# Development and Proof of Concept of an Audit Toolkit for the Safe Handling of Cytotoxic Drugs in Low- and Middle-Income Countries

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## ANNEX 1: Structured observation checklist for Prescriptions

| | **Rating**<br>*Circle the appropriate rating* | |
|---|---|---|
| **I. PRESCRIPTION FORMAT** | | **Comments** |
| Prescription exists in a written form, on a pre-formatted, printed prescription form or on prescription software | C PC NC NA | |
| No abbreviations | C PC NC NA | |
| **II. PRESCRIBER IDENTIFICATION** | | **Comments** |
| Prescriber's family name and given names | C PC NC NA | |
| Prescriber's telephone number | C PC NC NA | |
| Date of the prescription and prescriber's signature | C PC NC NA | |
| **III. PATIENT INFORMATION** | | **Comments** |
| Family name, given names, sex, identification number | C PC NC NA | |
| Date of birth (day/month/year) | C PC NC NA | |
| Inpatient/outpatient department | C PC NC NA | |
| Size and weight, body surface | C PC NC NA | |
| Diagnostic or diagnosis | C PC NC NA | |
| Relevant clinical parameters (renal or hepatic insufficiency) | C PC NC NA | |
| **IV. PROTOCOL** | | **Comments** |
| Protocol name (identification) | C PC NC NA | |
| Premedication and adjuvant treatments | C PC NC NA | |
| Chemotherapy drug(s) prescribed using INN | C PC NC NA | |
| Standard dosage and patient-adapted dosage | C PC NC NA | |
| Type and volume of solvent | C PC NC NA | |
| Pharmaceutical form and route of administration | C PC NC NA | |
| Cycle number and day | C PC NC NA | |
| Date and time of administration | C PC NC NA | |
| Duration and/or speed of administration | C PC NC NA | |
| Chronology of administration if several chemotherapy drugs | C PC NC NA | |

C = Compliant; PC = Partially Compliant; NC = Non-Compliant; NA = Not Applicable

**References:**

Quality Standards for the oncology pharmacy Service (Quapos) 6, European Society of Oncology Practice, 2018

Standards of Practice, International Society of Oncology Pharmacy Practitioners

2016 Updated American Society of Oncology/Oncology Nursing Society Chemotherapy Administration Standards, including Standards for Pediatric Oncology

**ANNEX 2: Structured observation checklists for Preparation**

A. Observation checklist for preparation without a biosafety cabinet or a cleanroom.
B. Observation checklist for preparation under a biosafety cabinet but without a cleanroom.
C. Observation checklist for preparation under a biosafety cabinet and inside a cleanroom.

## A. Observation checklist for preparation without a BSC or a cleanroom

| | **Rating**<br>*Circle the appropriate rating* | |
|---|---|---|
| **I. RECEIPT AND TRACEABILITY OF MATERIALS** | | **Comments** |
| Preparation of compounding worksheet (calculation of the volume of the anticancer drug to be drawn from the vial) | C PC NC NA | |
| Preparation of the chemotherapy formulation's label (identification of the patient, the product, the dosage, the route of administration, storage conditions, and time and date of expiry) | C PC NC NA | |
| Collection of equipment and ingredients for compounding based on the compounding protocol | C PC NC NA | |
| Documentation of product batch numbers and expiry dates on the compounding worksheet | C PC NC NA | |
| Double checking of the equipment and ingredients for compounding: verification of the drug name, dosage, quantity, type of solvent, equipment used, cleanliness, product batch n° and expiry dates, exactitude of the worksheets and the labels prepared | C PC NC NA | |
| **II. HYGIENE AND PPE** | | **Comments** |
| Operator wearing hospital uniform (not private clothes) | C PC NC NA | |
| Operator not wearing make-up or false nails | C PC NC NA | |
| Operator wearing no jewelry | C PC NC NA | |
| Operator washed hands hygienically (using soap and water as per WHO guidelines) | C PC NC NA | |
| Operator dried hands using single-use paper towels | C PC NC NA | |
| Donning of the following PPE | C PC NC NA | |
| □ hair cap | | |
| □ N95 or FFP2 mask | | |
| □ laboratory coat/coveralls | | |
| □ hospital clogs and/or overshoes | | |
| □ protection goggles | | |
| Operator disinfected hands with hydro-alcoholic solution | C PC NC NA | |
| Operator put on two pairs of gloves | C PC NC NA | |
| **III: PREPARATION ROOM** | | **Comments** |
| Room cleanliness (dust, waste, insects) | C PC NC NA | |
| No open windows or doors | C PC NC NA | |
| No concurrent activity occurring in the same room | C PC NC NA | |
| **IV. WORKBENCH SURFACE PREPARATION** | | **Comments** |
| No materials or equipment unnecessary to the drug preparation process are present | C PC NC NA | |
| Workbench surface decontaminated using ethanol 70% and then left to dry | C PC NC NA | |
| Presence of a waste bin | C PC NC NA | |
| Workbench surface is clean and tidy | C PC NC NA | |
| Only one drug at a time is in preparation on the workbench surface | C PC NC NA | |
| Preparation equipment and materials are properly laid out (following the correct preparation process) | C PC NC NA | |
| **V. HANDLING TECHNIQUES** | | **Comments** |
| Operator disinfects the vial septum and dries it if necessary (with sterile swabs) | C PC NC NA | |

| | | |
|---|---|---|
| The operator does not touch the different equipment tips (syringes, needles) | C PC NC NA | |
| Air pressure levels between the vials and the work area are correctly balanced (no pressure spikes, or air intake) | C PC NC NA | |
| Operator uses swabs when withdrawing needles from vials | C PC NC NA | |
| Operator properly recaps needles | C PC NC NA | |
| In-process monitoring procedure for volumes withdrawn from vials and in syringes (double-checking, gravimetry or otherwise) | C PC NC NA | |
| Strong management of supplies and production materials used (immediately thrown into waste bin or put far enough out of reach so as not to impede the order of drug preparation) | C PC NC NA | |
| **VI. END OF COMPOUNDING** | | **Comments** |
| The chemotherapy has been correctly labeled (identification of the patient, product, dosage, route of administration, conservation, date of administration, expiry time and date) | C PC NC NA | |
| The compounding process has been documented on the compounding worksheet | C PC NC NA | |
| Workbench cleanliness (elimination of waste products, spraying and cleaning with ethanol 70%) | C PC NC NA | |
| Appropriate management of left-over, unused drugs (labeling, expiry date in < 24 h, storage and conservation, sachets) | C PC NC NA | |
| **VII. REMOVING PPE** | | **Comments** |
| Operator removed PPE before leaving the drug preparation room area | C PC NC NA | |
| **VIII. RECONCILIATION before dispensing** | | **Comments** |
| There is a process for verifying that the chemotherapy formulation, the prescription and the compounding protocol match (verification of the compounding worksheet and the label) | C PC NC NA | |
| There is a visual inspection of the drug's container, its intactness and seals (also verify the type of tubing—with or without a filter) | C PC NC NA | |
| Visual inspection of the contents (color, clearness, lack of visible particles) | C PC NC NA | |
| Documentation of the reconciliation process on the compounding worksheet | C PC NC NA | |

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## B. Observation checklist for preparation under a biosafety cabinet but without a cleanroom

| | **Rating** *Circle the appropriate rating* | |
|---|---|---|
| **I. RECEIPT AND TRACEABILITY OF MATERIALS** | | **Comments** |
| Preparation of a compounding worksheet (calculation of the volume of the anticancer drug to be drawn from the vial) | C PC NC NA | |
| Preparation of the chemotherapy formulation's label (time and date of expiry (> 24 h), identification of the patient, the product, the dosage, the route of administration, storage and conservation) | C PC NC NA | |
| Collection of equipment and ingredients for compounding based on the compounding protocol | C PC NC NA | |
| Product batch numbers and expiry dates are traceable on the compounding worksheet | C PC NC NA | |
| Double checking of the equipment and ingredients for compounding: verification of the drug name, dosage, quantity, type of solvent, equipment used, cleanliness, product batch n° and expiry dates, exactitude of the worksheets and the labels prepared | C PC NC NA | |
| **II. HYGIENE AND PPE** | PC | **Comments** |
| Operator wearing hospital uniform (not private clothes) | C PC NC NA | |
| Operator not wearing make-up or false nails | C PC NC NA | |
| Operator wearing no jewelry | C PC NC NA | |
| Operator washed hands hygienically (using soap and water as per WHO guidelines) | C PC NC NA | |
| Operator dried hands using single-use paper towels | C PC NC NA | |
| Donning of the following PPE | C PC NC NA | |
| □ hair cap | | |
| □ mask | | |
| □ laboratory coat/coveralls | | |
| □ hospital clogs and/or overshoes | | |
| Disinfection of hands using an hydro-alcoholic solution | C PC NC NA | |
| Operator put on first pair of gloves | C PC NC NA | |
| **III: PREPARATION ROOM** | | **Comments** |
| Room cleanliness (dust, waste, insects) | C PC NC NA | |
| No open windows or doors | C PC NC NA | |
| No concurrent activity occurring in the same room | C PC NC NA | |
| **IV. PREPARING THE WORKBENCH** | | **Comments** |
| Laminar flow turned on at least 15 minutes before beginning any drug handling | C PC NC NA | |
| The biosafety cabinet is decontaminated (surfaces and sides) and allowed to dry | C PC NC NA | |
| Waste bin is correctly positioned beneath BSC | C PC NC NA | |
| Supplies and compounding ingredients placed under the laminar flow: one drug preparation at a time | C PC NC NA | |
| The operator removed outer packaging of sterile supplies (peeling technique) when placing them under the BSC | C PC NC NA | |
| Decontamination (spraying) of non-sterile supplies before placing them under the BSC | C PC NC NA | |
| Operator correctly put on sterile gloves | C PC NC NA | |
| Supplies and ingredients are correctly laid out (respecting clean zone, dirty zone, spacing) | C PC NC NA | |
| **V. HANDLING TECHNIQUES** | | **Comments** |

| | | | | | |
|---|---|---|---|---|---|
| The ventilation extraction grills have no obstructions | C | PC | NC | NA | |
| Operator makes no overly rapid movements | C | PC | NC | NA | |
| Vial septa are disinfected and dried if necessary (using sterile swabs) | C | PC | NC | NA | |
| Operator does not touch the different equipment tips/points (syringes, needles) | C | PC | NC | NA | |
| Air pressure levels between the vials and the work area are correctly balanced (if no spikes) | C | PC | NC | NA | |
| Operator uses swabs when withdrawing needles from vials | C | PC | NC | NA | |
| Needles are appropriately capped after use | C | PC | NC | NA | |
| In process verification of the volumes withdrawn from vials (double checking, gravimetry or otherwise) | C | PC | NC | NA | |
| Strong management of supplies and production materials used (immediately thrown into waste bin or put far enough out of reach so as not to impede the order of drug preparation) | C | PC | NC | NA | |
| **VI. END OF COMPOUNDING** | | | | | **Comments** |
| Chemotherapies are correctly labeled (time and date of preparation, for extemporaneous use, identification of the patient, product, dosage, route of administration, storage and conservation) | C | PC | NC | NA | |
| The BSC is cleaned at the end of the drug preparation session (waste removal, spraying with ethanol 70%, appropriate S-shaped cleaning technique) | C | PC | NC | NA | |
| Appropriate management of left-over, unused drugs (labeling, expiry date in < 24 h, storage and conservation, sachets) | C | PC | NC | NA | |
| **VII. REMOVAL OF PPE** | | | | | **Comments** |
| Operator removed PPE before leaving the drug preparation room area | C | PC | NC | NA | |
| **VIII. RECONCILIATION before dispensing** | | | | | **Comments** |
| There is a process for verifying that the chemotherapy formulation, the prescription and the compounding protocol match (verification of the compounding worksheet and the label) | C | PC | NC | NA | |
| There is a visual inspection of the drug's container, its intactness and seals (also verify the type of tubing—with or without a filter) | C | PC | NC | NA | |
| Visual inspection of the contents (color, clearness, lack of visible particles) | C | PC | NC | NA | |
| Documentation of the reconciliation process on the compounding worksheet | C | PC | NC | NA | |

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## C. Observation checklist for preparation under a biosafety cabinet and inside a cleanroom

| | **Rating** *Circle the appropriate rating* | |
|---|---|---|
| **I. RECEIPT AND TRACEABILITY OF MATERIALS** | | **Comments** |
| Preparation of compounding worksheet (calculation of the volume of the anticancer drug to be drawn from the vial) | C PC NC NA | |
| Preparation of the chemotherapy formulation's label (identification of the patient, the product, the dosage, the route of administration, storage and conservation, and time and date of expiry) | C PC NC NA | |
| Collection of equipment and ingredients for compounding based on the compounding protocol | C PC NC NA | |
| Product batch numbers and expiry dates are traceable | C PC NC NA | |
| Double checking of the equipment and ingredients for compounding: verification of the drug name, dosage, quantity, type of solvent, equipment used, cleanliness, product batch n° and expiry dates, exactitude of the worksheets and the labels prepared | C PC NC NA | |
| Decontamination of all equipment / and ingredients / and preparations before they are brought the cleanroom | C PC NC NA | |
| **II. HYGIENE AND PPE** | | **Comments** |
| Operator wearing hospital uniform (not private clothes) | C PC NC NA | |
| Operator not wearing make-up or false nails | C PC NC NA | |
| Operator wearing no jewelry | C PC NC NA | |
| Operator washed hands hygienically (using soap and water as per WHO guidelines) | C PC NC NA | |
| Operator dried hands using single-use paper towels | C PC NC NA | |
| Donning of the following PPE (in the airlock) | C PC NC NA | |
| □ hair cap | | |
| □ mask | | |
| □ laboratory coat/coveralls | | |
| □ hospital clogs | | |
| Operator put on overshoes on passing between the clean and dirty zones | C PC NC NA | |
| Operator disinfected hands using a hydro-alcoholic solution | C PC NC NA | |
| Operator put on first pair of gloves | C PC NC NA | |
| Sanitize gloves with ethanol 70% | C PC NC NA | |
| **III. PREPARATION OF THE WORKBENCH** | | **Comments** |
| Laminar flow turned on at least 15 minutes before beginning any drug handling | C PC NC NA | |
| The biosafety cabinet is decontaminated (surfaces and sides) and allowed to dry | C PC NC NA | |
| Waste bin is correctly positioned beneath the BSC | C PC NC NA | |
| Supplies and compounding ingredients placed under the laminar flow: one drug preparation at a time | C PC NC NA | |
| The operator removed outer packaging of sterile supplies (peeling technique) when placing them under the BSC | C PC NC NA | |
| Decontamination (spraying) of non-sterile supplies | C PC NC NA | |
| Operator correctly put on sterile gloves | C PC NC NA | |
| Supplies and ingredients are correctly laid out (clean zone, dirty zone, spacing) | C PC NC NA | |
| **IV. MANIPULATION TECHNIQUES** | | **Comments** |
| The ventilation extraction grills have no obstructions | C PC NC NA | |

| | | |
|---|---|---|
| Operator makes no overly rapid movements | C PC NC NA | |
| Vial septa are disinfected and dried if necessary (using sterile swabs) | C PC NC NA | |
| Operator does not touch the different equipment tips/points (syringes, needles) | C PC NC NA | |
| Air pressure levels are correctly balanced (no pressure spikes or air intake) | C PC NC NA | |
| Operator uses swabs when withdrawing needles from vials | C PC NC NA | |
| Needles are appropriately capped after use | C PC NC NA | |
| In process verification of the volumes withdrawn from vials (double checking, gravimetry or otherwise) | C PC NC NA | |
| Strong management of supplies and production materials used (immediately thrown into waste bin or put far enough out of reach so as not to impede the order of drug preparation) | C PC NC NA | |
| **V. END OF COMPOUNDING** | | **Comments** |
| The chemotherapy has been correctly labeled (identification of the patient, product, dosage, route of administration, conservation, date of administration, expiry time and date) | C PC NC NA | |
| The BSC is cleaned at the end of the drug preparation session (waste removal, spraying with ethanol 70%, appropriate S-shaped cleaning technique) | C PC NC NA | |
| Appropriate management of left-over, unused drugs (labeling, expiry date in < 24 h, storage and conservation, sachets) | C PC NC NA | |
| **VI. REMOVING PPE** | | **Comments** |
| Operator removes PPE before leaving the preparation area (in the airlock's "dirty" area) | C PC NC NA | |
| **VII. RECONCILIATION before dispensing** | | **Comments** |
| There is a process for verifying that the chemotherapy formulation, the prescription and the manufacturing protocol match (verification of the manufacturing worksheet and the label) | C PC NC NA | |
| There is a visual inspection of the drug's container, its intactness and seals (also verify the type of tubing—with or without a filter) | C PC NC NA | |
| Visual inspection of the contents (color, clearness, lack of visible particles) | C PC NC NA | |
| Documentation of the reconciliation process on the compounding worksheet | C PC NC NA | |

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## ANNEX 3: Structured observation checklist for the administration of iv chemotherapy

*Circle the appropriate rating*

| | | | | |
|---|---|---|---|---|
| **A** | **BEFORE ADMINISTRATION** | | | |
| I | PREPARATION OF EQUIPMENT AND MATERIALS | | | |
| 1 | Nurse disinfects hands using a hydro-alcoholic solution (as per WHO recommendations) throughout the treatment and care procedures | 8 stages, 20–30 seconds<br>Hand disinfection must take place at the WHO's Five Moments for Hand Hygiene | | C PC NC NA |
| 2 | Disinfection of the drug administration trolley or drug administration tray using an ad hoc disinfectant | | | C PC NC NA |
| 3 | Preparation of the equipment and supplies necessary for administration | e.g., swabs, waste bins, catheters, etc. | | C PC NC NA |
| II | NURSES CLOTHING | | | |
| 4 | Appropriate PPE | | | C PC NC NA |
| | Long-sleeved laboratory coat and/or coveralls □ | Pulled tight at the cuffs | | |
| | Mask □ | Surgical | | |
| | First pair of gloves □ | Non-sterile | | |
| | Protection goggles □ | If there is a risk of splashing or spillage | | |
| III | VERIFICATION THAT THE TREATMENT PROTOCOL MATCHES THE PRODUCT: checklist | | | |
| 5 | Verification that the treatment protocol matches the product administered | Possibly use a checklist | | C PC NC NA |
| | Methods of product storage and conservation □ | Refrigeration, room temperature, light sensitivity | | |
| | Patient identification □ | (e.g., family name, given names, date of birth, patient identification number) | | |
| | Name of the product to be administered □ | | | |
| | Dosage □ | | | |
| | Route of administration □ | Intravenous, intramuscular | | |
| | Today's date corresponds to the date of administration in the protocol □ | | | |
| | Date and time of treatment match □ | | | |
| | The drug will not expire before the end of the treatment □ | Date and time | | |

| | | | | |
|---|---|---|---|---|
| 6 | Removal and disposal of gloves as per the waste disposal plan | To avoid any contamination of the working environment, gloves must be removed and disposed of as soon as the drug administrator must touch any piece of equipment or material not used in drug administration | | C PC NC NA |
| 7 | Nurse disinfects hands using a hand disinfectant solution | | | C PC NC NA |
| IV | PREPARING THE PATIENT | | | |
| 9 | Verification of the patient's identity (family name, given names, date of birth) and that it matches with the patient identity on the drug treatment protocol | Family name, given names, date of birth | | C PC NC NA |
| 10 | Ensure that the patient has been informed and educated about the treatment he/she is going to receive | Effects, risks, and side-effects | | C PC NC NA |
| **B** | **DURING ADMINISTRATION** | | | |
| V | CHECKS | | | |
| 11 | Verification that the modalities of the drug's administration (route of administration, duration of administration, flow rate, etc.) agree with the medical treatment protocol, the nurse's protocol, and the product's specificities | Possibly use a checklist | | C PC NC NA |
| 12 | Documentation on the verification (point 11) is in the patient's record | | | C PC NC NA |
| VI | INTRAVENOUS ADMINISTRATION | | | |
| 13 | Nurse disinfects hands using an hydro-alcoholic solution | | | C PC NC NA |
| 14 | Nurse puts on the first pair of gloves | Non-sterile, non-powdered | | C PC NC NA |
| 15 | Placement and securing of a new, short peripheral venous catheter at a site with no prior puncture | Avoid the wrists, the elbow crease, and the backs of the hand, legs and feet.<br>If there is a prior puncture site, it is preferable to choose the other arm or, if this is impossible, a puncture site proximal to the first one<br>**Note: if the catheter was placed on the same day and there was venous reflux** | | C PC NC NA |
| 16 | Monitoring for potential venous reflux and rinsing of the catheter with 10 mL of NaCl | | | C PC NC NA |
| 17 | Nurse puts on the second pair of gloves over the first | Ensure that all appropriate PPE are being worn | | C PC NC NA |
| *ADMINISTRATION VIA PERFUSION* | | | | |

| | | | | |
|---|---|---|---|---|
| 18 | Connection of the perfusion to the catheter, which has been flushed using an isotonic solution | | | C PC NC NA |
| 19 | The infusion rate is set as per the protocol | | | C PC NC NA |
| 20 | Removal of both pairs of gloves and disposal as per the waste management plan | | | C PC NC NA |
| 21 | Disinfection of hands using an hydro-alcoholic solution | | | C PC NC NA |
| 22 | Clinical monitoring of the patient during the perfusion as per the drug administration plan | Pulse, blood pressure and body temp. | | C PC NC NA |
| 23 | Regular monitoring to ensure that there are no signs of extravasations | Attentive listening to the patient and monitoring of the puncture and for potential reflux | | C PC NC NA |
| 24 | Nurse puts on a new pair of gloves | Non-sterile, non-powdered | | C PC NC NA |
| 25 | The perfusion catheter is flushed with 50 mL of a compatible isotonic solution between each product and after the final one | | | C PC NC NA |
| 26 | The precise order of administration of the products is followed | | | C PC NC NA |
| 27 | At the end of the treatment, the catheter is withdrawn, and the puncture site is dressed using a dry bandage or the catheter is closed and left in place for the duration of the hospital stay | | | C PC NC NA |
| *INTRAVENOUS ADMINISTRATION using a short venous catheter* | | | | |
| 32 | Sterile swabs soaked in chlorhexidine alcohol or povidone-iodine are placed beneath the i.v. connector | This is unnecessary if it is a Luer-Lock syringe | | C PC NC NA |
| 34 | Connection of the cytotoxic drug's syringe | | | C PC NC NA |
| 35 | The injection duration indicated on the protocol is adhered to | | | C PC NC NA |
| 36 | Clinical monitoring of the patient during the injection as per the drug administration plan | Heart rate, blood pressure and temperature | | C PC NC NA |
| 37 | Monitoring to ensure that there are no signs of extravasations | Attentive listening to the patient and monitoring of the puncture and for potential reflux | | C PC NC NA |
| 38 | The perfusion catheter is flushed using 50 mL of a compatible isotonic solution between each product and after the final one | | | C PC NC NA |
| 39 | The order of administration of products is properly respected | | | C PC NC NA |
| 40 | At the end of the treatments, the catheter is withdrawn, and the puncture site is dressed using a dry bandage or the catheter is closed and left in place for the duration of the hospital stay | | | C PC NC NA |

**C AFTER ADMINISTRATION**

VII WASTE MANAGEMENT

| | | | | |
|---|---|---|---|---|
| 41 | All used consumable equipment and materials are disposed of directly into waste bins as per the waste management plan | (cytotoxic drugs, needles and sharps, infectious waste, PPE, excreta) | | C PC NC NA |
| 42 | Disinfection of the drug administration trolley or drug administration tray using an ad hoc disinfectant | | | C PC NC NA |
| 43 | Disinfection of the patient's armchair, bed, seat, and the base of the perfusion stand using an ad hoc disinfectant | | | C PC NC NA |
| 44 | Nurse removes and disposes of gloves | | | C PC NC NA |
| 45 | Nurse washes hands using soap and water as per WHO recommendations, then, after drying, disinfects hands using an hydro-alcoholic solution | | | C PC NC NA |
| VIII | DOCUMENTATION | | | |
| 46 | Details about the drug's administration are traceable in the patient's hospital records | | | C PC NC NA |
| 47 | There is appropriate documentation on patient monitoring (vital signs, health status etc.) | | | C PC NC NA |

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