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Compounding: Guidelines for Pharmacies

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Should denotes a recommendation, something that is advised but not mandatory.

7.3 Change control practices

Change control practices should be defined and implemented to ensure that changes to the system are introduced and managed in a systematic, controlled fashion, without unwanted consequences. All changes that might affect the quality of preparations shall be assessed, validated, and approved before they are adopted. Major changes shall be validated and sanctioned by the pharmacy manager or delegate. Minor changes (i.e., changes that have no direct effect on the quality of the final or in-process preparation) should be incorporated into policies and standard operating procedures and do not require validation.

Examples of major changes that should be validated include but are not limited to the following:

a) changes in heating, ventilation, air conditioning (HVAC) systems;

b) changes in cleaning procedures; and

c) changes in equipment.

7.4 Quality control program

The pharmacy department shall establish a quality control program of the necessary and relevant tests to assess compliance with quality requirements. These tests are not confined to the preparation activities.[6]

The quality control program shall specify which processes and preparations are to be tested. The program will involve validated tests, with documentation and review of test results, and follow up on test results that fail to meet specifications. Processes, equipment, and preparations with quality failing to meet or exceed the quality control specifications shall not be used.

7.5 Quality improvement program

An ongoing quality improvement program shall be in place to regularly assess and improve all aspects of the compounding program (or service), including personnel, physical environment, equipment and supplies, compounding processes, documentation, change control, quality control, and outsourcing, under which preparations are made.

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Shall denotes an expectation, or a practice that is widely accepted as being **required.**

The nonaseptic compounding of hazardous drug preparations may occur in a containment primary clean air device (PCAD) within a cleanroom, provided that the air quality of the cleanroom is not compromised.[29]

Minimizing injury or harm as a result of exposure to a hazardous substance is of utmost importance as delays in treatment can lead to serious harm. Emergency showers and eyewash stations shall be located such that persons can quickly and easily access them in the event of topical exposure. In facilities working with hazardous drugs, an eyewash station shall be located in the compounding area, and convenient access to an eyewash station and emergency shower shall be identified near (or in) the pharmacy department or other areas where work with hazardous drugs occurs.

All hazardous drugs, unless in a final, ready-to-use form, shall be stored in a negatively pressurized area separate from other, nonhazardous drugs and other inventory to prevent contamination and personnel exposure. Hazardous drugs that require refrigeration shall be stored in a designated refrigerator that is kept in the storage room that houses other hazardous drugs.[29]

9.2.2 Aseptic compounding

Aseptic compounding activities within a healthcare setting shall occur within a controlled work area in the pharmacy or satellite pharmacy, consisting of a physically enclosed cleanroom separated from the uncontrolled environment of surrounding areas by an anteroom.

Some exceptions to this requirement are indicated later in this document, insofar as they are deemed safe for the preparation and personnel and/or not making an exception would otherwise undermine the care or treatment being provided (e.g., in urgent or emergent care situations). For instances when aseptic compounding is to be undertaken in an uncontrolled physical environment, refer to Appendix A: Physical Environment for Aseptic Compounding Activity Occurring near Patient.

The controlled work area should be situated so that access points and activities directly related to aseptic compounding are out of high-traffic areas within the pharmacy department.

Provision should be made for personnel to change out of street clothes and into scrubs before entering the controlled work area.

Waste receptacles shall be provided at the location where the check of a preparation occurs (for disposal of materials once the check is complete).

Waste receptacles shall be removed from the compounding area and replaced at the end of each shift or more frequently.

All waste shall be stored and disposed of in accordance with the relevant federal, provincial/ territorial, and municipal legislation.

10.3.1 Waste generated by aseptic compounding

Waste receptacles inside the primary clean air device shall be used outside the critical area.

Waste receptacles outside the primary clean air device shall be placed in close proximity to the primary clean air device.

Waste receptacles shall be removed from the cleanroom and replaced at the end of each shift or more frequently. There should be provision for marshalling waste.

10.3.2 Waste generated by compounding with hazardous drugs

All hazardous waste must be disposed of separately from general waste, in hazardous waste receptacles with lids. Such hazardous waste receptacles must be available in all areas where hazardous drugs are received, stored, and prepared.

The distance from where hazardous waste is generated to the waste receptacle should be minimized.

Transferring hazardous drugs and contaminated supplies into waste receptacles may increase the risk of exposure.[43] Therefore, dedicated hazardous waste containment units should be easily accessible within the compounding area.

While awaiting removal from the facility for disposal, hazardous waste shall be stored in a secure area in securely sealed and properly labelled containers.

Aseptic compounding with hazardous drugs

All nonsharp waste generated inside the containment PCAD during compounding must be placed inside a hazardous drug waste receptacle (e.g., resealable bag or sharps container) within the containment PCAD for later removal and disposal into a larger hazardous waste receptacle.

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All alarms shall be documented, deviations from established limits investigated, and corrective measures taken. If an area does not have personnel coverage at all times, consideration should be given to redirecting alarms elsewhere in the facility to ensure that 24-hour response can be initiated.

11.3 Engineering of air supply systems

The air supply systems shall be engineered to support the required environmental conditions set forth in the air quality strategy.

PCAD: primary clean air device

11.3.1 Nonaseptic compounding area

The location of the air supply shall be such that it does not affect compounding activities.

The ductwork for supply air shall be cleaned regularly (at least annually) to minimize the release of dust and other particulates into (or over) the critical area.

Nonaseptic compounding with hazardous drugs

The physical environment where hazardous nonaseptic drugs are compounded shall protect the worker and the natural environment.

At a minimum, a containment device shall be used. If, on occasion, a hazardous nonaseptic preparation is compounded in a containment PCAD that is usually used to compound aseptic preparations, the device shall be thoroughly cleaned and disinfected before compounding of a sterile preparation is initiated in that containment PCAD.[29]

11.3.2 Anteroom

The anteroom serves as a buffer between the air in the uncontrolled environment and that in the cleanroom. It is therefore very important that any particles generated in this area be diluted and that airflow be configured to minimize entry of air into the cleanroom.

The anteroom shall be a grade C (ISO class 8) environment or better, supplied with HEPA-filtered air. The room shall be positively pressurized in relation to surrounding rooms of lower air quality classification, to reduce the opportunity for inflow of contaminants.

If a closet for the storage of cleaning supplies is located within the controlled work area, it should be under negative pressure sufficient to

PERSONAL HEALTH AND HYGIENE

Refer to the following sections of the *PIC/S Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments*.[1]

Main document
SECTION 2: Personnel; chapter 2.4 Hygiene
RELEVANCE: *General information*

All persons who enter the compounding areas shall maintain good personal hygiene.

The risk of particulate and microbial contamination of preparations, including contamination related to workers' illness, shall be minimized. To this end, assessment of the personal health of compounding personnel should be guided by policy and procedures within the pharmacy department, as well as the organization's health and safety requirements for employees, infection prevention and control practices, and safe practices for handling specific dangerous goods.

Hands shall be kept clean and nails kept trimmed short.

Persons with any of the following health conditions shall be assessed and exempted from responsibilities in the compounding area if necessary:[11, 17]

a) rashes;

b) burns to the skin;

c) open or weeping wounds;

d) active skin-shedding conditions;

e) uncontrolled symptoms of active allergic response (e.g., rhinitis, cough, pruritus);

f) contagious illness, including conjunctivitis and active respiratory infections; and

g) casts or other splint devices that inhibit proper hand hygiene.

Pharmacy personnel should be informed of how to recognize signs and symptoms of conditions that might arise from performing compounding activities (e.g., repetitive stress syndrome) and ways to mitigate these conditions.[7]

The requirements for hygiene procedures should be posted at all entrances to compounding areas, and these requirements apply to all persons entering the area.

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CLEANING, DISINFECTION, AND DECONTAMINATION

Refer to the following sections of the PIC/S *Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments*.[1]

Main document
SECTION 3: Premises and equipment
RELEVANCE: *General information*

Annex 1
SECTION 2: subsection Cleaning
RELEVANCE: *Aseptic compounding*

Annex 2
SECTION: Premises and equipment
RELEVANCE: *Nonaseptic compounding*

Cleaning and disinfection are essential elements of contamination control.

Everyone who is involved in compounding has a duty and responsibility to contribute to the cleanliness of the area where compounding activities are performed. The roles and responsibilities of every member of the team should be defined. If the team does not possess expertise in a particular area, additional individuals should be consulted as needed. For instance, consultation with the infection control and prevention department may be helpful in identifying any cleaning agents that should not be used.

A multidisciplinary team approach to maintaining cleaning and disinfection standards is important. To facilitate the fulfilment of responsibilities by pharmacy personnel, the pharmacy department should have an effective working relationship with the organization's housekeeping department and its infection control and prevention department.

With contributions from infection prevention and control personnel, decisions shall be made about the details of cleaning procedures, and the rationale for these decisions shall be documented. Procedures shall be written and endorsed by pharmacy management.

Any cleaning program should address the following questions:[69]

a) How is cleanliness defined?

b) How is cleanliness measured?

c) What cleaning materials can be used in each area?

d) When can each area be cleaned?

e) How frequently should each area be cleaned?

f) Who is responsible for cleaning each area or piece of equipment?

ANTICIPATION OF COMPOUNDING

Refer to the following sections of the PIC/S *Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments*.[1]

Main document
SECTION 5: Production; chapter 5.5 Starting materials
RELEVANCE: *General information*

Annex 1
SECTION 4
SECTION 5: subsection Quality control
RELEVANCE: *Aseptic compounding*

Annex 2
SECTION: Production
RELEVANCE: *Nonaseptic compounding*

Annex 3
SECTION 4: subsection Production
SECTION 5: subsection Quality control
RELEVANCE: *Radiopharmaceuticals*

Before compounding begins, a risk assessment should be conducted to define the level of quality assurance that should be applied to preparation of the compound. The physical environment, equipment, ingredients, supplies, and pharmaceutical knowledge and skill of personnel should be suitable for the preparation that is being compounded.[12]

Only physical environments, equipment, ingredients, and supplies that are fit for use shall be used for compounding.

All ingredients, supplies, equipment required to compound a preparation shall be assembled and placed in an area (e.g., bin) that reduces the likelihood of selection errors. Ideally, the person who assembles the items should not be the same person who is preparing the compound.[23]

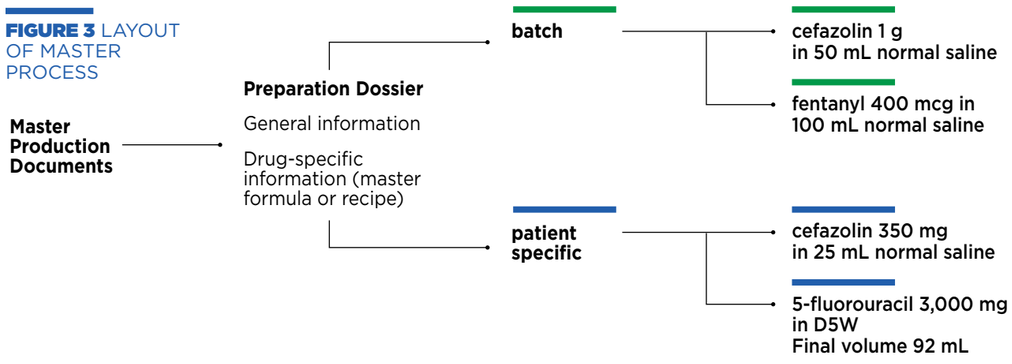
Work records and similar papers shall be contained in a protective sleeve or laminated.

Paper and other items from patient care and treatment areas (such as prescriber orders) shall not be brought into the areas where compounding occurs.

19.1 The master process

A master process shall be developed for each preparation to provide clear compounding instructions. A schematic of the master process is presented in Figure 3.

FIGURE 3 LAYOUT OF MASTER PROCESS



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Consideration shall be given at the facility level to determining the appropriateness of existing pneumatic tube systems for this use.

Hazardous preparations

Suitable safeguards, warnings, and other information shall be provided to protect persons who are involved in transporting sterile hazardous preparations.[17]

Preparations made with hazardous drugs should be packaged for transport in a sealed, leak-proof container with hazardous drug warning labels on the outside. Refer to section 19.6: "Packaging" for more information.

The method of transporting hazardous drugs shall not produce stress on the contents or packaging.

Pneumatic tube systems shall not be used to transport hazardous drugs. Such systems carry a risk of breakage and spillage[17] (especially for liquid formulations).

All preparations made with hazardous drugs should be placed within secondary packaging. Multiple hazardous preparations for a single patient may be placed in a single additional secondary package.

The transport of hazardous pharmaceuticals should comply with federal, provincial/territorial, and local requirements.

Radiopharmaceuticals

Special consideration should be given to the transportation of radiopharmaceuticals according to federal, provincial/territorial, and local transportation regulations.

27.1 Transportation involving a transport service

When a transport service (e.g., courier service) is involved in transporting preparations, the packages containing the preparation to be transported shall be labelled to promote safe transport and appropriate storage of the preparation en route.[17]

Communication with the transport service should convey information about the expected duration of the shipping period, safeguards to protect anyone handling the preparation, and the environmental

Shall denotes an expectation, or a practice that is widely accepted as being **required.**

n) records of process validation conducted.

Pharmacy service records may also include any of the following:

a) evidence that master formulae are periodically reviewed;

b) complete data derived from all tests necessary to ensure compliance with established specifications and standards, including process verification procedures and end-product testing;

c) records of third-party transport;

d) reports of complaints, recalls, and returns; and

e) individual prescriptions.

29.1 Documentation of work performed by nonpharmacy personnel

The identity of nonpharmacy personnel and their respective departments or organizations shall be recorded if they perform any of the following:

a) housekeeping;

b) equipment maintenance and certification;

c) environmental testing;

d) quality control testing; or

e) outsourced training or compounding.

Pharmacy services shall have access to the records created by these nonpharmacy personnel and shall ensure that the record-keeping practices comply with the specifications provided above and in these guidelines.

29.2 Policies and standard operating procedures

The pharmacy shall have documented, fully implemented policies and standard operating procedures that are specific to the practice of compounding, including the handling of radiopharmaceuticals and other hazardous products. All policies and standard operating procedures should be validated, approved, and regularly reviewed by designated personnel. Personnel who are expected to comply with the policies and procedures shall be informed of all changes to the policies and standard operating procedures.

THE AREA WHERE NONASEPTIC COMPOUNDING OCCURS

AREA	ACTIVITIES	FIXTURES, SUPPLIES	WORKING ENVIRONMENT	GARBING REQUIREMENTS	CLEANING SCHEDULE
Changing area	Changing garb Washing hands	Locker/clothes hooks Sink Mirror Chair	Grade - Unclassified	Clean, low-shedding clothes Clean shoes Gowns (or closed laboratory coats) Disposable hair coverings (e.g., hair nets) Facial hair coverings (as appropriate) Powder-free gloves Personal protective equipment, as appropriate	Waste receptacle – emptied at least daily; cleaned weekly Floors – daily Walls, mirrors, hooks – monthly Ceilings – monthly Chair – monthly Lockers – twice a year
Staging area	Storing materials, equipment, supplies Gathering materials Printing processing records Completing processing records Printing labels Washing hands	Shelves (compounding materials, pharmaceutical ingredients, containers, garb, cleaning supplies) Automated, mechanical or electronic compounding equipment Mirror Designated counter space Potable water/sink (hand and equipment washing) Purified water (for compounding and equipment rinsing) Dishwasher(s) Waste receptacle (Emergency shower and eye wash station)	Grade - Unclassified	As above	Waste receptacle – emptied at least daily; cleaned weekly Floors – weekly Shelving – monthly Walls – annually Ceilings – annually Sink – daily Compounding equipment – promptly following use Storage bins (e.g., for gloves – monthly) Refrigerator – monthly Emergency shower and eye wash station – run water weekly