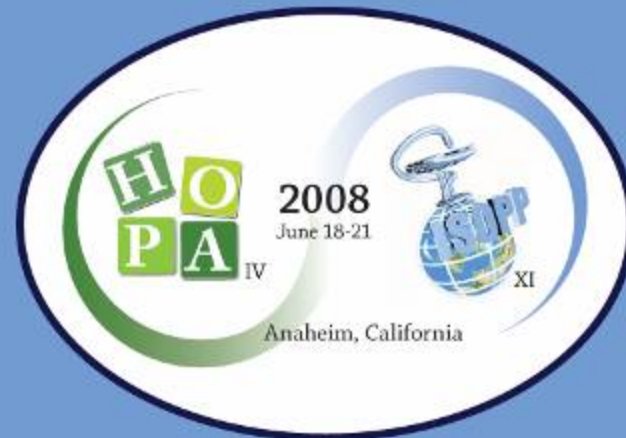


Safety in the Workplace

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Disclosure

- Sylvie Crauste-Manciet, PharmD, PhD has no apparent or real conflicts of interest to report

Learning Objectives

- Evaluate the risk in the workplace related to cytotoxic preparation. By reviewing the international studies, the possible sources of contamination in the workplace and the route of exposure will be identified.
- Develop a risk management strategy. In particular, develop skills related to technical aspects of collective equipment and personal protective equipment
- Discuss the use of environmental monitoring and biological monitoring for risk control

Workshop Plan

- Evaluate the risk in the workplace
 - Identify hazardous substances
 - Assess the risk to health
- Develop a risk management strategy
 - Control the risk to health
 - Assess the control measures implemented



Evaluate the Risk: Hazard Identification

IARC Classification

*(International Agency for
Research on Cancer)*

■ Antineoplastic drugs

- 1: Carcinogenic in humans
- 2A: Probably carcinogenic in humans
- 2B: Possibly carcinogenic in humans
- 3: Not classifiable
- 4: Not carcinogenic



WORLD HEALTH ORGANIZATION
INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans

Evaluate the Risk: Hazard Identification

■ 1 Carcinogenic in humans

- Azathioprine
- Chlorambucil
- Cyclophosphamide
- Myleran
- Melphalan
- Semustine
- Tamoxifen
- Thiotepa
- Treosulfan
- Mustargen-Oncovin-Procarbazine-Prednisone (MOPP)
- Etoposide-Cisplatin-Bleomycin (ECB)

■ 2A Probably carcinogenic in humans

- Azacitidine
- Bischloroethyl nitrosourea (BCNU)
- 1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU)
- Chlorozotocin Chlorozotocin
- Cisplatin
- Doxorubicin hydrochloride
- Mechlorethamine hydrochloride
- N-ethyl-N-nitrosourea
- Procarbazine
- Teniposide hydrochloride

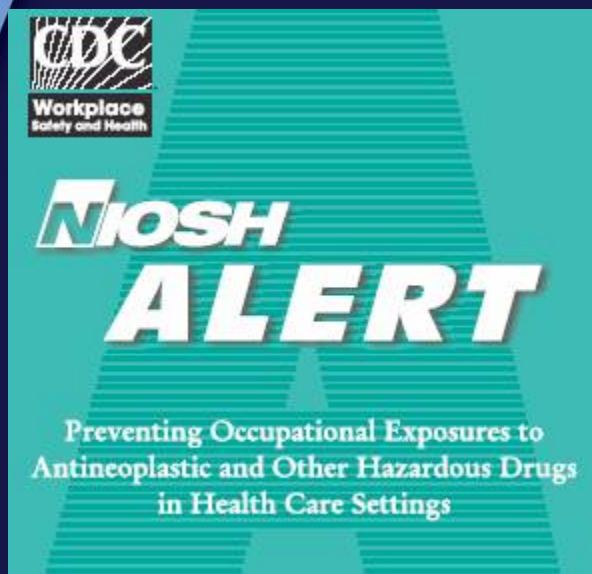


WORLD HEALTH ORGANIZATION
INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans

Evaluate the Risk: Hazard Identification

- *NIOSH definition of hazardous drugs*



1. Carcinogenicity
2. Teratogenicity or other developmental toxicity
3. Reproductive toxicity
4. Organ toxicity at low dose
5. Genotoxicity
6. Structure and toxicity profiles of new drugs that mimic existing drugs determined hazardous by the above criteria

Evaluate the Risk: Hazard Identification

2004 NIOSH Alert List Content

- Antineoplastics
- Antiretroviral agents
- Antivirals
- Androgens
- Estrogen agonist antagonists
- Progestins
- Contraceptives
- Gonadotropins
- Oxycytocics

- Immunomodulators
- Immunosuppressants

2006 Updated list

- Monoclonal antibodies ../..

NEW FDA DRUGS AND WARNINGS FITTING NIOSH CRITERIA FOR HAZARDOUS DRUGS 2006							
Proprietary Name	Established Name	NIOSH Hazardous Drugs Criteria					How Supplied
		Cancer	Preg Cat	Repro Tox	Organ Tox	Geno Tox	
Abilify	aripiprazole	+	C	+	+	+	Tablets
Alimta	pemetrexed	NT	D	+	+	+	IV infusion
Amevive	alfacept	+	B	--	+	--	Parenteral injection
Amitiza	lubiprostone	+	C	--		--	Capsules
Apokyn	apomorphine HCl	NT	C	+		+	Dermal injection
Arranon	nelarabine	NT	D	NT	+	+	IV infusion
Avastin	bevacizumab	NT	C	+	+	--	IV infusion

Workshop Plan

- Evaluate the risk in the workplace
 - Identify hazardous substances
 - Assess the risk to health
- Develop a risk management strategy
 - Control the risk to health
 - Assess the control measures implemented



What Are the Health Risks?

■ Acute health effects

- Irritation
- Headache
- Nausea, vomiting, diarrhea
- Allergy

■ Reproductive effects

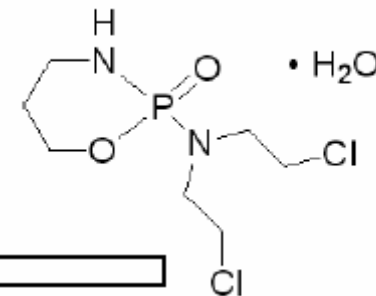
- Fetal loss
- Low birth weight
- Congenital abnormality
- Infertility

■ Chronic health effect

- Possibly cancer

Material Safety Data Sheet

Example: Cyclophosphamide



Baxter

Material Safety

MSDS Number:
Revision date:
Print date:

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION
 MSDS Number: 1118057
 Product name: Cyclophosphamide for Injection, USP
 Product code: NDC 10019-955-01, NDC 10019-956-01, NDC 10019-957-01

Synonyms:
Chemical Family:
Product Type:
Container Information:
Product Use:

Supplier:
BAXTER HEALTHCARE
DEERFIELD, ILLINOIS 6
(800) 422-9837 or (847) 1

Emergency telephone n

3. HAZARDS IDENTIFICATION

Emergency overview: **WARNING: HARMFUL IF SWALLOWED. CANCER SUSPECT. MAY CAUSE**

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Occupational Exposure Limits

Component	OSHA- Time Weighted Average:	OSHA- Short Term Exposure Limit:	OSHA- Ceiling Limits	ACGIH- Time Weighted Average:	ACGIH- Short Term Exposure Limit:	ACGIH- Ceiling Limit Value:
Cyclophosphamide 50-18-0	None	None	None	None	None	None

Principle routes

Inhalation:

Ingestion:

Engineering measures: Provide general or local

Handling must be limited.

EU EINECS List -

This product complies with EINECS

Risk Phrases:

- R22 - Harmful if swallowed.
- R41 - Risk of serious damage to eyes.
- R45 - May cause cancer.
- R46 - May cause heritable genetic damage.
- R48/23/24/25 - Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed.
- R61 - May cause harm to the unborn child.



Components to ensure that stable regulatory limits. If respiratory protection compliance with OSHA 29 er regions. Fire fighting s with full face piece and

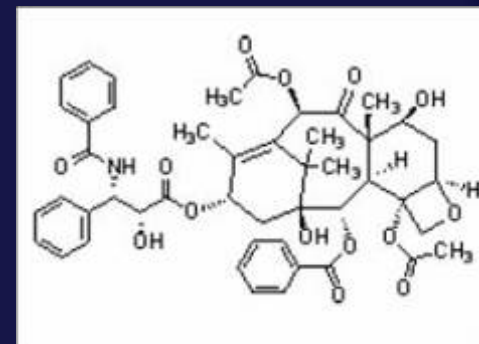
Safety Phrases:

- S53 - Avoid exposure - obtain special instructions before use.
- S15 - Keep away from heat.
- S26 - In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
- S45 - In case of accident or if you feel unwell, seek medical advice immediately (show label where possible).

ential exists for direct

Material Safety Data Sheet

- *Example: Paclitaxel*
- Hazard Code Xn (Harmful)



- Risk Statements 37/38-41-42/43-62-68
 - R37/38: Irritating to respiratory system and skin
 - R41: Risk of serious damage to eyes
 - R42/43: May cause sensitization by inhalation and skin contact
 - R62: Possible risk of impaired fertility
 - R68: Possible risk of irreversible effects
- Safety Statements 22-26-36/37/39-45
 - R22: Do not breathe dust
 - R26: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice
 - R36/37/39: Wear suitable protective clothing, gloves, and eye/face protection
 - R45: In case of accident or if you feel unwell, seek medical advice immediately (show label where possible)



Health Risks Assessment

T+ [highly toxic]



T+

T [toxic]



T

Xn [harmful]



Xn

Xi [irritant]



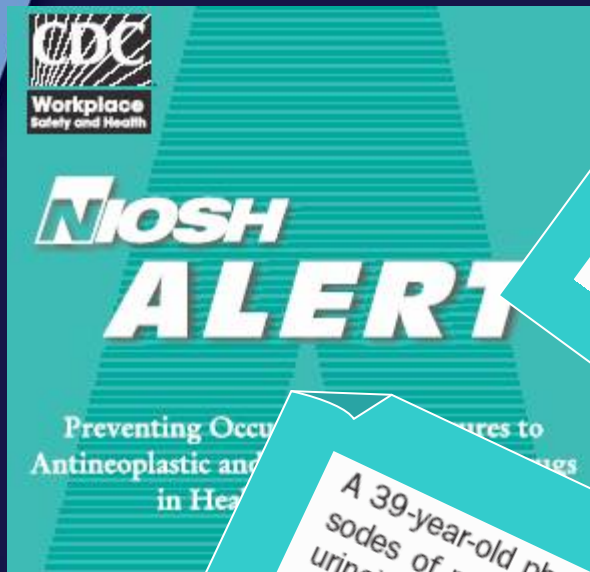
Xi

Hazard Class	Hazard Score
5	10 000
4	1000
3	100
2	10
1	1

Simplified method for risk assessment in the workplace. INRS [French National Research and Safety Institute (Institut National de Recherche et de Sécurité- France)]

Health Risks Assessment

CASE REPORTS



Gastrointestinal distress – cutaneous penetration of carmustine

A female oncologist reported a history of gastrointestinal distress and cutaneous penetration of carmustine. She had been working in an oncology ward for 10 years and had been exposed to carmustine for all of the time. She had been wearing gloves and a mask and leg and [unclear] (1988). Although

Allergic asthma – nurse working in oncology ward

A 41-year-old nurse working in an oncology ward for 10 years reported allergic asthma. She had been exposed to various drugs and had been wearing gloves and a mask. She had been working in an oncology ward for 10 years and had been exposed to various drugs for all of the time. She had been wearing gloves and a mask and leg and [unclear] (1988). Although

Allergic rash – patient care assistant working in oncology ward – handling patient urine

A 41-year-old patient-care assistant working in an oncology ward for 10 years reported an allergic rash. She had been exposed to various drugs and had been wearing gloves and a mask. She had been working in an oncology ward for 10 years and had been exposed to various drugs for all of the time. She had been wearing gloves and a mask and leg and [unclear] (1988). Although

Cancer – routine preparation of cytotoxic in horizontal laminar airflow hood

A 39-year-old pharmacist suffered two episodes of painless hematuria (blood in urine) and was found to have a grade II papillary transitional cell carcinoma [Levin et al. 1993]. Twelve years

Identify the Possible Exposure Routes

■ Dermal

- Contact
- Penetration

Sessink, et al. 1994.
Kromhout, et al. 2000.

■ Inhalation

■ Unexpected/accident

- Oral ingestion (hand-to-mouth)
- Percutaneous injury

Identify the Form of the Substance

- Liquid
- Powder
- Solid tablets
- Cream, ointments, lotions for topical application

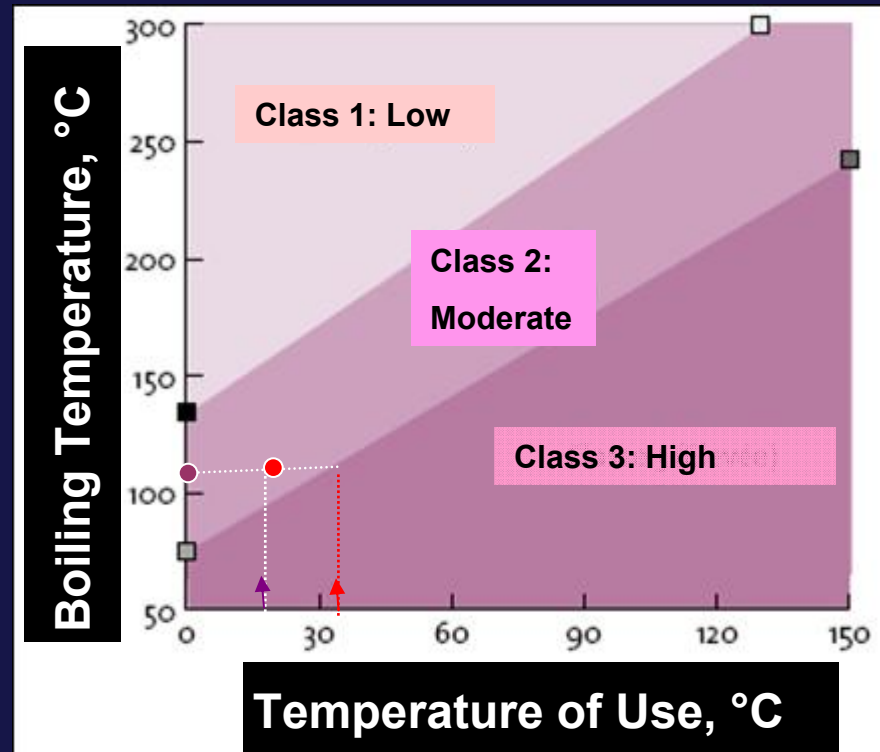


- Aerosols, droplets
- Vapors (cytotoxics able to vaporize at ambient temperature)
 - Cyclophosphamide
 - Ifosfamide
 - carmustine
 - Thiothepa

Identify the Physical State of the Substance

- Liquid
- Powder
- Solid tablets
- Cream, ointments, lotions for topical application

Liquid Volatility Class



Simplified method for risk assessment in the workplace. INRS [French National Research and Safety Institute (Institut National de Recherche et de Sécurité- France)]

Identify the Physical State of the Substance

- Liquid
- Powder
- Solid tablets
- Cream, ointments, lotions for topical application

Powder Volatility Class

Powder Type	Class	Score
Fine	1	100
Crystallized	2	10
Aggregated	3	1

Simplified method for risk assessment in the workplace. INRS [French National Research and Safety Institute (Institut National de Recherche et de Sécurité- France)]

Identify the Physical State of the Substance

- Liquid
 - Powder
 - Solid tablets
 - Cream, ointments, lotions for topical application
- Smaller particles
 - Higher emission
 - Increase transfer
 - Higher adherence to skin

Analyze the Quantities and Frequencies of Use

- Quantity
- Frequency
- Drug hazard score

- Score the exposure risk

Quantities Handled

- Q_i : quantities of the drug handled
- Q_{max} : highest quantities of drugs handled

Quantity Class	Q_i / Q_{max}
1	< 1%
2	1–5%
3	5–12%
4	12–33%
5	33–100%

Simplified method for risk assessment in the workplace. INRS [French National Research and Safety Institute (Institut National de Recherche et de Sécurité- France)]

Frequencies of Use

- Frequency class

Use	Rare	Intermittent	Frequent	Permanent
Per day	< 30 min	30–120 min	2–6 h	> 6 h
Per week	< 2 h	2–8 h	1–3 d	> 3 d
Per month	< 1 d	1–6 d	6–15 d	> 15 d
Per year	< 5 d	15 d–2 m	2–5 m	> 5 m
Class	1	2	3	4

Simplified method for risk assessment in the workplace. INRS [French National Research and Safety Institute (Institut National de Recherche et de Sécurité- France)]

Exposure Class

Quantity Class						
5	0	4	5	5	5	
4	0	3	4	4	5	
3	0	3	3	3	4	
2	0	2	2	2	2	
1	0	1	1	1	1	
	0	1	2	3	4	Frequency class

Simplified method for risk assessment in the workplace. INRS [French National Research and Safety Institute (Institut National de Recherche et de Sécurité- France)]

Vincent R, et al. INRS *Cahier de Notes Documentaires*, ND 2233-200-05. 2005;200:39-62.

Potential Risk of Exposure

Exposure Class						
5	100	1000	10 000	100 000	1 000 000	
4	30	300	3000	30 000	300 000	
3	10	100	1000	10 000	100 000	
2	3	30	300	3000	30 000	
1	1	10	100	1000	10 000	
	1	2	3	4	5	Hazard Class

Simplified method for risk assessment in the workplace. INRS [French National Research and Safety Institute (Institut National de Recherche et de Sécurité- France)]

Risk Priority: Priority Score

Score	Priority
$\geq 10\ 000$	HIGH
100-10 000	MODERATE
< 100	LOW

- Priority score

Risk Assessment

- Nature of work involving cytotoxics
- Sources of contamination
 - External surface of vials
 - Process
 - External surface of final product
 - Patient

Identify the Nature of the Work Involving Cytotoxic Drugs

■ Where are cytotoxics used in the workplace?

- Pharmacy (drug reception and storage)

- Pharmacy (drug preparation)

- Pharmacy (drug destruction)

- Handling transport disposition (cytotoxic drug and cytotoxic waste)

- Ward, daycare center (drug administration)

- Patient care after administration (drug excretion)

Exposure risk assessment: international studies results

- Evidence for worker exposure

- Environmental contamination in the workplace

- Biological exposure of handlers

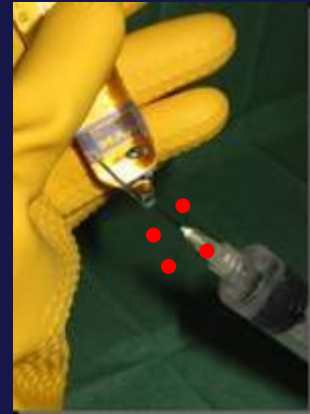
PHARMACY:

External Surface Vials Contamination

- Connor TH, et al. *Am J Health-System Pharm.* 2005; 62:475-84.
- Delporte JP, et al. *Eur Hosp Pharm.* 1999;5:119-21.
- Favier B, et al. *Oncol Pharm Pract.* 2003;9:15-20.
- Hepp R, et al. *Krankenhauspharmazie.* 1998;19:22-7.
- Mason HJ, et al. *Ann Occup Hyg.* 2003;47:681-685.
- Nygren O, et al. *Ann Occup Hyg.* 2002;46:555-7.
- Ros JJW, et al. *Ziekenhuisfarmacie.* 1997;13:168-71.



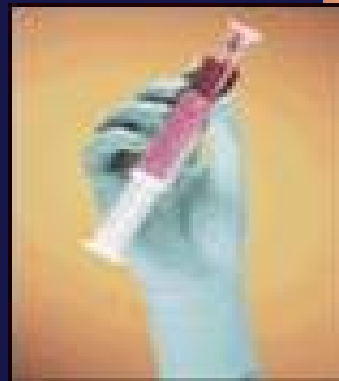
PHARMACY: Compounding Process as Source of Contamination



- Reconstitution
- Withdrawal of the solution
- Transfer of the solution into bags

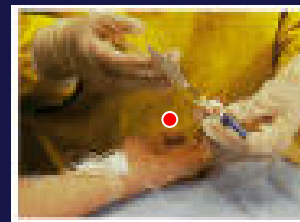
PHARMACY / WARD: External Surface of Final Product

- Contamination is transferred during the compounding process



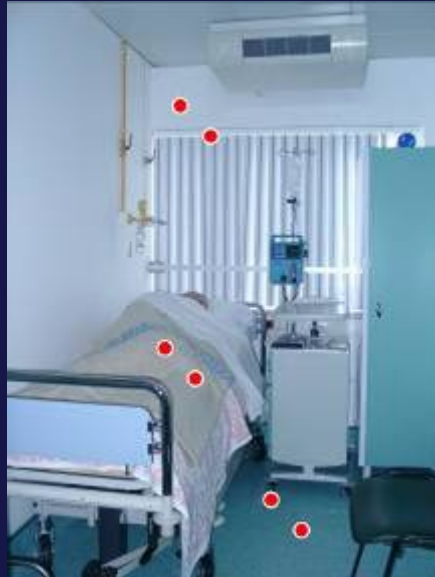
WARD: Drug Administration

- Injection
- Remove perfusion line



WARD: Patient Care

- Excreta
 - Urine
 - Fecal
 - Sweat
 - Vomit



- Handling patient urine
- Washing a patient
- Removing bed sheets
- Cleaning patient toilets

Environmental contamination with cyclophosphamide

- Surface contamination¹
- Air contamination (0,5- 1,7 ng/m³)¹
- Bed sheets, towels²



1. Kromhout H, et al. *Ann Occup Hyg.* 2000;44:551-60.

2. Fransman W, et al. *Ann Occup Hyg.* 2004;48:237-44.

Dermal Exposure Assessment

- Potential dermal exposure function of task
(*RISKOFDERM Model*)

Task	Default values	Reasonable Worst Case Exposure	
		mg	mg/cm ²
Washing patient		25000	30.5
Mixing small quantities of cytotoxic drugs in hospital pharmacies		0.53	0.00065
Pouring of urine contaminated with cytotoxics		18.0	0.022

Exposure risk assessment: international studies results

- Evidence for worker exposure
 - Environmental contamination in the workplace
 - Biological exposure of handlers

Biological Exposure

Cyclophosphamide in Urine

Subject	No. of Positive Samples(%)	Range of Concentration
Nurses	8/87 (9.2%)	0.35–9.08 µg/L ¹
Pharmacy technicians	5/20 (25%)	0.70–2.70 µg/24h ²
Pharmacy technicians	8/9 (88.9%)	0.20–19.40 µg/L ³
Nurses	20/25 (80%)	0.02–9.14 µg/24h ⁴
Pharmacy technicians and nurses	106/1415 (7.5%)	0.05–0.76 µg/L ⁵
Pharmacy technicians and nurses	18/62 (29%)	0.05–10.03 µg/L ⁶

1. Hirst, et al. *Lancet* 1984;1:186-8.

2. Evelo, et al. *Int Arch Occup Environ Health*. 1986;58:151-5.

3. Sessink PJM, et al. *Arch Environment Health*. 1994;49:165-9.

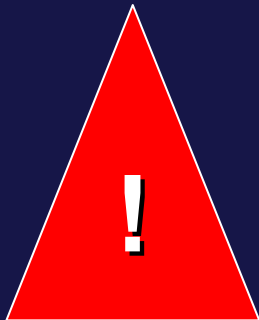
4. Burgaz S, et al. *Mutation Res*. 1999;439:97-104.

5. Pethran et al. *Int Arch Occup Environ Health*. 2003;76:5-10.

6. Turci R, et al. *Toxicol letters* .2002;134:57-64.

Biological Exposure

- Pharmacy technicians and pharmacy assistants (not directly involved in preparation)
 - 57/87 positive urine samples (at least one positive result)
 - No difference between subjects working either as manufacturer or assistant



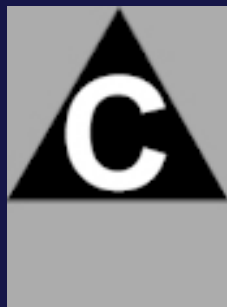
Drugs	Range of Concentration
CP	0.04–0.76µg/L
IF	0.07–2.00µg/L
Epirubicine/ doxorubicine	4.5–196 µg/L

CP = cyclophosphamide; IF = ifosphamide.

Schreiber C, et al. *Int Arch Occup Environ Health*. 2003;76:11-6.

Workshop Plan

- Evaluate the risk in the workplace
 - Identify hazardous substances
 - Assess the risk to health
- Develop a risk management strategy
 - Control the risk to health
 - Assess the control measures implemented



Control Measures

- Acceptable level of exposure of workers does not exist for pharmaceutical products
- Occupational Exposure Limits (OEL) ???
- Control measures must be implemented to reduce exposure to low level “as low as reasonably achievable” (ALARA)

Control Measures: General Considerations

SUBSTITUTION

CLOSED COLLECTIVE PROTECTION

OTHER COLLECTIVE PROTECTION

PERSONAL PROTECTION

WORK PRACTICE PROCEDURES



Efficiency of the Measure



Residual Risk

“Closed” Collective Protection

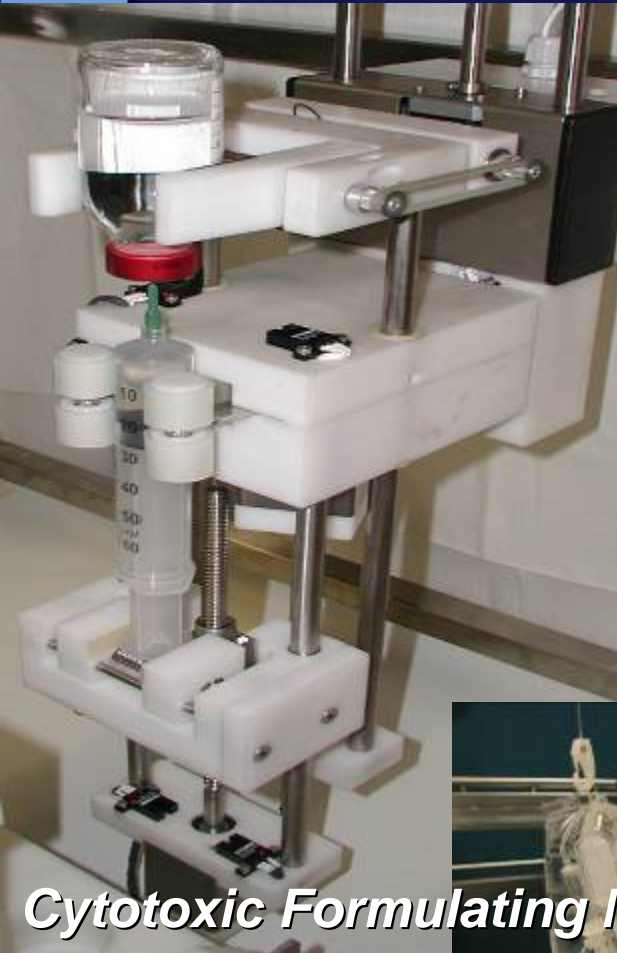
- System allowing a **total and permanent** containment
- System where all the operations processes, transfers, transportation, cleaning, maintenance.../... are physically and permanently separated from the toxic product....
- **Need the development of automation** of the tasks including transportation and cleaning
- Preparation should potentially be automated

CLOSED COLLECTIVE PROTECTION

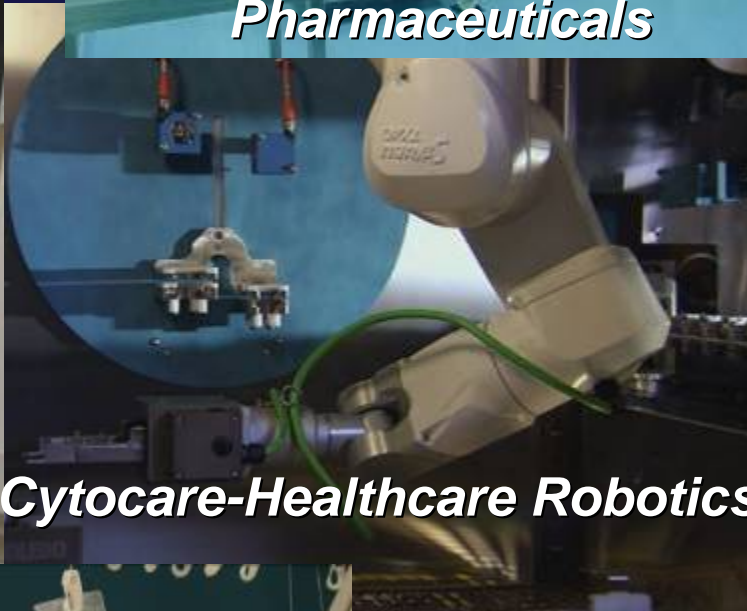
Automation



*API- Sintetica SA
Pharmaceuticals*



Cytotoxic Formulating Machine – MDS



Cytocare-Healthcare Robotics



*Intellifill i.v.™ –
Forhealth
Technology, Inc.*



Other Collective Protection

- Use ventilation systems



BSC IIB (minimum)



BSC III

Air must be vented
outside the building

- Use barrier systems



Isolator



OTHER COLLECTIVE PROTECTION

Laminar Airflow / Biohazard Safety Cabinets



Horizontal airflow is not allowed for cytotoxics preparation

Laminar Flow Cabinets (LFCs) are not suitable for the preparation of hazardous drugs. Biohazard safety cabinets (BSCs) should be used instead, with a vertical downward air flow exhausting vertically from the cabinet and not towards the operator



PHARMACEUTICAL INSPECTION CONVENTION
PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

Biohazard Safety Cabinets



- Class II B1
 - Recirculated air inside the cabinet
 - Exhaust downflow air through HEPA filter to the atmosphere
 - All contaminated ducts and plenums under negative pressure
- Class II B2 (total exhaust)
 - Without air recirculation inside the cabinet

HEPA = high efficiency particulate arresting.

NIOSH National Institute for Occupational Safety and Health. 2004. NIOSH publication N°2004-165, Washington DC.

Biohazard Safety Cabinets



■ Class III

- **Totally enclosed**
- **Gas-tight**
- **Preparation with attached rubber gloves through a non-opening view window**
- **Negative pressure**
- **HEPA filtration (inlet and outlet air)**
- **Passage of material through double-door or pass-through box**



ISOLATOR Definition: USP <797> 2008

- Compounding aseptic containment isolator (CACI)

Compounding Aseptic Containment Isolator (CACI)—A compounding aseptic isolator (CAI) designed to provide worker protection from exposure to undesirable levels of airborne drug throughout the compounding and material transfer processes and to provide an aseptic environment for compounding sterile preparations. Air exchange with the surrounding environment should not occur unless the air is first passed through a microbial retentive filter (HEPA minimum) system capable of containing airborne concentrations of the physical size and state of the drug being compounded. Where volatile hazardous drugs are prepared, the exhaust air from the isolator should be appropriately removed by properly designed building ventilation.

Isolator Definition PIC/S Guidelines 2008

Pharmaceutical Isolator

A containment device which utilises barrier technology to provide an enclosed, controlled workspace.



PHARMACEUTICAL INSPECTION CONVENTION
PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME



- Rigid or soft wall
- Turbulent airflow
- Double HEPA air filtration (inlet and outlet)
- Positive or negative pressure
- Preparation with attached rubber gloves/half suit
- Sterile (gas sterilization: H_2O_2 , peracetic acid)
- Containment transfer systems

Personal Protective Equipment

■ Gloving and gowning

- “Chemotherapy” gloves
- Double gloving
- Change every 30 minutes or when torn, punctured or contaminated
- Inspect before use
- Wash hands with soap before donning and after removal



■ Use disposable sleeve cover

■ Use polyethylene



PERSONAL PROTECTION

Gloves / Cloth Exposure Prevention

- Hierarchic order for dermal risk exposure

- No cloth : 1
- Woven clothing: 0.3
- Non woven clothing-permeable: 0.1
- Non-woven clothing impermeable: 0.03

- Double gloving > simple gloving

- Replacement frequency of the inner glove

Work Practice Procedures

- Insufficient on their own
- Improvement of the protection
 - Use of containment systems
 - Compounding process
 - Administration
 - Transport of drugs and waste
 - Education and training

WORK PRACTICE PROCEDURES

Improve Compounding Process

- Transfer devices which are able to decrease aerosolization of toxic drugs during the preparation

- Compounding devices



Codan



ICU-
Hospira



B Braun



Baxter



Teva



ICU Medical



Carmel

<797> PHARMACEUTICAL
COMPOUNDING—
STERILE PREPARATIONS

“When closed-system vial-transfer devices (CSTDs) (ie, vial-transfer systems that allow no venting or exposure of hazardous substance to the environment) are used, they shall be used within the ISO class 5 environment of a BSC or CACI.”

Improve Administration

- Personal protective equipment
- Containment tubing
- Containment connection



ICU Medical



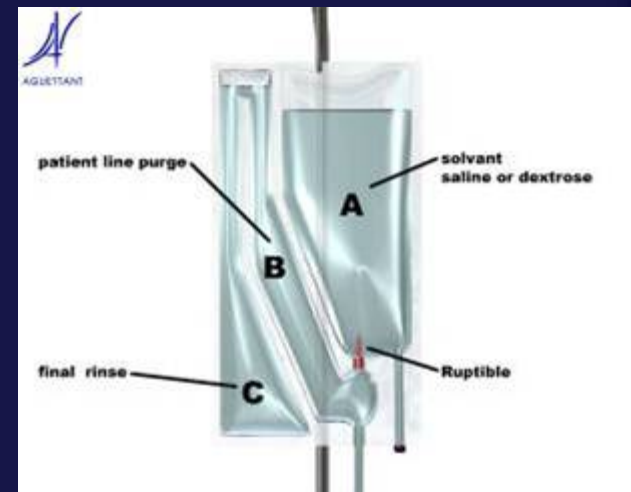
Carmel



Codan



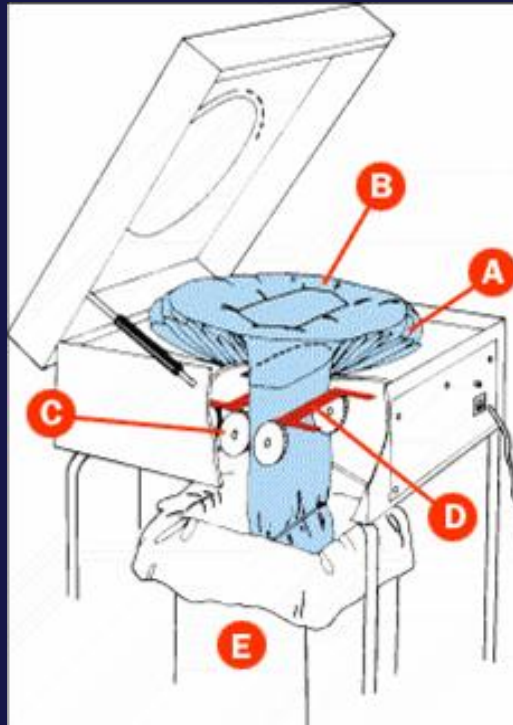
Macopharma



Aguettant

Improve Containment of Products and Waste

- Disposable transport bags
- Disposable sealed plastic bags
- For BSC'S



Improve Containment of Products and Waste

- For isolators

Double interlocking doors

- Disposable sealed sterile plastic bags



Tubing®, La Calhène



Biosafe®, IDC



Beta Bag®, La Calhène

Education

se croire en sécurité, c'est risqué!



“Feel safe, it is risky !”



“Protecting oneself is not ridiculous !”

toujours réfléchir avant d'agir



“Always think before doing !”

Education

“Disposable gloves are single use”

“Fit your mask on face, ... it is vital !”

“After use, discard your disposable gloves”



Training: USP <797>

- Full training for all personnel compounding hazardous drugs
 - Storage
 - Handling
 - Disposal of the drug
- Training verification
 - prior compounding
 - Tested at least annually
 - Documented
- Overview of hazardous drugs (mutagenic teratogenic carcinogenic properties)

■ Contents

- Safe aseptic manipulation practice
- Negative pressure technique when utilizing BSC or CACI
- Correct use of closed system transfer devices
- Containment cleanup, disposal procedure, and procedures for breakage and spills
- Treatment of personnel contact and inhalation exposure

BSC Biological Safety Cabinet

CACI Compounding Aseptic Containment Isolator

Evaluation of Protective Measures

- Environmental monitoring

- Useful tool for:

- Assessment of environmental basic level in the workplace: benchmark
- Assessment of protective measure implemented
- Detect failure in the process

- Cytotoxic drugs commonly used as markers:

Cyclophosphamide / Ifosphamide
5 FU
Methotrexate
Platinum
[cisplatin, carboplatin, oxaliplatin]
Doxorubicin / epirubicine
Paclitaxel

Evaluation of Protective Measures

- Environmental monitoring
- Surface contamination sampling
- Filter paper or tissue wipe
- Solvent system for helping drug recovery (ie, HCl, NaOH)

- Sensitive analytical method

GC-MS GC-MS-MS

LC-MS-MS

ICP-MS

Adsorptive Voltammetry

GC-MS Gas chromatography Mass Spectrometry

GC-MSMS Gas chromatography tandem mass spectrometry

LC-MSMS Liquid Chromatography tandem mass spectrometry

ICP-MS Inductively coupled plasma mass spectrometry

Surface Environmental Sampling Recommendation USP <797> 2008

- **Frequency:**
 - Initially
 - At least every 6 months

- **Sample localizations:**
 - *Working area of BSCs and CACIs*
 - *Counter tops (finished preparation)*
 - *Areas adjacent to BSCs / CACIs (Floor)*
 - *Patient administration areas*

BSC Biological Safety Cabinet

CACI Compounding Aseptic Containment Isolator

- ***If measurable level of contamination:***

- Identify cause of contamination
 - Document
 - Contain
- Retraining
 - Cleaning (high-pH soap and water)
 - Improving engineering controls

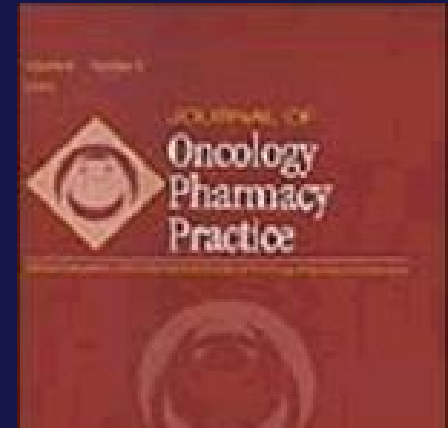
- **Engineering controls improvements:**

- Venting BSCs/CACIs 100% to the outside
- Implement CSTD
- Re-assessing type of BSCs/CACIs

CSTD Closed System Transfer Device

References - Guidelines

- Table of contents
 - Transport of cytotoxics
 - Personnel
 - Education and training
 - Hierarchic order in protection measures
 - Facilities for sterile cytotoxic reconstitution and personal protective equipment
 - Special devices
 - Ventilation tools
 - Nonsterile preparations
 - Chemical contamination monitoring
 - Checking procedures
 - Administration of cytotoxic drugs
 - Cleaning procedures
 - Cytotoxic spills, extravasation and other incidents
 - Waste handling and patient excreta
 - Laundry
 - Warning staff of presence of cytotoxic agents
 - Home care
 - Risk management
 - Medicine management



**ISOPP Standards of Practice
Safe handling of cytotoxics**

References - Guidelines

- *ASHP guidelines on handling hazardous drugs. Am J Health Syst Pharm. 2006,63:1172-93.*
- NIOSH (National Institute for Occupational Safety and Health). 2004. *Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings.* NIOSH Publ No 2004-165. Washington, DC:U.S. Government Printing Office.
- *USP<797> Pharmaceutical compounding-Sterile preparations.* The United State Pharmacopeial Convention. *revision bulletin, 2008.*
- *PIC/S guide to good practices for the preparation of medicinal products in healthcare establishments.* Pharmaceutical Inspection Convention-Pharmaceutical Co-operation Scheme. April 2008.