وزارة الصحة
سياسات وإجراءات

إجراءات التشغيل القياسية لتحضير الأدوية الكيماوية (SOPs of chemotherapeutic drug preparation)	رمز الوثيقة: MOH SOP D MM 21
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وزارة الصحة
مديرية التطوير المؤسسي وضبط الجودة
السياسات والإجراءات
Policies & Procedures
٢١ كانون الثاني ٢٠٢٥
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Introduction:

Chemotherapeutic drugs (CDs) are cytotoxic and have shown to be mutagenic, and/or teratogenic. Toxicities can occur acutely, after administration, within hours or days; or chronically, from weeks to years. Because of these drugs' toxicities, and to ensure best patient care and outcomes, Healthcare Professionals (HCPs) require special training and experience to manage, prescribe, reconstitute, and administer these drugs effectively and safely.

Standard Operating Procedures (SOPs) are essential documents in the pharmacy that provide detailed guidelines for the consistent and standardized preparation of Chemotherapy. These procedures are designed to ensure the quality, safety, and efficacy of (CDs) throughout the entire preparation process, it describes how will safely handle a hazardous chemical, including the amount and concentration will be used, how to obtain or create the working solution, and special handling procedures, and personal protective equipment (PPE).

Definitions:

1. **Chemotherapeutic drugs (CDs):** all systemic parenteral drugs that control, kill, alter, or slow the reproduction of rapidly growing cancer cells, they are used to treat many different disorders including but not limited to cancers of different types, in addition to autoimmune diseases.
Similar drugs are also known as antineoplastic and cytotoxic.
2. **Material Safety data sheet (MSDS):** Sheet provided by the manufacturer that summarizes the chemical properties and hazards of a specific chemical and outlines ways in which workers can protect themselves from exposure to the chemical.
3. **Preparation**: mixing of ingredients to prepare a drug for patient use, including dilution, admixture, repackaging, reconstitution or other manipulation of sterile drugs.

4. **Health care Professionals (HCP):** Any worker who is involved in the care of patients. The category includes pharmacists, pharmacy technicians, nurses (registered nurses, licensed practical nurses, nurses' aides, etc.), physicians, home health care workers, and environmental services workers (housekeeping, laundry, and waste disposal).
5. **Licensed Healthcare Facility**: a hospital providing Healthcare Services in accordance with the applicable regulations, rules, standards and policies.
6. **Personal protective equipment (PPE):** equipment used to protect healthcare providers during preparation of CDs such as protective gloves, goggles, gowns, respiratory protection, eye protection, lab coats, and respirator.
7. **Clean Room**: a room which is constructed and used in a manner to control and minimize the introduction, generation and retention of particles inside it, and in which relevant parameters, e.g. temperature, humidity and air pressure are controlled as necessary.
8. **ISO Class 7 Clean Room**: a room that has no more than 352,000 particles per cubic meter equal to and larger than 0.5 microns. For ISO Class 7, the Fed Std. 209E rating is Class 10,000.
9. **HEPA Filter**: High-efficiency particulate air filter rated 99.97% efficient in capturing 0.3-microndiameter particles
10. **Primary engineering control (PEC):** A ventilated device designed and operated to minimize worker and environmental exposures to CDs by controlling emissions of airborne contaminants, such as a biosafety cabinet (BSC) or preparation aseptic containment isolator (CACI), used in sterile chemotherapeutic preparation
11. **Isolator**: preparation aseptic biological safety cabinet (AII / BII)
12. **Biological safety cabinet (BSC) class II type BII**:

BSC are cabinets designed to prevent biological exposure to personnel and the environment and to protect experimental material from contamination when appropriate practices and procedures are followed

Class II have been adopted for use in compounding CDs as they protect the product, the worker, and the environment.

Type BII is the one where 0% of airflow recirculated and 100% of airflow directly exhausted.

Objectives of SOP:

1. To establish a systematic and controlled approach to various activities, from handling to the final delivery of high-quality CDs to patients.
2. To minimize variations, errors, and risks associated with the preparation process.
3. To ensure the accurate and consistent execution of preparation processes according to the guidelines.
4. Safety: Chemotherapy must be managed in a safe environment where the qualified personnel, facilities, equipment, and emergency procedures are immediately achieved to protect workers and environment from chemical risks and potential accidents.
5. To serve as valuable training tools for new employees, ensuring that they understand and follow established protocols.
6. Regular review and updates of SOPs allow for continuous improvement in processes based on feedback and evolving pharmacy standards.

Scope: The scope of this (SOPs) is extensive and critical to ensure the safety and efficacy of CDs. They are applicable to all (HCP) licensed by MOH.

Roles and responsibilities:

1. **Preparation Supervisor:**

1.1 Overseeing the entire Chemotherapy preparation process.

1.2 Planning and scheduling preparation activities.

1.3 Ensuring adherence to preparation timelines and targets.

1.4 Managing resources efficiently.

1.5 Overseeing compliance with SOPs and safety protocols and regulatory requirements.

1.6 Ensuring a safe working environment during chemical preparation.

1.7 Ensuring suitable and secure storage space for consumables, equipment, pharmaceutical drugs required for chemotherapy.

1.8 Providing training on safety procedures.

1.9 Monitoring the use of (PPEs).

1.10 Investigating and reporting safety incidents

2. Preparation Pharmacists/Technicians:

2.1 Executing specific tasks related to chemical preparation.
2.1.1 Following SOPs for material handling and mixing.
2.1.2 Monitoring equipment during preparation.
2.1.3 Reporting equipment malfunctions or abnormalities.
2.1.4 Maintaining cleanliness and order in the preparation area.

2.2 Ensuring overall compliance and quality assurance in the preparation process.
2.2.1 Conducting audits to verify compliance with SOPs.
2.2.2 Managing version control of SOPs.
2.2.3 Training personnel on proper documentation procedures.
2.2.4 Reviewing and approving documentation and record-keeping.
2.2.5 Collaborating with other departments to address and resolving quality-related issues.

Specific materials and chemicals required for Chemotherapy preparation:
1. Chemicals: Hydrogen Peroxide, Potassium permanganate, Potassium hypochlorite, Alcohol 76%

2. Cleaning Agents: Chemicals for equipment cleaning and sterilization e.g Surfanios.

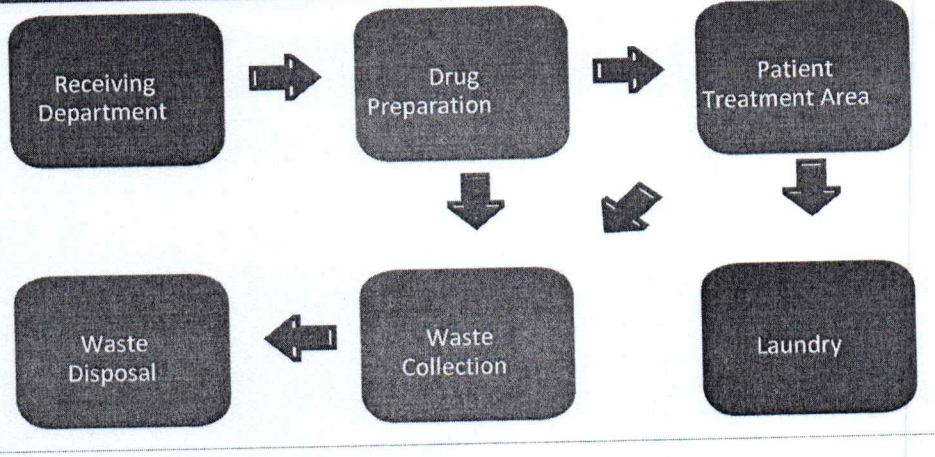
Safety Equipment and Elements required for Chemotherapy preparation:

1. An approved (BSC) for the preparation of CDs to provide protection of personnel, drug and environment – Preference is for a Class II Type BII cabinet or Isolator Cabinet System – located in an ISO Class 7 Clean Room environment.
2. The exhaust system discharge must be HEPA filtered, with fan connected to an emergency power supply and status (run/off) locally monitored and alarmed.
3. Hand wash stations must be provided where contact with CDs can occur, i.e. preparation rooms and patient treatment areas.
4. An ante room used for transiting from external circulation space.
5. Personal protective equipment (PPE) such as protective gloves, goggles, gowns, respiratory protection, eye protection and lab coats.
6. Administrative controls (training and education programs; availability of safety data sheets; established work practices, policies, surveillance).

Flow of CDs through the Hospital or Clinic:

The pharmacy and patient treatment areas (clinic or ward) have been the focus of concern with respect to exposure of health care workers to CDs.
These locations include the areas for receiving, storage, and preparation of drugs; areas through which drugs are transported; patient treatment areas; laundry services; and waste collection and storage areas (Figure 1).
Workers in all these areas are at risk for exposure. Therefore, they should have appropriate hazard awareness and job task training; training in the selection and use of (PPE), especially a respirator (typically an N-95); and training in the use of CD spill kits and should take precautions to reduce exposure as much as possible.

Figure 1. Flow of CDs through the Hospital or Clinic



1. **Receiving CDs from the Distributor,** the following recommendations should be put into place for all personnel involved in receive, storage, retrieval, or inventorying of CDs:

1.1 All personnel who receive CDs from manufacturers or distributors must be trained to wear full PPEs and to use a respirator.

1.2 There should be a storage area specifically for CDs and it should be labeled as such. The physical storage requirements set out on the label should be met (e.g. refrigeration between 2-8 degrees Celsius), Store materials according to their specific requirements (temperature, humidity, etc.).

1.3 CDs spill kits must be readily available in the receiving and storage area, and all personnel must be trained to perform spill cleanup and remove the damaged drug containers and packaging.

1.4 Personnel should wear one or two pairs of gloves that have been tested and approved for use with CDs (ASTM 2005).

1.5 Material Safety Data Sheet (MSDS) should be provided from the manufacturer for each CDs.

1.6 The storage area for CDs must have appropriate ventilation. Ideally, storage areas should have negative air pressure in relation to surrounding areas, with at least 12 air changes per hour to reduce drug residue in breathable air.

1.7 Storage areas must be cleaned at least every 30 days with detergent solution. Diluted bleach solution may also be used if the container is resistant to damage from bleach. Wipe, don't spray, CD storage bins.

1.8 Implement a first-in, first-out (FIFO) inventory system.

1.9 Stocks of CDs should be distinctively labelled with visual warning signs in separate bins or shelves, segregated from other drugs.

2. Preparation of CDs: Strict aseptic technique should be used in the preparation of all sterile doses, whether the drug is hazardous or not. For CD preparation, it is critical to remember that the sterile dose must remain sterile but that the CD must be contained within the CD container, syringe, and IV bag and must not be allowed to contaminate the work area.

2.1 Safe Handling and Management of CDs:

- All preparation of CDs should be performed over plastic-backed absorbent pads in a BSC.
- Pads should be disposed of immediately upon contamination and after completion of tasks.
- Donning Full PPE including a coated gown, eye protection, and a respirator should be worn for preparation in the anti room.
- Double chemotherapy- tested gloves should be worn for all procedures involving preparation and administration of CDs (one under the cuff of the gown and one over the gown cuff) and change them at least every 30 to 60 minutes, after each use, immediately when torn, punctured, or when contaminated.
- A specific CDs sharps container should be in the immediate vicinity for safe sharps disposal.

- Clean containers before they are removed from BSC.
- Clean the BSC upon completion of tasks with [cleaning solution].
- Place all contaminated disposable items in bags before disposal.
- Non-disposable utensils, glassware, and other surfaces contaminated with CDs must be decontaminated at the end of the laboratory work session.
- When the work is completed and before donning PPE, remove gloves and wash hands with soap and water.
- CDs should be prepared within the pharmacy department or in a pharmacy-controlled facility within a clinical area, No CDs should be prepared out of a pharmacy controlled facility.
- In every instance, CDs should be prepared to the same standard out of hours as within normal working hours.
- All CDs should be prepared by appropriately trained and competent staff.
- All CDs prepared by a pharmacy department will have a shelf-life assigned to it, based on the stability of the drug.
- If CDs are prepared in an environment other than the pharmacy department (a pharmacy-controlled facility within a clinical area), they should be used immediately after preparation. The administration of infusions produced in this way should be completed ideally within 12 hours of preparation with a maximum of 24 hours' timeframe.
- Proper manipulative technique to maintain the sterility of the drug and to prevent the generation of contaminants must be used consistently.
- MSDS immediately available in work place.
- A PEC must be disinfected with 70% isopropyl alcohol prior to sterile preparation; it should be cleaned with a detergent and bleach solution, and then thoroughly rinsed with sterile water, following CD preparation.
- If no PEC is available, CD should be prepared in a quiet workspace, away from heating and cooling vents and away from other personnel. Good technique is critical.
- Select the appropriate syringes and needles to compound the dose. Syringes and IV sets with Luer-Lok™ fittings should be used since they are less prone

to separate than friction fittings. Care must be taken to ensure that all connections are secure.

- Select syringes that will be no more than three-quarters full when they contain the partial or full drug dose to prevent the risk of the plunger dislodging from the barrel. If more than one syringe will be needed, select them all before beginning the preparation.
- Select a needle of appropriate gauge and length for the vial and final container. If more than one needle will be needed, select them all before beginning the preparation.
- If the dose is to be placed into an IV bag, select the appropriate IV infusion set so that the IV bag can be spiked and the IV tubing primed prior to the addition of the CD.
- Assemble all non-CD drug containers, solution containers, and supplies, including waste containment bags and disposal containers. A CD spill kit have to be readily available.
- Prepare CD drug containers by removing outer packaging and wiping off all vials or ampoules before use by a wiper wetted with alcohol or another appropriate solution; discard wiper in containment bag for appropriate disposal. Never spray the CD container directly, as that transfers contamination to the air and other surfaces.
- Remove and contain outer gloves for appropriate disposal. Sanitize the fresh outer glove with isopropyl alcohol gel prior to preparation.
- If the dose is to be placed into an IV bag, manipulations for spiking, priming, and closing the administration tubing must all be done prior to the addition of the CD. Fasten the clamps on the IV infusion set and place a cap or connector on the end of the tubing, spike the IV bag, open the clamps, and prime the IV tubing. Be sure to keep the bag and tubing sterile.
- If using a Close System Transfer Devise (CSTD) with bag adapter, prepare the bag and tubing prior to the addition of the CD. Spike the IV bag with the bag adapter, clamp the IV tubing, and spike the IV tubing into the CSTD bag

adapter. Open the clamp and prime the IV tubing. Fasten the tubing clamps and place a CSTD closed male luer connector on the end of the tubing. Be sure to keep the bag and tubing sterile.

2.2 Final Doses

CD doses must be in final ready-to-administer form when transported to the patient. Doses in IV bags must have the IV tubing connected and the line primed with non-CD-containing solution. Doses in syringes must be clear of air and not require any further manipulation. Final doses are placed into thick, sealable plastic bags for transport to patients. In addition to patient-specific labeling, auxiliary labels of "Chemotherapy Drug" should be affixed to the dose and the transport bag

2.3 Containment and Disposal:

Once preparation is complete and the dose has been prepared for transport:

2.3.1 All disposable equipment and supplies must be contained and disposed of as CD-contaminated waste in blue bags or containers.

2.3.2 Remove all PPE except for inner gloves and contain in sealable bag for disposal.

2.3.3 Remove inner gloves, contain, and dispose of as CD waste.

2.3.4 Wash hands after completing preparation.

2.4 Emergency Procedures

2.4.1 Working in the open eliminates the protections conferred by engineering controls, which increases the risk of personnel harm if there is leakage or spillage during the preparation process.

2.4.2 It is critical that anyone prepare CD doses have immediate access to emergency supplies (e.g. eyewash stations and spill kits) and be trained to use them.

2.4.3 If there is a leakage or spill that more than or equal 10 ml, a pre specified code is called for chemical leakages (e.g. code green)

3. Transporting prepared CDs from the Pharmacy to the Patient Care Area

3.1 All CD doses should be double-bagged or placed in a sealed container for transport to the patient care area. If the bag is dropped and the container breaks or leaks, there is another barrier to prevent the CD from spilling on the handler or the external environment.

3.2 All compounded sterile preparation (CSP) of a CDs are required to be taken to the area manually, rather than by mechanical transport (such as a pneumatic tube system), which may damage the CSP and result in breakage or leakage.

3.3 Use of the transport bag prevents the handler from being exposed to CDs that could have been deposited on the external surface of the finished drug through the preparation process or as a result of leakage during transport.

3.4 CD spill kits should be on the transport cart in case of an accident during transport. Only personnel trained to clean up a CD spill may transport CD doses.

4. Handling Chemotherapeutic Waste

The hospital or clinic needs to determine the process for handling the waste of CDs generated during preparation and administration or during spills (e.g. blue bags for CD wastes, code green for spills), as well as wasted (bulk) drugs . If situations vary, it is important to determine state local regulations governing waste disposal and air and water quality to ensure compliance.

Waste handling efforts should minimize the chance of contaminating the local water supply and/or soil with CDs, as they are toxic.

Incineration is the preferred disposal method for most CD waste, although only special incinerators are effective in removing some of the CD residue. CD waste should never be discarded into wastewater (sink or toilet) or into a landfill.

5. Labeling: All containers should be labeled, as a minimum, with the following:

5.1. Patient's Name and identifier, if applicable;

5.2. Prescribing physician name, if applicable;

5.3. Name of sterile compounded drug including strength or concentration;
5.4. Date prepared and Expiration date;
5.5. Name or initials of pharmacist who prepared the drug;
5.6. Directions, if applicable;
5.7. Route and rate of administration, if applicable;
5.8. Prescription number (if applicable);
5.9. Physical storage requirement;

6. Safety Measures:

6.1 Personal Protective Equipment (PPE): emphasize the importance and the necessity of wearing PPEs when handling and preparing CDs. Conduct regular training sessions on the correct use and disposal of PPEs and clean up the spill.
6.2 Implement comprehensive training programs on the safe handling, storage, and disposal of chemicals.
6.3 Ensure easy access to and understanding of Material Safety Data Sheets MSDS for all chemicals used.
6.4 Conduct regular emergency response drills for personnel and ensure the availability and proper functioning of emergency equipment, such as eyewash stations and fire extinguishers.
6.5 Establish clear procedures for the proper disposal of hazardous waste and Conduct regular audits to ensure compliance with waste disposal regulations.

References:

- ASHP Guidelines on Handling Hazardous Drugs 2006, Drug Distribution and Control: Preparation and Handling–Guidelines (p. 132-164)
- Physical Environment Provisions of USP "Hazardous Drugs — Handling in Healthcare Settings", The American Society for Health Care Engineering (ASHE) 2019
- Safe Handling of Hazardous Chemotherapy Drugs in Limited-Resource Settings, Pan American Health Organization / World Health Organization regional office for the Americas.