCO/ONS Chemotherapy Administration Safety Standards used for QOPI Certification

(standards are written out completely in Table in Section IV above):

Standards:  1, 2, 6, 11, 15, 16, 17, 18, 19, 21, 22, 24, 26, 27, 28, 29, 31, 33, 34, 35
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D. QOPI Core Certification Measures:

<b>Core Measures</b>
1. Pathology report confirming malignancy
2. Staging documented within one month of first office visit
6. Pain addressed appropriately
9. Documented plan for chemotherapy, including doses, route, and time intervals
10. Chemotherapy intent (curative vs. palliative) documented
21a. Smoking status/tobacco use documented in past year
24. Patient emotional well-being assessed by second office visit
<b>Symptom/Toxicity Management Module measures</b>
27. Corticosteroids and serotonin antagonist prescribed with moderate/high emetic risk Chemotherapy
33. Infertility risks discussed prior to chemotherapy with patients of reproductive age
<b>End of Life Care Module measures</b>
38. Pain assessed appropriately at EOL (defect-free measure)
45a. Hospice enrollment and enrolled > 7 days before death (defect free measure)
<b>Breast Cancer Module measures</b>
53. Combination chemotherapy received within 4 months of diagnosis by women under 70 with AJCC stage I (T1c) to III ER/PR negative breast cancer*
54. Test for Her-2/neu gene overexpression
56a. Trastuzumab not received when Her-2/neu is negative or undocumented
57. Trastuzumab received by patients with AJCC stage I (T1c) to III Her-2/neu positive breast cancer*
59. Tamoxifen or AI received within 1 year of diagnosis by patients with AJCC stage I (T1c) to III ER or PR positive breast cancer*
<b>Colorectal Cancer Module measures</b>
66. CEA within 4 months of curative resection for colorectal cancer
68. Adjuvant chemotherapy received within 4 months of diagnosis by patients with AJCC stage III colon cancer*
72. Adjuvant chemotherapy received within 9 months of diagnosis for patients with AJCC stage II or III rectal cancer*
73. Colonoscopy before or within 6 months of curative colorectal resection or completion of primary adjuvant chemotherapy.
74. KRAS testing for patients with metastatic colorectal cancer who receive MoAb therapy.
75a. Anti-EGFR MoAb therapy not received by patients with KRAS mutation.
<b>Non-Small Cell Lung Cancer Module measures</b>
81. Adjuvant cisplatin-based chemotherapy received within 60 days after curative resection – stage II or IIIA NSCLC.
84. Performance status documented for patients with initial stage IV or distant metastatic NSCLC.
85. Platinum doublet first-line chemotherapy or EGFR-TKI (or other targeted therapy with documented DNA mutation) received by patients with initial AJCC stage IV or distant metastatic NSCLC with performance status of 0 – 1 without prior history of chemotherapy.
88. Positive mutation for patients with stage IV NSCLC who received first-line EGFR tyrosine kinase inhibitor or other targeted therapy.

## II. CMS Value Based Purchasing (VBP)/Shared Savings Program (SSP)<sup>19</sup>

- A. Established by Affordable Care Act of 2010 to use patient satisfaction measures and clinical outcome data to influence payment from Medicare to hospitals
- B. VBP – applies to nearly all providers in all settings
  - 1. Involves nearly all acute care programs
  - 2. Impacts 1% of payment in initial year and increases to 2% by 10/2017
  - 3. Current measures include process of care, patient experience and outcomes
  - 4. Rewards achievement and improvement
  - 5. Quality Incentive Program applies to renal dialysis centers
  - 6. Physician payments adjusted up or down based on performance of quality and cost metrics
  - 7. Domains of quality measurement – safety, patient and caregiver centered experience and outcomes, care coordination, clinical care, population/community health, and efficiency/cost reduction
  - 8. Sample report for patient satisfaction survey data used for VBP:

	VBP Achievement Threshold (50th Nat'l Percentile)	VBP Benchmark (Mean of Top Decile)	Unit A		Unit B		Unit C		Unit D	
			N	Score	N	Score	N	Score	N	Score
<b>Communication with Nurses</b>	<b>75.79</b>	<b>84.99</b>	<b>239</b>	<b>68.83</b>	<b>178</b>	<b>84.40</b>	<b>276</b>	<b>71.27</b>	<b>32</b>	<b>82.29</b>
Nurses listened carefully to you			234	64.53	178	79.78	270	66.30	32	75.00
Treated w/ courtesy/respect by nurses			237	76.37	177	92.09	275	81.09	32	90.63
Nurse explained things understandably			238	65.55	177	81.36	273	66.30	32	81.25
<b>Communication with Doctors</b>	<b>79.57</b>	<b>88.45</b>	<b>239</b>	<b>69.70</b>	<b>175</b>	<b>80.73</b>	<b>277</b>	<b>76.48</b>	<b>32</b>	<b>75.00</b>
Drs listened carefully to you			232	68.53	171	80.70	272	75.00	32	68.75
Drs explained things understandably			234	65.38	174	74.14	276	69.93	32	71.88
Treated w/ courtesy/respect by Drs			237	75.11	174	87.36	277	84.48	32	84.38
<b>Responsive of Hospital Staff</b>	<b>62.21</b>	<b>78.08</b>	<b>223</b>	<b>47.50</b>	<b>171</b>	<b>60.17</b>	<b>266</b>	<b>56.07</b>	<b>32</b>	<b>64.44</b>
Help going to bathroom as soon as needed			100	50.00	71	60.56	153	60.13	13	61.54
Got help as soon as wanted			220	46.36	170	60.00	259	53.67	32	65.63
<b>Pain Management</b>	<b>68.99</b>	<b>77.92</b>	<b>165</b>	<b>58.54</b>	<b>113</b>	<b>71.62</b>	<b>229</b>	<b>64.62</b>	<b>23</b>	<b>71.74</b>
Did everything to help your pain			165	67.88	112	83.93	228	76.75	23	82.61
Pain well controlled during stay			163	49.08	110	59.09	227	52.42	23	60.87
<b>Communication about Medicines</b>	<b>59.85</b>	<b>71.54</b>	<b>129</b>	<b>55.73</b>	<b>124</b>	<b>74.80</b>	<b>172</b>	<b>59.47</b>	<b>26</b>	<b>69.23</b>
Told what medicine was for			127	71.65	124	85.48	169	74.56	26	76.92
Staff described med side effects			126	39.68	122	63.93	169	44.38	26	61.54
<b>Cleanliness and Quiet of Hospital Env.</b>	<b>63.54</b>	<b>78.10</b>	<b>461</b>	<b>50.98</b>	<b>345</b>	<b>73.04</b>	<b>543</b>	<b>46.41</b>	<b>62</b>	<b>61.29</b>
Room kept clean during stay			233	60.52	175	77.14	272	58.46	31	64.52
Quiet around room at night			228	41.23	170	68.82	271	34.32	31	58.06
<b>Discharge Information</b>	<b>82.72</b>	<b>89.24</b>	<b>215</b>	<b>81.18</b>	<b>162</b>	<b>95.67</b>	<b>258</b>	<b>92.56</b>	<b>27</b>	<b>92.59</b>
Talked about help you would need			211	78.67	162	94.44	256	91.80	27	92.59
Received info re: symptoms to look for			214	83.64	161	96.89	255	93.33	27	92.59
<b>Overall Hospital Rating</b>	<b>67.33</b>	<b>82.55</b>	<b>233</b>	<b>63.09</b>	<b>175</b>	<b>86.29</b>	<b>272</b>	<b>65.81</b>	<b>31</b>	<b>83.87</b>

C. SSP<sup>20</sup>

1. Establishes Accountable Care Organizations (ACOs) that take full responsibility for the health of a patient or community (Medicare beneficiaries).
2. If an ACO succeeds in delivering high quality care at a reduced cost – it will share the savings that Medicare achieves.
3. ACOs may consist of physician practices, hospitals employing physicians, or partnerships between hospitals and physician groups.
4. Measures for ACO Quality Performance include:
  - a. Patient and caregiver experience
  - b. Care coordination transition teams
  - c. Care coordination information teams
  - d. Patient safety



- e. Preventative health: At-risk populations including diabetes, heart failure, coronary artery disease, hypertension, COPD and frail elderly patients

### III. **CMS Oncology Care Model (OCM)**<sup>21</sup>

- A. The innovation Center at CMS published the first major payment modification for oncology services in February 2015. The OCM focuses on an episode of cancer care, specifically a chemotherapy episode of care.
- B. The goals of OCM are to utilize appropriate aligned financial incentives to improve:
  - 1. Care Coordination
  - 2. Appropriateness of care
  - 3. Access for Medicare beneficiaries undergoing chemotherapy
- C. Financial incentives encourage participating oncology practices to work collaboratively to comprehensively address the complex care needs of beneficiaries receiving chemotherapy treatment and encourage the use of services that improve health outcomes.
- D. How will the OCM work?
  - 1. Episode based: Payment model targets chemotherapy and related care during a 6 month period following the initiation of chemotherapy treatment.
  - 2. Emphasizes practice transformation: Physician practices are required to engage in practice transformation to improve the quality of care they deliver.
  - 3. Multi-payer model: Includes Medicare fee-for-service (FFS) and other payers working in tandem to leverage the opportunity to transform care for oncology patients across the population.
- E. Physician practices that are Medicare providers and furnish chemotherapy may apply to participate in OCM – there are six requirements for participation:
  - 1. Provide 24/7 patient access to an appropriate clinician who has real-time access to the patient’s medical records.
  - 2. Use an ONC-certified EMR and attest to Stage 2 of meaningful use (MU) by the end of the third model performance year and MU Stage 1 by the end of the first model performance year.
  - 3. Utilize data for continuous quality improvement – The CMS Innovation Center will provide participating practices with rapid cycle data feedback reports to aid in quality improvement. Practices are expected to use this data to continuously improve OCM patient care management.
  - 4. Provide core functions of patient navigation: Practices are required to provide patient navigation to all OCM patients. The National Cancer Institute provides a sample list of patient navigation activities.
  - 5. Document a care plan for every OCM patient that contains the 13 components in the Institute of Medicine’s Care Management Plan. Plan components include treatment goals, care team, psychosocial support and estimated out-of-pocket costs.
  - 6. Treat patient with therapies consistent with nationally recognized clinical guidelines. Practices must report which clinical guidelines (NCCN® or ASCO) they follow for OCM patients or provide a rationale for not following the clinical guidelines.

- F. Payers
  - 1. OCM covers Medicare fee-for service (OCM-FFS) other payers (OCM-OP). Other payers may include commercial payers, state Medicaid agencies, or other governmental payers (including Tricare, FEHBP and state employee health plans).
  - 2. Payer participation will drive the geographic scope of the model. The CMS Innovation Center will publish lists of payers and practices who submit letters of intent to participate in OCM and expects other payers to plan for OCM participation with their associated practices.
- G. Operations of OCM:
  - 1. Commit to participation in OCM for its 5 year duration and begin performance period within 90 days.
  - 2. Sign a memorandum of understanding with the Innovation Center.
  - 3. Enter into agreements with OCM practices that include requirements to provide high quality care.
  - 4. Share model methodologies with the Innovation Center.
  - 5. Provide payments to practices for enhanced services and performance as described in the RFA (request for applications).
- H. Quality Improvement Measures – Align practice quality and performance measures with OCM.
- I. Data Sharing – Provide participating practices with aggregate and patient-level data about payment and utilization for their patients receiving care in OCM, at regular intervals.
- J. Medicare beneficiaries who meet each of the following criteria will be included in OCM-FFS:
  - 1. Eligible for Medicare Part A and enrolled in Medicare Part B.
  - 2. Have Medicare FFS as their primary payer.
  - 3. Do not have end-stage renal disease.
  - 4. Are not covered by United Mine Workers.
  - 5. Receiving treatment with chemotherapy for cancer under management of an OCM participating practice.
- K. Episode Definition:
  - 1. OCM-FFS includes nearly all types of cancer.
  - 2. Episodes initiate when a beneficiary starts chemotherapy
  - 3. The Innovation Center has devised a list of chemotherapy drugs that trigger OCM-FFS episodes, including endocrine therapies but excluding topical formulations of drugs.
  - 4. All Medicare A and B services that Medicare FFS beneficiaries receive during episodes will be considered included services. Certain Part D expenditures will also be included.
  - 5. OCM-FFS episodes extend 6 months after a beneficiary’s chemotherapy initiation.
  - 6. Beneficiaries may initiate multiple episodes during the 5 year model performance period.
- L. Payment:
  - 1. Per-beneficiary-per-month (PBPM) payment
    - a. \$160 PBPM payment for enhanced services required by OCM that is paid during the chemotherapy episode.
    - b. OCM-FFS practices are eligible for the PBPM monthly payment for each month of the 6 month episode, unless the beneficiary enters hospice.
  - 2. Performance-based payment
    - a. Incentive to lower the total cost of care and improve quality of care for beneficiaries over the 6 month episode period.

- b. Retrospective payment that is calculated based the practice's historical Medicare expenditures and achievement on selected quality measures.
- c. CMS will calculate benchmark episode expenditures participating practices based on historical data, geographical variation and trended to applicable performance period.
- d. A discount will be applied to the benchmark to determine a target price for OCM-FFS episodes. (e.g., Benchmark = \$100 with 4% Discount = Target Price of \$96.
- e. If actual OCM-FFS episode Medicare expenditures are below target price, the practice could receive a performance-based payment. (e.g., Actual cost = \$90 from example (d) above the performance-based payout could be up to \$6.)
- f. The amount of the performance-based payment may be reduced based on the participant's achievement and improvement on a range of quality measures.
- g. Risk Arrangement for Shared Savings may be one-sided or two-sided:
  - a. One-sided: participants are NOT responsible for Medicare expenditures that exceed target price; Medicare discount 4%; must qualify for performance-based payment by the end of year 3.
  - b. Two-sided: participants are responsible for Medicare expenditures that exceed target price; option to take downside risk beginning in year 3; Medicare discount 2.75%; must qualify for performance based payment by end of year 3.
  - c. Clinical trial participants are included.
- h. Risk adjustments will be made for episodic expenditures including beneficiary expenditures, episode characteristics, disease characteristics and type of service furnished.

M. Quality Measures:

1. Clinical quality of care
2. Communication and care coordination
3. Person and caregiver centered experience and outcomes
4. Population health
5. Efficiency and cost reduction
6. Patient safety
7. Quality measures are culled from data sources such as practice-reported data, Medicare claims and patient surveys.

Quality Domain	Recommended Practice Requirement or Quality Measurement	NQF #	Source
Communication and Care Coordination	# of ED visits per OCM-FFS beneficiary per episode		Claims data
Communication and Care Coordination	# of hospital admissions per OCM-FFS beneficiary per episode		Claims data
Communication and Care Coordination	% of all Medicare FFS beneficiaries managed by the practice admitted to hospice for < 3 days	#0216	Claims data
Communication and Care Coordination	% of all Medicare FFS beneficiaries managed by the practice who experience ≥ 1 ED visit in the last 30 days of life	#0211	Claims data
Person- and Caregiver-Centered Experience and Outcome	% of OCM-FFS beneficiaries face-to-face encounters with the participating practice in which there is a documented plan of care for pain and pain intensity is quantified	#2100	Reported by practice
Person- and Caregiver-Centered Experience and Outcome	Score on patient experience survey (modified CAHPS)		Administered by CMS contractor
Person- and Caregiver-Centered Experience and Outcome	% of OCM-FFS beneficiary face-to-face encounters in which the patient is assessed by an approved patient-reported outcomes tool and that receive psychosocial screening/intervention at least once per episode		Reported by practice

#### N. Monitoring and Evaluation

1. Tracking of claims data
2. Patient surveys
3. Site visits
4. Analysis of quality measurement data
5. Time and motion studies
6. Medical record audits, tracking of patient complaints and appeals
7. OCM will use match-comparison groups to detect changes in utilization, costs and quality that can be attributed to the model

O. Learning and Diffusion

1. Topic-specific webinars that allow OCM participants to learn from each other
2. Online portal to support learning through shared resources, tools, ideas, discussions, and data-driven approaches to care
3. Action Groups in which practices work together virtually to explore critical topic areas and build capability to deliver comprehensive oncology care
4. Coaching to help practices overcome barriers to improvement

**IV. Other general quality improvement tools used in oncology pharmacy:**

A. Six Sigma – Philosophic approach to eliminating defects and work variation through prevention and process improvement using a team based approach.<sup>22</sup>

1. DMAIC – Define, Measure, Analyze, Improve, Control
2. Utilizes quantitative and qualitative statistically based tools for data analysis (e.g. control charts)
3. Goal is to reduce error rate to 3.4 per million
4. Requires extensive staff training awarding belt colors (similar to martial arts) to delineate competence

B. Lean – Elimination of waste based on Toyota Production System<sup>23</sup>

1. Methodology – Breakdown a process into individual components and eliminate steps that do NOT provide value
2. Kaizen philosophy – employee-led continuous improvement by specifying value of a process; value stream can be mapped to eliminate non-value added steps
3. Kaizen Events – Rapid improvement initiative focused on a specific process with a well defined scope
  - a. An example would be a Kaizen event focused on improvement drug dispensing time in an outpatient oncology infusion center partnering pharmacy with nursing.

C. Root Cause Analysis (RCA) – structured, step-by-step techniques for problem solving. The goal is to determine and correct the ultimate cause(s) of a problem, not just the visible symptoms, to ensure that it does not occur again.<sup>24</sup>

1. RCA consists of determining what happened, why it happened and what can be done to prevent it from happening again
2. The Joint Commission requires all accredited organizations to conduct an RCA of any sentinel event (an unexpected occurrence involving death or serious physical or psychological injury, or risk thereof).

3. The five whys technique – consists of asking why an event occurred repeatedly until the root issue is uncovered.
  4. Cause and effect diagram – can use a “fishbone” diagram where the head of the fish is the problem and branches are considered different categories of causes.
- D. Failure Mode Effects Analysis (FMEA) – originally developed by the US military in the 1940’s to assess equipment failure. It has since been adopted in many industries to evaluate service failure. Joint Commission requires use of FMEA or a similar tool to reduce the potential for failure of a process. FMEA classically involves the following steps:<sup>25</sup>
1. Identification of the process to be evaluated.
  2. Team training; use of FMEA in health care will typically involve personnel from multiple department – e.g. pharmacy, nursing, environmental services, laboratory, etc.
  3. Develop a detailed process flowchart, including all steps in the process.
  4. Identify each step in the process
  5. Identify potential failures (e.g. failure modes) at each step in the process
  6. Determine the worst possible outcome of each failure mode.
  7. Identify the contributory factors for each potential failure.
  8. Identify any failure “controls” that are currently present. A control reduces the likelihood of a failure event or reduces the severity of the consequences of a failure.
  9. Rate the severity of each failure (typically a 1 to 10 scale).
  10. Rate the likelihood that each failure cause will occur (typically a 1 to 10 scale).
  11. Rate the effectiveness of each control (again, a 1 to 10 scale).
  12. Multiple the three above ratings by each other to obtain the risk priority number (RPN) for each cause or contributory factor.
  13. Use the RPNs to prioritize problems for corrective actions.
  14. Develop an improvement plan to address the targeted causes.
- E. Medication Use Evaluation (MUE)
1. Performance improvement method that focuses on evaluating and improving medication-use processes with the goal of optimal patient outcomes.
  2. MUE may be applied to a medication or therapeutic class, disease state or condition, a medication-use process (e.g. prescribing or dispensing medications) or specific outcomes.

3. ASHP outlines MUE objectives, methodology and pharmacists' role in MUEs in their published guidelines for MUE.<sup>26</sup>

F. Institute for Safe Medication Practices (ISMP)- only non-profit organization devoted entirely to medication error prevention and safe medication use.<sup>27</sup> Certified as a Patient Safety Organization by the US Agency for Healthcare Quality and Research.

1. Maintains a national voluntary medication error-reporting system where anonymous reports are shared via a newsletter (ISMP Medication Safety Alert).
2. Provides consulting services to pharmaceutical industry and hospital to identify risk point for medications errors.
3. Offers self-assessments for institution to benchmark their medication safety practices with other participating institutions.
4. Conducts ongoing continuing education efforts via webinar or at professional meetings on medication safety topics.
5. Established targeted medication safety best practices for hospital for 2014-15.
  - a. **Best practice #1 – Dispense vincristine (and other vinca alkaloids) in a mini bag of a compatible solution and not in a syringe.**
  - b. **Best practice #2 – Use a weekly dosage regimen default for oral methotrexate. If override to daily require a hard stop verification of an appropriate oncologic indication. Provide patient education by a pharmacist for all weekly oral methotrexate orders.**
  - c. Best practice #3 – Measure and express patient weights in metric units only. Ensure that scales used for weighing patients are set to measure only in metric units.
  - d. Best practice #4 – Ensure that all oral liquids that are not commercially available as unit dose products are dispensed by pharmacy in an oral syringe.
  - e. Best practice #5 – Purchase oral liquid dosing devices (oral syringes / cups / droppers) that only display the metric scale.
  - f. Best practice #6 - Eliminate glacial acetic acid from all areas of the hospital.

## INFORMATICS

- I. Electronic Medical Record (EMRs) – oncology EMRs have lagged behind other computerized physician order entry applications<sup>28</sup>**
- A. Clinical components of an EMR: Results reporting information system (RRIS), computerized physician order entry, clinical decision support system (CDSS)
  - B. Baseline elements in oncology-specific EMR: Tumor staging; multidisciplinary and data-intensive workflow; chemotherapy dosing and administration; toxicity assessment and management; clinical trial and protocol management; drug inventory management; survivorship care.
  - C. Oncology specific EMR functionalities identified by ASCO: Chemotherapy/drug management; oncology-specific billing; calendar/scheduler; clinical trials and research; compliance safeguards.
  - D. Error rates are significant in oncology patients given the complexity of treatment regimens – 7% in outpatient adults and 18% in pediatrics<sup>29</sup>
  - E. Commonly used EMRs for oncology<sup>30</sup>

Vendor	Pros	Cons
Epic - Beacon	Highly rated by KLAS on sales/contracting and implementation/training Decision support for pharmacists/physicians Supports inpatient and outpatient use Functions on hand-held devices KLAS Rating – 85.42 out of 100	Rated well below average on Ease of Use Rated below average in needed functionality CPOE for chemotherapy, not radiation therapy Each site has to build its own treatment regimens
Mosaiq - Elekta	Obtained 2011 best in KLAS award for software and services Used globally by oncology practitioners Above average rating for keeping promises Solutions for medical and radiation oncology Linked to NCCN Guidelines® Certified EHR/demonstrate Stage 1 Meaningful Use KLAS Rating – 79.24 out of 100	Below average rating in overall product, product response time , integration and needed functionality Poor executive involvement Poor implementation and insufficient training of the product Not an part of an integrated EMR
I Know Med (G2) – McKesson/US Oncology	Can be used for all size practices HL7 Compliant Windows and Web based Supportive radiation oncology Supports US Oncology clinical trials Certified EHR/demonstrate Stage 1	Requires an additional interface to a health-system EMR Use is largely limited to outpatient setting with US Oncology physician office based practices Chemotherapy orders may be processed prior to having physician



	Meaningful Use	e-signature Flexibility is limited for building new regimens due to pathway use by US Oncology physicians
Cerner – Power Chart Oncology	HL7 Compliant Windows and Web based Certified Stage 2 Meaningful Use Supports inpatient and outpatient chemotherapy ordering Supports Stem Cell Transplantation CDSS integrated into ordering template	No solution for ordering chemotherapy drugs by non-oncologists Does not support radiation oncology Functionality for ordering subsequent cycles with modifications to the original order template is flawed

\*KLAS – independent auditor of health care information technology

\*\*Other major vendors such as Meditech, Cerner and Allscripts have oncology EMRs in various stage of development

## II. Other relevant technology

- A. Automated dispensing cabinets (e.g. Pyxis, Omnicell) – guidelines for safe use provided by ISMP<sup>31</sup>
- B. DoseEdge/MedKeeper- utilizes digital photo and barcoding to verify step by step compounding of sterile intravenous products
- C. Oncology Clinical Pathways:<sup>32,33</sup>
  1. Goal is to standardize practice for ordering chemotherapy regimens with use of evidenced-based clinical pathways based on disease and stage.
  2. Compliance – goal for on-pathway rate approximates 70 to 80% taking into account patient-specific factors such as end-organ dysfunction, tumor genomics, patient performance status and access to care.
  3. Major commercial vendors: Via Oncology – University of Pittsburgh Medical Center; US Oncology – McKesson; Cardinal Health.
  4. Clinical data:
    - a. Data from eight community practices for treatment of NSCLC patients – drug costs: On-pathway - \$18,042 vs. Off-pathway \$27,737; no difference in overall survival.<sup>32</sup>
    - b. Utilization of clinical pathways among multiple private oncology physician practices demonstrated an 88% compliance rate with physicians and a decrease in regimen usage from 168 to 136.<sup>33</sup>

## III. Meaningful Use - The Medicare and Medicaid EHR Incentive Programs provide financial incentives for the “meaningful use” of certified EHR technology to improve patient care.<sup>34</sup> To receive an EHR incentive

payment, providers have to show that they are “meaningfully using” their EHRs by meeting thresholds for a number of objectives. CMS has established the objectives for “meaningful use” that eligible professionals, eligible hospitals, and critical access hospitals (CAHs) must meet in order to receive an incentive payment.

A. Staged in three steps:

1. Stage I – 19 of 24 objectives must be met for incentive payments
2. Stage II – must meet Stage I requirements with additional objectives – starts in 2014
3. Stage III – starts in 20**FINANCE**

**I. Reimbursement for outpatient oncology drugs:**

- A. Reimbursement rates under Medicare for IV drugs provided by hospitals/office-based clinics in the outpatient setting —the average sale price (ASP) of the drug plus 6%.
- B. The federal government sequester has reduced the payment from ASP plus 6% to ASP plus 4.3%. Payment limits are updated quarterly on the CMS website.<sup>35</sup>

Select chemotherapy drugs with J-code, drug name, billing unit and reimbursement per billing unit<sup>35</sup>

J9033	Bendamustine injection	1 MG	21.347
J9035	Bevacizumab injection	10 MG	65.664
J9040	Bleomycin sulfate injection	15 UNITS	18.779
J9041	Bortezomib injection	0.1 MG	45.567
J9042	Brentuximab vedotin inj	1 MG	106.856
J9043	Cabazitaxel injection	1 MG	139.036
J9045	Carboplatin injection	50 MG	3.152
J9047	Injection, Carfilzomib, 1 mg	1 MG	29.291
J9050	Carmustine injection	100 MG	1424.261
J9055	Cetuximab injection	10 MG	52.540
J9060	Cisplatin 10 MG injection	10 MG	2.075
J9065	Inj cladribine per 1 MG	1 MG	22.262
J9070	Cyclophosphamide 100 MG inj	100 MG	52.458
J9098	Cytarabine liposome inj	10 MG	544.543
J9100	Cytarabine hcl 100 MG inj	100 MG	0.942
J9120	Dactinomycin injection	0.5 MG	645.749
J9130	Dacarbazine 100 mg inj	100 MG	4.000
J9150	Daunorubicin injection	10 MG	26.121
J9155	Degarelix injection	1 MG	3.515
J9160	Denileukin diftitox inj	300 MCG	1646.180
J9171	Docetaxel injection	1 MG	3.980
J9175	Elliotts b solution per ml	1 ML	4.157
J9178	Inj, epirubicin hcl, 2 mg	2 MG	1.213
J9179	Eribulin mesylate injection	0.1 MG	98.239
J9181	Etoposide injection	10 MG	0.730
J9185	Fludarabine phosphate inj	50 MG	71.075
J9190	Fluorouracil injection	500 MG	2.123
J9200	Floxuridine injection	500 MG	69.388
J9201	Gemcitabine hcl injection	200 MG	7.403
J9202	Goserelin acetate implant	3.6 MG	194.420
J9206	Irinotecan injection	20 MG	4.539
J9207	Ixabepilone injection	1 MG	68.646
J9208	Ifosfamide injection	1 GM	35.813
J9209	Mesna injection	200 MG	2.936
J9211	Idarubicin hcl injection	5 MG	35.678
J9214	Interferon alfa-2b inj	1 MIL UNITS	20.654
J9217	Leuprolide acetate suspension	7.5 MG	209.085
J9218	Leuprolide acetate injection	1 MG	8.762
J9225	Vantas implant	50 MG	2941.839
J9226	Supprelin LA implant	50 MG	16632.025
J9228	Ipilimumab injection	1 MG	128.966

C. Medicare Part D for prescription drug coverage:<sup>36</sup>

1. Offers beneficiaries the option of enrolling for prescription drug coverage administered by a private insurer starting in 2006.
2. Costs have been 40% lower than originally forecast by the Congressional Budget Office largely due to competition between plans, use of generic drugs and beneficiary choice of low-premium plans.
3. Most plans have a deductible with a co-insurance of 25%. Once a cumulative expense of approximately \$3,000 is reached the patient is responsible for the full cost of the drugs until total expenditure reaches approximately \$5,000. This is coverage gap has been termed the “doughnut hole”. The Affordable Care Act will gradually phase out the doughnut hole by 2020.
4. Subsidies are available for economically disadvantaged patients.
5. Medication Therapy Management (MTM) being incorporated into multiple plans and disease states.

II. **Diagnostic related group (DRG) payment (Medicare Part A benefit):** CMS payment method for inpatient hospitalization. Chemotherapy drugs are not individually reimbursed as part of a hospitalization stay and therefore the cost would be deducted from a DRG payment to the hospital for a specific hospital admission.<sup>37</sup>

Case:

A metastatic NSCLC patient is admitted to a hospital for exacerbation of pain. The hospitalization is 3 days and the third day happens to coincide with the patient’s next schedule infusion appointment for pemetrexed. If the hospital administers the pemetrexed on day #3 following admission at a cost of approximately \$5,000, what will be the impact on the hospital’s bottom line if the DRG reimbursement is \$4,000 notwithstanding the costs of hospitalization?

- A. No impact on the hospital bottom line
- B. The hospital will realize \$9,000 in margin following reimbursement
- C. The hospital will realize \$1,000 in margin following reimbursement
- D. The hospital will lose \$1,000 following reimbursement

III. **Patient assistance programs**

- A. New oncology drugs (oral and IV) have patient assistance programs available through the manufacturer – contact information is typically available on the drug’s website
- B. Co-pays can be a formidable cost for many patients receiving high-cost oncology drugs even with insurance

### C. Patient assistance funds

Cancer Care Foundation : [www.cancercarecopay.org](http://www.cancercarecopay.org)

Chronic Disease Fund (CDF): [www.cdfund.org](http://www.cdfund.org)

Healthwell Foundation : [www.healthwellfoundation.org](http://www.healthwellfoundation.org)

Leukemia and Lymphoma Society :

<http://www.lls.org/#/diseaseinformation/getinformationsupport/financialmatters/>

National Organization for Rare Disorders (NORD) [www.rarediseases.org](http://www.rarediseases.org)

Patient Access Network Foundation: [www.panfoundation.org](http://www.panfoundation.org)

Patient Advocate Foundation: <http://www.patientadvocate.org/> or [www.copays.org](http://www.copays.org)

Patient Services Incorporated (PSI): <https://www.patientservicesinc.org/>

## IV. Drug purchasing

### A. Heterogeneity in Drug Pricing:<sup>38</sup>

1. Average Wholesale Price (AWP) – “sticker price” – that does not directly correspond to any actual market transaction. It is not an average of prices charged by wholesalers to providers but a price reported to publishing houses (e.g. Redbook). Medicare’s use of AWP for payment on pharmaceuticals ended in January 2005.
2. Wholesale Acquisition Price (WAC) – this “list” price from wholesalers may not accurately reflect what is being paid by providers due to discounts and price concessions offered by manufacturers. In general terms:  $AWP = 1.2 \times WAC$
3. Average Sales Price (ASP) – Replaced AWP as the basis for most drugs covered under Medicare’s medical benefit (Part B) in January 2005. ASP is calculated by CMS based on market data for manufacturer selling price which includes rebates, volume discounts, etc. Many private payors have gravitated to ASP to base their reimbursement for oncology drugs.
4. 340B – federal program requiring manufacturers to provide significant discounts for outpatient drugs by eligible covered entities. These covered entities include public and not-for-profit hospitals, children’s hospitals, critical access hospitals and federally qualified health centers and specialty clinics that serve a disproportionate percentage of low-income patients (approximately 12% or greater of payor mix). In 2010, the Accountable Care Act expanded the 340B eligibility to free standing cancer centers.<sup>37</sup>
  - a. Physician office practices or inpatient settings are not eligible for 340B drug pricing
  - b. Patients must receive services from providers at the covered entity to be eligible for 340B

- c. For cancer clinics to be eligible for the 340B program they must be listed on the Medicare cost report for the facility, the clinic must be located within 35 miles of the main hospital campus, the clinic must operate under the same license as the hospital, clinical and financial operations must be integrated between the clinic and hospital (including physician and administrative oversight), medical records must be integrated between the clinic and hospital and the clinic must publicly declare its affiliation with the 340B hospital.
  - d. An oncology clinic may retain eligibility for 340B even if the physicians are not employed by the hospital as long as the requirements listed in C above are met and the hospital retains ownership of the clinic and purchases the drugs.
  - e. A non-340B hospital may form a contractual agreement with a 340B hospital for joint ownership or equity in a clinic that may be that clinic eligible for 340B if the requirements in C above are met.
  - f. Typically, eligibility for a new clinic for 340B is determined the following summer following the end of the year of the clinic was reported on the 340B hospital's Medicare cost report. The clinic is not eligible to purchase drugs at the 340B pricing until approved by Health Resources and Services Administration (HRSA) of the federal government, which administers the program.
  - g. Medicaid patients are not eligible for 340B drug pricing since they already qualify for discounted drug pricing.
5. Average Manufacturer Price (AMP): created by OBRA 1990 for the purpose of calculating rebates paid by manufacturers to states for drugs dispensed to their Medicaid beneficiaries. AMP is defined as the price available to the retail class of trade and reflected any discounting or rebates to the purchasing entity. In 2005, the federal government mandated that AMP be used instead of AWP to calculate the Federal Upper Limit (FUL) for reimbursement to outpatient prescriptions for the facilities classified as retail class of trade (community pharmacies, mail order pharmacies, and physician offices).
6. Group Purchasing Organizations (GPO): Alliances of health care providers or pharmacies that form an alliance to increase negotiating leverage by increasing purchasing volume.

7. Sample table comparing drug acquisition costs for a hospital through a wholesaler comparing 340B vs. GPO vs. WAC pricing:

	340B (in \$ per vial)	GPO (in \$ per vial)	WAC (in \$ per vial)
Drug A	102.39	217.38	222.22
Drug B	132.1	204.11	391.03
Drug C	895.61	942.75	931.44
Drug D	4725.62	6274.07	6274.07
Drug E	683.02	768	1600
Drug F	1258.14	1592.25	1681.4
Drug G	1275	1658	1658
Drug H	1926	2637	2596
Drug I	1735	3599	3512

B. Drug Shortages –plagued oncology drugs (including supportive care for several years)

1. Up to date information: ASHP website<sup>40</sup> and FDA website.<sup>41</sup>
2. Impact on providers<sup>42</sup>
3. Impact on patients:
  - a. Resulted in treatment modifications in 9.8% of adult patients<sup>43</sup>
  - b. Survey data from HOPA membership (n = 243) 93% reported treatment changes or delays in treatment; 85% reported increased drug costs and 10% reported reimbursement challenges.<sup>44</sup>

V. Oncology pharmacist work metrics

- A. Staffing – HOPA survey from spring 2009 newsletter presented data on staffing levels in outpatient oncology infusion centers.

Characteristic	Hospital-Based (n = 46)	Physician office –based (n=12)
# patients per day	84.5	84.4
Pharmacist FTE	4.7	2.2
Pharmacy tech FTE	4	3

B. Intervention data – outcome data is limited; table below summarizes some published literature

Author	Patient population	Intervention	Outcome
Ryan et al. <sup>45</sup>	Cancer pain (n=44)	Follow-up to pain clinic visits	2.3 interventions per patient; 85 minutes spent on each patient in follow-up consisting of refilling prescriptions, altering the medication regimen and contacting other providers
Verbrugge et al. <sup>46</sup>	Oral meds	Adherence to oral anticancer drugs	Review of 25 studies yielded adherence rates influenced by disease factors, patient perception of treatment importance, toxicity and duration of therapy. High cost and younger age were negative predictive factors
Mancini R <sup>47</sup>	Ambulatory oncology clinic (n=75)	Symptom assessment tool	Duplicative meds (46%), drug interactions (44%), toxicity (75%), treatment modification (95%).
Valgus JM et al. <sup>48</sup>	Ambulatory hem/onc clinic in university setting (n=89)	Supportive care management, patient education, teaching, improved efficiency in infusion room	Pharmacist made 186 interventions, wrote 136 prescriptions, and provided 900 bill-able education session over 18 months
Jones KL et al. <sup>49</sup>	Ambulatory breast cancer clinic (n=145)	Pharmacist-managed anticoagulation	53% of lab draws were in goal INR range of 2 -3; recurrent thrombosis 4.1% ; minor bleeding 18.6%; major bleeding 2.1%

**Pharmacy Advocacy Organizations:**

Organization	Website	Mission
Academy of Managed Care Pharmacy (AMCP)	<a href="http://www.amcp.org">www.amcp.org</a>	Provides clinical, educational, and business management services to pharmacists and health care providers involved with pharmacy benefits management.
American Association of Colleges of Pharmacy (AACP)	<a href="http://www.aacp.org">www.aacp.org</a>	Partners with pharmacy schools to promote scholarship, education standards and research to benefit



		society as a whole.
American Association of Pharmaceutical Scientists	<a href="http://www.aaps.org">www.aaps.org</a>	Organization comprised of pharmaceutical researchers that promotes research, scientific standards and advocacy.
American Association of Pharmacy Technicians	<a href="http://www.pharmacytechnician.com">www.pharmacytechnician.com</a>	Professional society dedicated to fostering the education and practice standards of pharmacy technicians.
American College of Clinical Pharmacy (ACCP)	<a href="http://www.accp.com">www.accp.com</a>	Support of expansion of clinical services, education, research and training of pharmacists.
American Society of Health System Pharmacists (ASHP)	<a href="http://www.ashp.org">www.ashp.org</a>	Advocacy, education and accreditation standards for pharmacists practicing in hospitals and health care institutions.
American Pharmacists Association (APhA)	<a href="http://www.pharmacist.com">www.pharmacist.com</a>	Largest pharmacy professional society with 62,000 members. APhA focuses on societal awareness of pharmacist value in supporting appropriate medication use, fostering pharmacist professional development and promoting disseminating of professional practice standards among its membership.
Hematology Oncology Pharmacy Organization (HOPA)	<a href="http://www.hoparx.org">www.hoparx.org</a>	Facilitates education, practice standards, research and advocacy for pharmacy practitioners that practice in hematology/oncology.
International Society of Pharmaceutical Compounding	<a href="http://www.isphc.org">www.isphc.org</a>	Disseminate standards of practice and education for pharmacists for extemporaneous compounding.
National Community Pharmacists Association	<a href="http://www.ncpanet.org">www.ncpanet.org</a>	Promotes education, networking, professional standards and advocacy for community pharmacy practitioners.

## RECOMMENDED READING AND REFERENCES

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