Handling Cytostatic Drugs

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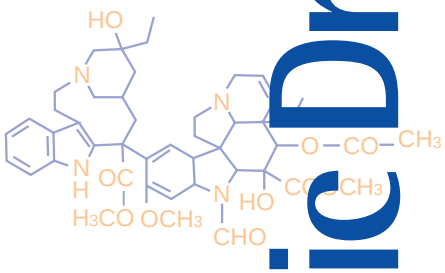

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Preface

Oncological patients are the focus of our attention and actions. In order to effectively combat their disorder and to meet their needs, everyone involved in their treatment must be able to perform various tasks in accordance with the latest medical insights and practices.

Over the last few years, impressive progress has been made not only in research and clinical application, but also in clinical and pharmaceutical practice – where we find a growing demand for specialist skills to meet these requirements. Further training and specialization are therefore a high priority. When addressing the handling of cytostatic agents in pharmacies, the assessment of drug safety factors is gaining in importance.

It is suspected that even the smallest doses of cytostatic agents have an irreversible and cumulative effect and, although they do not have a threshold value, they represent a low but nevertheless clearly defined risk as a consequence. For this reason, all responsible bodies are in agreement that the risks involved in handling cytostatic agents must be minimized.

The quality standard for pharmaceutical-oncological service, developed in Germany, has become the working standard throughout Europe. Rules and guidelines, which may help to prevent contamination and ensure uniform safety and quality, need to be defined for all areas involved in handling cytostatic agents.

ISOPP, the "International Society of Oncology Pharmacy Practitioners", is endeavoring to meet the ever-increasing demand for communication and collaboration in this sector. The society therefore supports every measure that furthers this objective. For this reason we warmly welcome the publication of this booklet and hope that it will enjoy the popularity and appreciation it deserves.

Klaus Meier
President, International Society of Oncology Pharmacy Practitioners

Contents

Handling Cytostatic Drugs: Contents

Introduction

Handling cytostatic drugs requires a number of organizational and technical systems in order to guarantee the best possible protection for personnel. This booklet focuses on various ways of protecting personnel from potential hazards through the careful handling of cytostatic drugs, and for this reason, product protection is only briefly discussed. Furthermore, we have chosen not to present different national legal requirements. Instead, we have tried to describe best practices to ensure the highest possible degree of protection for humans and the environment. In particular, we have concentrated on putting theoretical knowledge into practice. Therefore, you will find a checklist to test your knowledge in the Appendix.

This booklet does not claim to be complete and does not substitute for direct contact with your local pharmacist. Some of the specific recommendations described may not be consistent with accepted practices and/or environmental, health and safety regulations in the US and several other countries. With regard to legal requirements, it is your responsibility to be informed. For additional information – in particular, product specific information such as safety data sheets or legal regulations – you should contact the manufacturers or your local authorities.
A collection of forms, i.e., operating procedures to make your work easier, is also listed in the Appendix.

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Please contact us if you have any suggestions for improvement or corrections, so we can include them in the next updated version to make this booklet even more practical, relevant, and helpful for all persons involved in handling cytostatic drugs.

Cytostatic Drugs – What They Are and What They Do

Cytostatics are drugs used to block the growth of cancer cells. They achieve this by influencing cell metabolism during the cell cycle (Fig. 1) so that cell division and cell reproduction is inhibited. Cytostatics can be classified according to their action mechanisms and their points of attack. An overview of the most important groups is given in Table 1 (p. 8).

The mechanisms of cytostatic action are very likely to lead to carcinogenic, mutagenic, and teratogenic effects. Consequently, pregnant women should avoid all contact with cytostatic drugs. This is required by law in most European countries, but not in all countries (e.g., in the U.S.), so it is necessary for facilities to check local regulations.

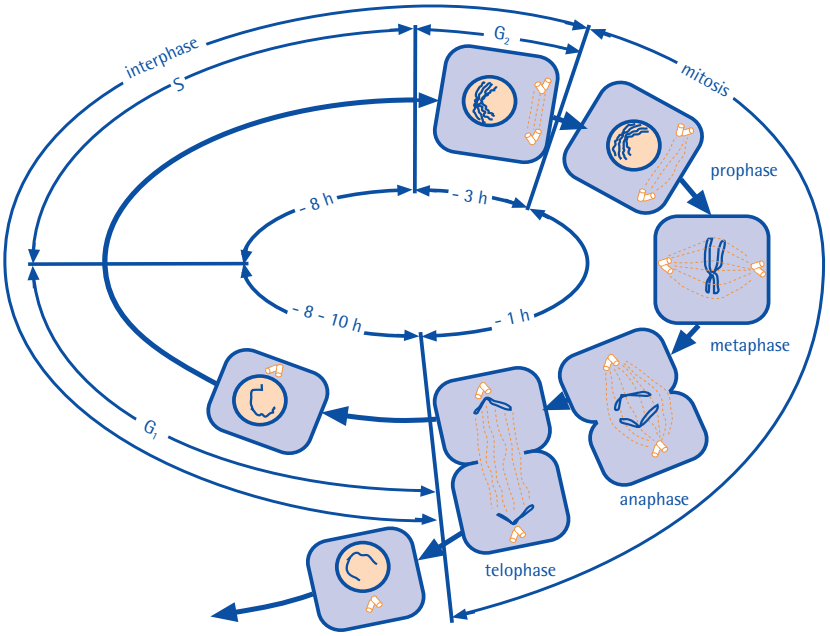


Fig. 1: Cell cycle

Cell growth and cell division are divided into several phases: synthesizing and doubling of the DNA take place in the S-phase (synthesis). During the M-phase (mitosis), two daughter cells are developed. Before and after the mitosis, there are two "resting" phases (G_1- and G_2-phase).

Source: Pschyrembels Medizinisches Wörterbuch. de Gruyter Verlag, Berlin

Mode of Action

Since cancer cells hardly differ physiologically from healthy cells, cytostatic drugs do not specifically affect cancer cells, but all dividing cells. Therefore, substantial side effects may occur such as nausea, hair loss, and immunosuppression.

These unwanted side effects occur not only in the chemotherapeutically treated patients, but also pose a health hazard for the staff, especially when they are involved in cytostatic drug preparation (pharmacy) and administration (nursing).

Moreover, personnel involved in delivery, transport, and disposal of cytostatic drugs may be affected, as well as technical and laboratory staff (for example during maintenance of safety cabinets or the analysis of patient blood or urine).

Evidence of an increased health risk from improper work practices is suggested in the literature. For example, the occurrence of side effects, such as nausea and eyelash loss in nursing personnel, has been reported (Jung 1990). Furthermore, in several studies cytostatic drugs were detected in the urine of pharmacy and nursing personnel (Sessink et al. 1992, 1994).

The literature contains contradictory data regarding the mutagenic effect of cytostatic drugs on exposed personnel. Some studies report mutagenic effects in the urine of nurses (e.g., Falck et al. 1979), whereas other studies could not confirm this (e.g., Cooke et al. 1991).

These contradictory results contribute to the uneasiness and uncertainty of the personnel concerned. In the earlier studies, the safety precautions for personnel were not as great as they are today. Additionally, the long-term risk for health care workers is not yet known. In order to ensure optimal protection, it is advisable to assume the worst case and to take comprehensive and effective protection measures.

Mode of Action

Table 1:
Cytostatic mechanisms of action of selected active substances

Type of cytotoxic agent	Selected active substances	Mechanism of action	Main effect phase in the cell cycle
Alkylating agents	Ifosfamide Cyclophosphamide Treosulfane Carboplatin Cisplatin	Alkylating of DNA ▼ Cross-linking ▼ Prevention of DNA-replication	Non-specific in all cycle phases
Antimetabolites	Cytarabine 5-Fluorouracil Gemcitabine Mercaptopurine Methotrexate*	Incorporation into DNA as fraudulent nucleotide ▼ Inhibition of enzymes in DNA-synthesis	S-phase
Mitotic inhibitors	Paclitaxel Vinorelbine Docetaxel Vincristine Vinblastine Vindesine	Disturbance of spindle foundation ▼ Arresting of mitosis during metaphase	M-phase
Cytotoxic antibiotics	Daunorubicin Doxorubicin Epirubicin Mitozantrone	Intercalation between DNA-bases ▼ Inhibition of DNA-biosynthesis	S-phase G_2-phase
Topoisomerase I- **and** **II-inhibitors**	Etoposide Teniposide Topotecane	Inhibition of Topoisomerase I, which removes the torsion of the DNA Inhibition of Topoisomerase-II, which catalyzes the torsion of the DNA and others	S-phase G_2-phase M-phase S-phase

* does not act as fraudulent nucleotide, inhibits folic acid metabolism

Safe Handling of Cytostatic Drugs

Consideration of product safety must be heeded when cytostatic drugs are handled. For example, in order to prevent the infection of patients, care must be taken that the substances are not microbially contaminated.

Additionally, consideration of personnel safety mentioned in this booklet must be observed.

In order to ensure the most comprehensive protection possible, protective measures must be taken simultaneously, such as blocking cytostatic drugs by several barriers and thus preventing health hazards for personnel (multi-barrier concept).

Combining both technical mechanisms and personal protective equipment (protective clothing) is the best way to combat the different means of contamination.

Some cytostatic drugs can be absorbed through the skin or through the respiratory tract by aerosolization. In order to protect individuals, it is particularly important that the handling of cytostatic drugs is properly managed. The greatest potential for improvement is in this area. The best protective equipment will not work if personnel are insufficiently trained and suitable protective equipment is lacking.

Therefore, in the following section, recommendations are presented for the highest levels of safety at different stages in the handling of cytostatic drugs.

Management

The number of persons handling cytostatic drugs should be kept to a minimum. The reconstitution of cytostatic drugs should be centralized. In larger hospitals, drug solutions should be reconstituted and delivered to the wards by the internal pharmacy. Hospitals without an internal pharmacy and/or oncological practices should be provided with ready-made solutions by regional or, even better, local pharmacies using the appropriate technical equipment. Due to the limited stability of the solutions, transport distances should be kept as short as possible. For transport, liquid-proof, shatterproof, and easy-to-clean containers (e.g., plastic boxes) should be used.
Generally, containers for internal and external transport are to be clearly labeled in order to indicate their hazardous potential (see Fig. 2).

Fig. 2: Example for a warning label

The areas in which cytostatic drugs are handled should meet the following requirements:

- Reconstitution of cytostatic drugs should be carried out within a separate area, away from general wards and/or pharmacy activities and busy thoroughfares inside the building.
- Reconstitution should be performed in a biological safety cabinet (BSC) and should be clearly separated from areas of other activities. This should be a separate, labeled, and draft-free area.
- A separate area for changing clothes and separate storage of protective and normal clothing should be situated outside the entrance to the reconstitution area.
- The free space in the work area should be at least 1.5 m^2 and be at least 1 m wide. The room should be at least 10 m^2. There should be no drafts.
- The construction of the area should allow for thorough cleaning. There should be as few objects as possible placed in the area, the floor covering should be made of synthetic material, and the floor should extend approximately 10 cm up the walls, which are coated with washable paint.
- Access to the work area should be restricted to authorized and trained personnel only.
- Food or drink must not be consumed in areas in which cytostatic drugs are handled. There must be no smoking within these areas. Only cytostatic drugs and working equipment may be stored in this area: strictly no food or beverages.
- Ideally, in pharmacies and wards, cytostatic drugs are to be stored separately in a ventilated safety cabinet with removable drip trays. If necessary, store cytostatics in a refrigerator which can be cleaned easily after spillage, in compliance with appropriate preventive measures (see the "Cleaning Procedures after Accidents" section).
- After completing procedures involving cytostatic drugs and removing protective equipment, employee should throroughly wash hands and face.

All new employees handling cytotoxic materials should receive adequate education and training, and should be regularly retrained.
The employees must be aware of the hazards, able to act responsibly, and know how to react in emergencies. The training measures are to be documented, continuously improved and updated. An important component of any training program is practical experience based on a theoretical foundation. A recommended training outline is provided in the Appendix. In order to be able to look up necessary information, participants of the training should be supplied with detailed reference material.

For all areas in which cytostatic drugs are handled, separate operating procedures containing the following points are to be provided:
- Hazards for humans and the environment
- General handling
- Emergency response
- First aid
- Spill clean-up
- Waste disposal
- Training documentation for each person

Standard operating procedures for different areas are provided in the Appendix.

The work area should be monitored after a spill and periodically e.g., once a year, by analyzing wipe and air samples for cytostatic drugs (if analysis methods are available). Contact the drug manufacturer for methods and procedures available.

Through monitoring, the improper handling of cytostatic drugs can be detected (during in-house investigations in hospital pharmacies, traces of cyclophosphamide were even found on door handles). In addition, the efficiency of cleaning procedures can be closely monitored.

Personnel handling cytostatic drugs should be examined regularly (at least once annually) as part of an occupational health program.
The main parts of the examination should be tests regarding disturbance of the respiratory organs, therapy-resistant skin irritations, as well as liver, renal, and haematological malfunctions. If substantial contamination is suspected, biological monitoring by analysis of the urine and blood for cytostatic drugs handled by the person or other appropriate assays, may be recommended by the examining health care professional.

Wholesale, Pharmaceutical Shipment, and Storage

Generally, every delivery of medicines should be checked for cytostatic drugs. If broken packages are detected, they are to be handled within a separate work area (e.g., a safety cabinet). Because wholesalers usually only handle medications that are packed in several layers, there is little health risk for personnel during routine activities. Therefore, protective clothing need only to be worn after accidents or if any container appears broken or leaking. The recommended procedures in this case are described in the "Cleaning Procedures after Accidents" and "First Aid" sections and in the operating instructions. The larger the quantities of cytostatic drugs to be supplied, stored, transported, and delivered, the greater the likelihood of accidents. Therefore, to avoid glass breakage, special care is necessary when loading and unloading packages (which can be broken and therefore contaminated) as well as when storing them on high-rise shelves.

Tips for Pharmaceutical Wholesalers

- Wear protective clothing after accidents.
- Take special care when loading, unloading, and storing on high shelves to avoid possible glass breakage.
- Handle broken packages in a separate work area (e.g., a safety cabinet).
- If an accident occurs, notify regulatory authorities if required by law.

Reconstitution of Intravenously Administered Cytostatics

The reconstitution of cytostatic solutions should be performed according to good manufacturing practice (GMP) in safety cabinets. Safety cabinets provide personnel with protection from aerosols and dust (in particular by air movement and filtering – see Fig. 3).

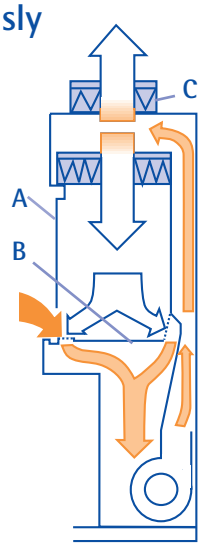


Fig. 3:
Biological Safety Cabinet

The airflow within the cabinet must be **laminar and vertical**. The exhausted air is ideally ducted outside of the building.

Ambient Air
Contaminated Air
Filtered Air

A: Sash
B: Working Surface
C: Exhaust Filter

The biological safety cabinet is to be maintained regularly by trained technical personnel in accordance with the manufacturer's recommendations and regulatory requirements. Maintenance is to be documented. It is very important to control the work environment when changing filters. Newer safety cabinets have a pre-filter integrated into the work surface, which can be changed more easily than the large exhaust filters. Thus, the time-consuming changing of the main filter is needed less frequently. Contractors specializing in servicing biological safety cabinets should be used. If they are not available only well-trained maintenance staff should be in the room while the filter or pre-filter is being changed. A respirator mask, safety goggles, a protection suit, and protection gloves are to be worn as protective gear. A full protection suit is recommended when changing the main filter. After the filter has been changed, the room must be thoroughly cleaned.

Tips for the Safety Cabinet

- Use a liquid-proof absorbing mat.
- Airflow is vertical; therefore no objects may be located above the work surface (e.g., shelves or containers hung on the wall).
- Within the safety cabinet, the quality of airflow may not be equal in all regions. Therefore, work at least 10 - 15 cm away from all side edges.
- Always leave the safety cabinet turned on (24 hours a day, 7 days a week); if there is no one working there for longer periods, such as at night and at weekends, reduce but do not stop the airflow.
- Do not cover the ventilation slots.
- Before beginning to work, make sure that all necessary equipment is available on the work surface.
- During maintenance of the safety cabinet, in particular when the filter is changed, cytostatic drug particles can get into the environment. Therefore, thoroughly clean the room after maintenance.

Safety

For work in a safety cabinet, a liquid-proof gown (that covers the torso) as well as double-layer sleeve-covering gloves are recommended as protective clothing. The glove material should be to at least 0.3 mm thick. Glove materials include latex, neoprene, polyurethane and nitrile. Powder-free latex and nitrile gloves are available in adequate thickness. Because neither of these materials is completely impermeable to every cytostatic agent, the gloves are to be changed at least every 20 minutes or immediately in case of visible contamination or damage. When working with very lipophilic cytostatic drugs, such as carmustine, gloves are to be changed immediately after reconstitution.

Damaged gloves can be readily identified if two pairs of gloves are worn with an integrated biogel indicator. The inner and outer gloves are different colours and are provided with a biogel system. Thus, a pinhole in the outer glove results in a clearly visible dark discoloration of the inner glove, when there is any liquid contact (Krammer and Carstens 1997).

For spill clean-up and where additional protection may be needed a respirator mask such as a high-efficiency particulate (HEPA) and safety goggles should be used as additional protective equipment (see p. 20 for more details on spill cleanup).

Since vials could be broken in transport or contaminated on the outside when filled with medicines, gloves and a gown must be worn during unpacking. Wherever possible, use sealed transport systems. Any contaminated parts after a leakage must not be touched directly with the gloves alone, use an additional swab or similar material. When substances must be dissolved in sealed vials, a positive pressure inside the vial may result from the solvent injection, increasing the risk of aerosol releases or splashing when the needle is removed. Therefore, reconstitution devices like chemo mini-spikes and liquid-proof absorbent mats are recommended.

Waste materials are to be collected and disposed of in appropriate containers in accordance with their degree of contamination (see the section on "Disposal of Cytostatic Waste").

After finishing work in the safety cabinet, the work surface is to be cleaned as described in the section "Routine Cleaning Procedures". The inner and outer walls of the safety cabinet should be cleaned regularly at least once per week.

Handling of Orally Administered Cytostatic Drugs

Since cytostatic drugs are rarely administered orally, personnel are often insufficiently informed about the hazards and the handling of such medications. The following recommendations should be considered when handling orally administered cytostatic drugs:

- All packages containing cytostatic drug tablets should carry a clearly visible warning label.
- Tablets should only be counted with powder-free gloves.
- A dedicated counting tray and disposable tongue depressors should be used when counting oral agents. The use of an automatic counting machine should be restricted because of cross contamination and dust generation concerns.
- When tablets have to be broken, a plastic bag should be used.
- Counted tablets are to be placed into separate, labeled dosage boxes.
- Use tweezers for administration. Do not touch the tablets with bare hands.
- Although a non-routine use, if tablets must be grounded to a powder to administer though a feeding tube (or if capsules must be opened to remove powder for administration via a feeding tube) these operations should only be done under a biological safety cabinet by personnel wearing personal protection equipment.

Administration

The hospital wards are supplied with the ready-prepared drug solution by the central reconstitution service (e.g., the hospital pharmacy). Administration consists only of connecting the solution (bottle, bag, or syringe) with the infusion system or the perfusor, which was previously filled with physiological saline solution*. Therefore, the risk of aerosol production during administration is clearly lower than during reconstitution. To avoid personnel health hazards, the following precautions should be taken:

- The ready-prepared drug solutions should be stored separately from other medications.
- A gown, protective gloves, and a liquid-proof absorbent mat are to be used as protective equipment. The skin should be completely covered.
- There is increased risk for personnel if infusion bottles or bags are dropped and burst. Therefore, trousers and closed shoes should always be worn while handling these materials.

Tips for the Administration of Cytostatic Solutions

- Use a swab or a cotton pad when injecting into a cytostatic drug solution.
- Fill the infusion system with the carrier solution (usually physiological saline solution).
- Always inject into standing infusion bottles. Never inject into hanging bottles.
- When the application is finished, do not remove the infusion system from the bottle and do not break it off, but dispose of the bottle and infusion system as a unit.

*All connections should be made with a Luer Lock system to ensure correct and safe connection even under pressure.

Nursing of Patients Receiving Cytostatic Drugs

When nursing chemotherapeutically treated patients, special care is required in handling patient excretions. Bleomycin, for example, is excreted unchanged in the urine up to 70 percent within 24 hours. Frequently, cytostatic drugs are metabolized within the body, however their metabolites retain their cytostatic effect. Some cytostatic drugs are activated by metabolism.

An example of this is cyclophosphamide, which can be recovered in the urine with approximately 20% in its original form and approximately 40% as partially active (alkylating) metabolite. Moreover, in some cases, the excretion over a long period of time of some cytostatic drugs must be considered. Thus, the excretion of vincristine, vinblastine, and vindesine in feces can last over 3 weeks. An overview of the excretion rates of different cytostatic drugs is provided in the Appendix.

Tips for Nursing Patients Receiving Cytostatic Drugs

- Cover the mattress of the patient bed with a protective plastic layer.
- Dispose of patient excretions into the sewage system, if this conforms to local regulations.
- Wear protective gloves and a gown while handling patient excretions. Special care is needed when cleaning the containers.
- Contaminated linen should be put into the laundry bag immediately. Wear protective gloves and a gown to do so. The laundry bag is to be clearly labeled to inform the laundry personnel of potential hazards.

Extravasations

If extravasations occur, the following rules are to be followed:

1. Stop the infusion – Do not remove the canula!
2. Inform a physician.
3. Aspirate the extravasated drug.

The subsequent therapy of extravasations is controversial and depends on the particular cytostatic drug (see references in the Appendix and contact the manufacturer).

Special Requirements for Home Care

Due to cost or patient convenience, chemotherapy is increasingly being shifted from hospitals to homes. The preventive measures do not differ in principle from those for in-patient treatment, however, the following additional management concerns must be addressed:

- The administration of the cytostatic drug solution is best performed in oncological practices.
- The reconstitution of the ready-prepared cytostatic drug solutions takes place in a local pharmacy, which receives and disposes of the bulk-contaminated wastes. Waste disposal has to be coordinated with the pharmacy.
- To collect the strongly contaminated wastes at the home of the patient and to transport these to the pharmacy, sturdy, firmly sealable and labeled containers must be available for home health care personnel.
- Because the majority of the time the patient is not nursed by professional staff, but by relatives, the hazards should be pointed out to the caretakers. The caretakers should be trained in handling cytostatic drugs.
- For the patients and those in close contact with them, a team of well-trained personnel must be available for further inquiries and support around the clock (at least by telephone in a hospital with oncological expertise). The team should be made up of at least oncological nursing professionals, cancer specialists and pharmacists.

Disposal of Cytostatic Waste

By law, cytostatic waste has to be disposed of as hazardous waste by incineration in most countries. Unfortunately, there is no further detail regarding the degree of contamination, or exactly what is to be considered a cytostatic waste. Most guidelines recommend a differentiation between trace and bulk-contaminated waste (OSHA – Occupational Safety and Health Authority, ASHP – American Society of Hospital Pharmacists, LAGA – Länderarbeitsgemeinschaft Abfall, ÖNORM – Österreichische Norm).

While trace-contaminated waste (e.g., swabs, gloves, and empty infusion bottles) can be disposed of together with household waste, bulk-contaminated waste (e.g., partly empty infusion bottles or syringes) requires special treatment, normally high temperature incineration e.g., > 1000°C.

In fixing the residues, the National Institutes of Health (U.S.) recommend the limit of 3 percent of the net weight of the container contents.

Advice regarding a definition of residual materials may be taken from local waste regulations. In any event, it is necessary to adhere to appropriate safety measures in order to avoid exposing personnel.

Highly-concentrated cytostatics (e.g., stock solutions or perfusor syringes) generally have to be disposed of as hazardous waste.

Disposal

Before disposal in special containers, the strongly contaminated cytostatic drug wastes are to be sealed into plastic bags. Special devices are not necessary, and a domestic heat sealer is sufficient. Cytostatics can also be inactivated by chemical reactions. Most inactivation methods are very complicated and should be carried out with well-founded chemical knowledge and duly observing industrial safety standards. In a hospital, this is only possible in laboratories or in the pharmacy.

Furthermore, it must be noted which substances and metabolites result from this treatment and the degree of their risk-potential. In addition, it must be proven that a mutagenic potential no longer exists. The remaining solutions cannot simply be flushed away in the sewage system. In most countries, they must be disposed of in accordance with their potential hazard. For these reasons, chemical inactivation of the cytostatic drugs is not advised.

Tips for Disposal of Cytostatic Waste

- Dispose of trace-contaminated waste (e.g., swabs, gloves, empty infusion bottles) together with domestic waste.
- Dispose of bulk-contaminated waste or highly concentrated solution as special waste (in accordance with local requirements).
- Seal bulk-contaminated waste in plastic bags (domestic bags and heat sealers are sufficient).
- Use high temperature incineration for special waste, e.g., > 1000°C.
- Dispose of patient excretions into the sanitary sewage system (in accordance with local requirements).

Cleaning Procedures After Accidents

If cytostatic drug solutions or powder are spilled (e.g., by bursting of infusion bags or breaking of ampules), the affected area must be isolated, labeled and cleaned immediately. If necessary, contaminated persons must be decontaminated at once. During cleaning, a protective suit (or a gown and overshoes), protective gloves, safety goggles, and a respirator mask should be worn. To clean up after accidents, spill kits with the following contents should be kept in or near work areas:

- two pairs of protective gloves
- a liquid-proof gown
- safety goggles
- respirator mask (high-efficiency particulate (HEPA))
- overshoes
- a sufficient quantity of absorbent cloth (cellulose, ChemoSorb, etc.)
- a small plastic scoop and tongs to collect glass fragments
- easy to seal waste disposal bags labeled "Cytostatic Drugs"
- hazard signs or barrier tape

The contaminated area is first to be covered carefully with a thick layer of cellulose or other absorbing material, in order to soak up the substance without producing splashes. Use dry cellulose for spilled solutions and damp cellulose for spilled powder (see "Tips for Clean Up After Accidents"). Thereafter, the surface (which should be as dry as possible) has to be cleaned with cellulose soaked in 70 percent alcohol and afterwards with cellulose soaked in a soap solution.

Under no circumstances should aerosol or dust be produced by direct spraying of water or cleaning solution or by using brooms or vacuum cleaners.

In order to avoid skin or eye contact with the residue of the spilled material, special care is required while taking off protective clothing.

Tips for Clean Up After Accidents

- Isolate the affected areas, ideally consult a second person as "supervisor".
- Use hazard signs or barrier tape.
- Wipe up spilled liquids with dry cellulose.
- First cover spilled powder carefully with damp cellulose. Then wipe up the damp substance with dry cellulose.
- Collect glass fragments with tongs and a scoop.
- Dispose of waste and heavily contaminated clothing in suitable containers.

Routine Cleaning Procedures

No special cleaning methods are necessary for daily room cleaning – the use of water and cleaning agents is normally sufficient.

Work surfaces and walls of safety cabinets are to be cleaned first with water and afterwards with 70 percent alcohol. To prevent explosions, alcohol must not be applied in large quantities (< 50ml/m²) and the cleaning cloth should only be dampened.

The requirements for cleaning personnel, including the selection of personal protection equipment, will depend on the exposure during handling of cytostatic drugs:

- In areas in which cytostatic drugs are not handled very often (e.g., laboratories), the cleaning personnel should be informed that cytostatic drugs may be present. While cleaning the work surfaces and using the cleaning solution, protective gloves should be worn.

- In areas in which cytostatic drugs are handled more often (e.g., reconstitution areas or oncological wards), cleaning personnel should be trained to handle cytostatic drugs (hazardous potential, protection measures, and waste disposal). During cleaning, skin contact with cytostatic drugs should be avoided by wearing protective gloves as well as proper clothing (e.g., trousers and closed shoes).

First Aid

In case of contamination of the skin with cytostatic drugs, different first aid measures are to be taken depending upon the type of cytostatic drug. In many cases, immediate thorough washing with water is sufficient. For cytostatic drugs where this is not sufficient, specified recommended measures are provided in the Appendix.

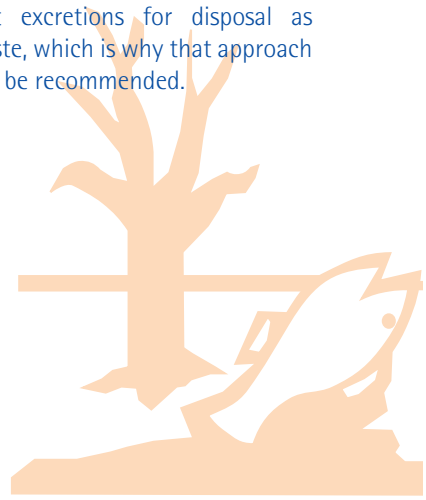
Furthermore, if there is eye contact with a cytostatic drug, contact an eye specialist immediately. If a cytostatic drug has been swallowed unintentionally, a physician is to be contacted immediately. The nearest poison control center should be consulted for specific advice, if necessary (the telephone number should be specified in the operating procedures). Any accident must immediately be reported to the designated occupational physician and documented. An example of an accident report form is provided in the Appendix.

Environmental Impact of Cytostatic Drugs

Cytostatic drugs can pass into wastewater, both through liquid residues and through patient excretions. Since the majority of cytostatic drugs are not rapidly biologically degraded, traces can pass though the wastewater treatment plants and reach surface water, as has been shown for cyclophosphamide and ifosfamide. After entry into the aquatic environment, cytostatic drugs may be degraded in other ways such as by sunlight or hydrolysis. Some cytostatic drugs, such as epirubicin, are strongly adsorbed by sewage sludge. If this sludge is then used agriculturally, it might affect soil (micro) organisms.

The occurrence of cytostatic drugs in drinking water has not been documented. As a precaution, however, the entry of cytostatic drugs into the environment should be minimized. The concentrations in patient excretions are so small that based on present knowledge, a hazard for human health and the environment is unlikely.

It is possible, however, that a potentially higher exposure risk for health care personnel would result from the collection of patient excretions for disposal as special waste, which is why that approach should not be recommended.



Contents

Checklist for Self-Testing

1. Which of the following substances are potentially cytotoxic?
A) Cisplatin.
B) Paclitaxel.
C) Ifosfamide.
D) Acetylsalicylic Acid.
E) Epirubicin.
F) A, B, C and E.
G) Ciprofloxacin.

2. To minimize the risk for personnel and the environment, institutions in which cytostatic drugs are handled should provide:
A) Written operating procedures for all areas.
B) Periodic training of personnel.
C) Periodic personnel monitoring by occupational health services.
D) Comprehensive technical and personal protection equipment.
E) Brooms and scoops for cleaning up after accidents.
F) All of the above.
G) A, B, C and D.

3. Practical experience is an important component of any training program.
A) True. B) False.

4. Areas, in which cytostatic drugs are handled, should meet the following requirements:
A) Separation of non-contaminated and potentially contaminated areas is achieved by installing a specific room for changing clothes in front of the entrance to the reconstitution area.
B) Separate storage areas are provided for cytostatic drugs and food.
C) Thorough cleaning should be easy to perform.
D) Access to the work area is possible for all personnel.
E) The work area must be clearly separated from areas for other activities.
F) For better air circulation, a work area as drafty as possible should be chosen (i.e., behind swinging doors)
G) A, B and E.
H) A, C and E.
I) A, C, E and F.

5. Airflow within safety cabinets must be:
A) Laminar and horizontal.
B) Laminar and vertical.
C) Turbulent.

6. The exhausted air should be ducted:
A) To the outside.
B) Into the room.
C) After being filtered into the room.

7. Due to the high consumption of electrical energy, safety cabinets should be turned off after use.
A) True.
B) False.
C) Reduce airflow during the night.

8. Protective gloves should be changed:
A) Every 60 minutes.
B) Every 20 minutes.
C) After accidents or visible glove-contamination.

9. When working outside a safety cabinet, which of the following should be worn as additional protective clothing beside protective gloves and a gown?
A) Respirator mask.
B) Overshoes.
C) Safety goggles.
D) All above.
E) A and C.

10. Injection in cytostatic drug solutions before administration is to be performed:
A) Into standing bottles.
B) Into hanging bottles.
C) Either is acceptable

11. When the administration is finished, dispose of infusion system and bottle/bag:
A) As a unit.
B) Separately.

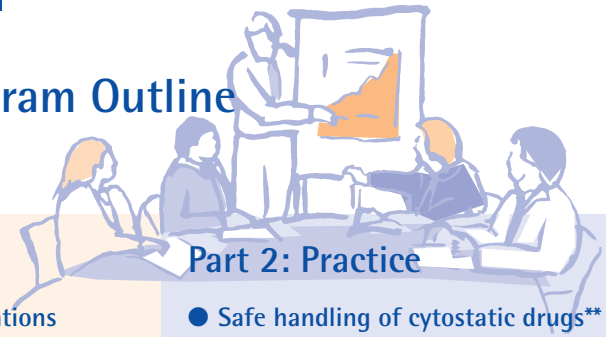
12. Cytostatic waste is to be disposed of:
A) As special waste.
B) Together with domestic waste.
C) According to its level of contamination, as special waste or together with domestic waste.

13. Spilled cytostatic drugs are cleaned:
A) By using a broom or a vacuum cleaner.
B) By wiping them up with an absorbent material without producing splashes.
C) After isolating the affected areas.
D) A and C.
E) B and C.

14. Generally, in waste water treatment plants cytostatic drugs degrade well.
A) True.
B) False.

Solutions: 1 - F, 2 - G, 3 - A, 4 - H, 5 - B, 6 - A, 7 - B, C, 8 - B, C, 9 - E, 10 - A, 11 - A, 12 - C, 13 - E, 14 - B

Training Program Outline



Part 1: Theory

- **Effects of the medications**
  - Mechanisms of action
  - Side effects
  - Hazardous potential
- **Legal regulations***
  - Occupational health
  - Waste
  - Waste water
  - Hazardous substances
- **Safe handling of cytostatic drugs**
  - Management
  - Operation instructions
  - Personal protective equipment
  - Technical protective equipment
  - Maintenance of technical protective equipment (procedures and intervals)
- **General cleaning procedures and intervals**
- **Behaviour in emergencies**
  - First aid measures
  - Contact persons (Health Surveillance Services, Poison Control Center)

* Further requirements should be adopted according to local requirements.

Part 2: Practice

- **Safe handling of cytostatic drugs****
  - Correct handling of personal and technical protective equipment
  - Maintenance of protective equipment
  - Avoidance of aerosols, splashes and dust-raising
  - Disposal of cytostatic waste
- **Cleaning procedures**
  - Handling of protective clothing
  - Spillage of powders and solutions
  - Location of the spill kit
- **Behaviour in emergencies**
  - Isolation of the affected areas
  - Cleaning procedures
  - Providing first aid

**During exercises in handling cytostatic drugs, dyestuffs can be used to show the proper and improper handling of the substances.

Training Documentation Form

Subject of course:

Date: Location:

Subjects:

Topics discussed:

Trainer:

Participants:

Name	Signature

	Operating Procedures	Number: Signature: Date:

Cytostatic Drugs

Reconstitution of Cytostatic Drug Solutions

Examples for Hazards

Highly flammable (F)

Irritant (Xi)

Toxic (T)
Very toxic (T^+)

Dangerous for the environment (N)

Hazards for humans and the environment

- Irritant effects or allergic reactions are possible after eye or skin contact.
- Side effects to bone marrow, digestive tract, gonads, and immune system are possible.
- Carcinogenic, mutagenic, and teratogenic effects cannot be excluded.
- Pregnant women and minors (e.g., less than 18 years old) must not have any contact with cytostatic drugs.
- Cytostatic drugs are not usually biodegradable and are therefore hazardous to the environment.

General handling

- Reconstitution has to take place in a safety cabinet with laminar and vertical airflow.
- Wear liquid-proof protective gloves and a liquid-proof gown.
- Change gloves frequently, e.g., at least every 20 minutes, or immediately in the case of visible contamination.
- Use a liquid-proof absorbent mat and reconstitution devices when reconstituting in sealed vials.
- Leave ventilation slots uncovered.
- After finishing work, clean the work surface with water and afterwards with 70 percent alcohol.
- Do not turn off the safety cabinet, even after use.
- Service the safety cabinet periodically, in accordance with the manufacturer's recommendations.
- Label the containers for in-house transport.

Behaviour in emergencies (Emergency Tel.: _____)

- After spillage of cytostatic drugs, the contaminated area is to be isolated and cleaned immediately.
- Wear liquid-proof gloves and a gown, a respirator mask, and safety goggles during cleaning.
- Use a spill kit.
- Soak up spilled substances with sufficient quantities of absorbent material; avoid dust-raising and aerosol production.
- Clean biological safety cabinet first with 70 percent alcohol and then with a detergent solution.
- Dispose of contaminated materials as special waste.

First Aid (Emergency Tel.: _____ Poison Control Center Tel.: _____)

- Flush with plenty of cold water immediately; in addition, consult first aid chart.
- Seek medical attention immediately.
- Eye contact: flush with plenty of cold water immediately; in addition, consult first aid chart. Contact an eye specialist.
- Ingestion: seek medical attention immediately. Contact the nearest Poison Control Center.

Organisational requirements of the work place

Restrictions

Waste disposal (Contact person Tel.: _____)

- Collect trace-contaminated waste (e.g., gloves) separately from other waste in resistant and liquid-proof containers and dispose of it with domestic waste.
- Seal bulk-contaminated waste (e.g., remaining solutions) in plastic bags and dispose of it in liquid-proof and labeled containers as special waste.

For additional information, ask your doctor or pharmacist, or your safety or environmental expert.

	Operating Procedures	Number: Signature: Date:

Cytostatic Drugs

Administration of Cytostatic Drugs - Nursing of Patients Receiving Cytostatic Drugs

Examples for Hazards

Highly flammable (F)

Irritant (Xi)

Toxic (T)
Very toxic (T^+)

Dangerous for the environment (N)

Hazards for humans and the environment

- Irritant effects or allergic reactions are possible after eye or skin contact.
- Side effects to bone marrow, digestive tract, gonads, and immune system are possible.
- Carcinogenic, mutagenic, and teratogenic effects cannot be excluded.
- Pregnant women and minors (e.g., less than 18 years old) should not have any contact with cytostatic drugs.
- Cytostatic drugs are not usually biodegradable and are therefore hazardous for the environment.

General handling

- Wear liquid-proof protective gloves and a liquid-proof gown; cover skin completely.
- Use a liquid-proof absorbent mat; cover mattress of patient bed with a protective layer.
- Use a swab or a cotton pad when injecting into a cytostatic drug solution.
- Always inject into standing infusion bottles. Never inject into hanging bottles
- Fill the infusion system with the carrier solution (usually physiological salt solution).
- When the application is finished, do not remove infusion system from the bottle and do not break it off, but dispose of bottle and infusion system as a unit.

Behaviour in emergencies (Emergency Tel.:)

- After spillage of cytostatic drugs, the contaminated area is to be isolated and cleaned immediately.
- Wear liquid-proof gloves and a gown, a respirator mask, and safety goggles during cleaning.
- Use a spill kit.
- Soak up spilled substances with sufficient quantities of absorbent material; avoid dust raising and aerosol production.
- Dispose of contaminated materials as special waste.
- Put contaminated linen immediately into the laundry bag.
- Clean contaminated protective mattress coverings with soap and water.

First Aid (Emergency Tel.: Poison Control Center Tel.:)

- Flush with plenty of cold water immediately; in addition, consult first aid chart.
- Seek medical attention immediately.
- Eye contact: flush with plenty of cold water immediately; in addition, consult first aid chart. Contact an eye specialist.
- Ingestion: seek medical attention immediately. Contact the nearest Poison Control Center.

Organisational requirements of the work place

Restrictions

Waste disposal (Contact person Tel.:)

- Dispose of trace-contaminated waste (e.g., gloves, swabs) in sealable plastic bags together with domestic waste.
- Seal bulk-contaminated waste (e.g., remaining solutions and partially emptied infusion bags) in plastic bags and dispose of in liquid-proof and labeled containers as special waste.
- Dispose of patient excretions into the sewage system.

For additional information, ask your doctor or pharmacist, or your safety or environmental expert.

	Operating Procedures	Number: Signature: Date:

Cytostatic Drugs

Handling of Cytostatic Drugs at the Pharmaceutical Wholesaler, Pharmacies, and Warehouses

Examples for Hazards

Highly flammable (F)

Irritant (Xi)

Toxic (T)
Very toxic (T^+)

Dangerous for the environment (N)

Hazards for humans and the environment

- Irritant effects or allergic reactions are possible after eye or skin contact.
- Side effects to bone marrow, digestive tract, gonads, and immune system are possible.
- Carcinogenic, mutagenic, and teratogenic effects cannot be excluded.
- Pregnant women and minors (e.g., less than 18 years old) should not have any contact with cytostatic drugs.
- Cytostatic drugs are not usually biodegradable and are therefore hazardous to the environment.

General handling

- Check whether delivery contains cytostatic drugs.
- Handle with special care to prevent spills and breakages.
- Do not touch broken bottles, vials, or packages with bare hands.
- For damaged or moisture soaked packaging, immediately place the entire package and the materials using appropriate protective measures into a chemically resistant air-tight container. Finally, check the contents in an approved area (for example, a laboratory safety hood) while observing safety measures.
- If, during handling, the cytostatic materials appear to have contaminated the packaging or other materials, all materials should be placed in a chemically resistant, air-tight container and removed to an approved area for further handling (e.g., a laboratory safety hood).

Behaviour in emergencies (Emergency Tel.: _____)

- After spillage of cytostatic drugs, immediately isolate and clean the affected area.
- Wear a protective suit (or a gown and overshoes), gloves, a respirator mask, and goggles when cleaning spills.
- Use a spill kit.
- Soak up spilled solutions with plenty of dry absorbent material; avoid aerosol production.
- Remove spilled powder with plenty of damp disposable absorbent material; avoid raising dust.
- Take up glass fragments with a scoop and dispose of in proper containers.
- Clean surface with detergent solution and disposable towel, twice followed by clean water rinses.
- Use particular care when removing protective clothing to avoid contact of skin or eyes with residues of spilled material.

First Aid (Emergency Tel.: _____ Poison Control Center Tel.: _____)

- Flush with plenty of cold water immediately; in addition, consult first aid chart.
- Seek medical attention immediately.
- Eye contact: flush with plenty of cold water immediately; consult first aid chart. Contact an eye specialist.
- Ingestion: seek medical attention. Contact Poison Control Center.

Organisational requirements of the work place

Restrictons

Waste disposal (Contact person Tel.: _____)

- Dispose of product and contaminated material as special waste.
- Use liquid-proof, resistant, and clearly labeled containers for disposal.
- For disposal as special waste, refer to the local regulations.

For additional information, ask your doctor or pharmacist, or your safety or environmental expert.

Excretion Rates of Selected Cytostatic Drugs

Cytostatic drug	Excretion rate	Duration after therapy for which protective clothing is recommended when handling excreta*	
5-Fluorouracil	**Urine:** unchanged up to 15 % over 24 h	**Urine:** 2 days	**Faeces:** 5 days
Amsacrin		**Urine:** 3 days	**Faeces:** 2 days
Bendamustin		**Urine:** 6 days	
Bleomycin	**Urine:** unchanged up to 68 % over 24 h	**Urine:** 3 days	
Busulfan		**Urine:** 1 day	
Carboplatin	**Urine:** 60 % over 24 h	**Urine:** 1-2 days	
Carmustin	**Urine:** 55-65 % over 24 h	**Urine:** 4 days	
Chlorambucil		**Urine:** 1-2 days	
Cisplatin	**Urine:** unchanged and metabolized up to 75 % over 5 days	**Urine:** 7 days	
Cyclophosphamide	**Urine:** unchanged up to 25 % over 48 h; unchanged and metabolized up to 62 % over 48 h **Faeces:** up to 4 % after i.v.-dose Traces detected in sweat and saliva (in saliva up to 77 % of plasma concentration)	**Urine:** 3 days	**Faeces:** 5 days
Cytarabin	**Urine:** 90 % within 24 h	**Urine:** 1 day	
Dacarbazin		**Urine:** 1 day	
Dactinomycin	**Urine:** 20 % within 24 h	**Urine:** 5 days	
Daunorubicin		**Urine:** 7 days	**Faeces:** 7 days
Docetaxel	**Urine:** 60 % within 24 h	**Urine:** 1 day	**Faeces:** 2 days
Doxorubicin	**Urine:** unchanged and metabolized up to 15 % over 5 days **Faeces:** unchanged and metabolized up to 85 %	**Urine:** 6 days	**Faeces:** 7 days
Epirubicin	**Urine:** unchanged up to 11 % over 24 h	**Urine:** 3 days	
Etoposide	**Urine:** unchanged 40 to 50 % over 24 h **Faeces:** unchanged 2 to 15 % over 24 hours	**Urine:** 3 days	**Faeces:** 5 days
Fludarabine	**Urine:** 40-60 % over 24 h	**Urine:** 3 days	
Gemcitabine		**Urine:** 1 day	
Hydroxycarbamide	**Urine:** 50-80 % over 24 h	**Urine:** 2 days	
Ifosfamide		**Urine:** 2 days	
Idarubicine		**Urine:** 3 days	**Faeces:** 2 days
Lomustine	50-66 % over 24 h	**Urine:** 2 days	**Faeces:** 2 days

Cytotoxic	Excretion rate	Duration after therapy for which protective clothing is recommended when handling excreta*	
Melphalan	30-60 % over 24 h	**Urine:** 2 days	**Faeces:** 7 days
Mercaptopurine	**Urine:** unchanged 10 to 20 % over 24 h metabolized 10 to 40 % over 24 h	**Urine:** 2 days	**Faeces:** 5 days
Methotrexate	**Urine:** unchanged and metabolized 40 to 50 % (at low doses) and up to 90 % (at high doses) over 48 h **Faeces:** up to 9 %	**Urine:** 72 hours	**Faeces:** 7 days
Mitomycine		**Urine:** 1 day	
Mitozantrone	**Urine:** unchanged up to 6.5 % over 5 days metabolized up to 3.6 % over 5 days **Faeces:** up to 18 % over 5 days	**Urine:** 6 days	**Faeces:** 7 days
Nimustine	**Urine:** unchanged up to 13 %	**Urine:** 4 days	
Oxaliplatin	**Urine:** 40-50 % over 24 h	**Urine:** 3 days	
Paclitaxel	**Urine:** unchanged up to 13 % over 24 hours **Faeces:** more than 13 % over 24 hours		
Procarbazine	**Urine:** unchanged 5 % over 72 h metabolized 25-70 % over 72 h	**Urine:** 3 days	
Teniposide		**Urine:** 3 days	
Thioguanine		**Urine:** 1 day	
Thiotepa		**Urine:** 3 days	
Topotecan		**Urine:** 2 days	
Treosulfan	**Urine:** 90 % over 6 h	**Urine:** 1 day	
Trofosfamide	**Urine:** 60 % over 6 h	**Urine:** 1 day	
Vinblastine	**Urine:** unchanged and metabolized 13 to 33 % over 72 h; **Faeces:** unchanged and metabolised 10 up to 41 % over 72 h	**Urine:** 4 days	**Faeces:** 7 days
Vindesin		**Urine:** 4 days	**Faeces:** 4 days
Vincristine	**Urine:** unchanged 8 % over 72 h metabolized 4 % over 72 h **Faeces:** unchanged 30 % over 72 h metabolized 40 % over 72 h	**Urine:** 4 days	**Faeces:** 7 days
Vinorelbine		**Urine:** 4 days	**Faeces:** 7 days

*If not specified, at least 48h.

Sources: Harris and Dott (1985); Cass and Musgrave (1992); Graijny et al. (1993); Micromedex™ Drug Data Base (1997); Dimtscheva et al. (1998)

First Aid Measures*

Substance	Measures after contamination
Amsacrine	Immediate and thorough washing with soap and water.
Bleomycin	Immediate and thorough washing with soap and water.
Carboplatin	Immediate and thorough washing with soap and water. Apply a mild cream, if any transient stinging is experienced.
Carmustine	Immediate and thorough washing with soap and water. In cases of local irritation apply sodium bicarbonate solution.
Cisplatin	Immediate and thorough washing with soap and water. Apply a mild cream, if any transient stinging is experienced.
Cyclophosphamide	Immediate and thorough washing with soap and water. After eye contact, immediately irrigate with 0.9% sodium chloride solution.
Cytarabine	Immediate and thorough washing with soap and water. After eye contact, immediately irrigate with 0.9% sodium chloride solution.
Dactinomycin	Wash with water or sodium phosphate solution.
Daunorubicin	Immediate and thorough washing with soap and water or with sodium bicarbonate solution. After eye contact, immediately irrigate with 0.9% sodium chloride solution.
Doxorubicin	Immediate and thorough washing with soap and water or with sodium bicarbonate solution. After eye contact, immediately irrigate with 0.9% sodium chloride solution.
Epirubicin	Immediate and thorough washing with soap and water or with sodium bicarbonate solution. After eye contact, immediately irrigate with 0.9% sodium chloride solution.
Etoposide	Immediate and thorough washing with soap and water.
5-Fluorouracil	Immediate and thorough washing with soap and water.
Gemcitabine	Immediate and thorough washing with water. After eye contact, immediately, irrigate with 0.9% sodium chloride solution.
Idarubicine	Immediate and thorough washing with soap and water or with sodium bicarbonate solution. After eye contact, immediately irrigate with 0.9% sodium chloride solution.
Methotrexate	Immediate and thorough washing with water. Apply a mild cream, if any transient stinging is experienced. After eye contact, immediately irrigate with water or 0.9% sodium chloride solution.
Mitomycin	Very strong irritant; neutralize with several washes of 8.4% sodium bicarbonate solution followed by soap and water; avoid hand creams.
Others	Immediate and thorough washing with plenty of cold water is sufficient.

Source: Allwood, Wright and Stanley (1997) The Cytotoxics Handbook

* For further information see material safety data sheet supplied by the manufacturer

Contamination of Personnel with Cytostatic Drugs

date/time of the accident: **department/ward:**

1. Personal data

first name: **last name:**

activity:

❑ reconstitution ❑ application ❑ nursing
❑ other:

2. Accident

name of the cytostatic drug:

form of the cytostatic drug:

❑ original product ❑ reconstituted solution ❑ patient excretion
❑ contaminated material ❑ other:

means of contamination:

❑ skin contact ❑ eye contact ❑ inhalation
❑ ingestion ❑ other:

affected part of body:

protective clothing worn:

❑ gown ❑ gloves ❑ goggles
❑ respirator mask ❑ other:

short description of accident:

first aid measures:

doctor contacted:

Example for

Documentation of Cytostatic Drug Handling

Employee: _____

Date	working hours (h)	handled substance	amount in mg	remarks
7/15/98	4.5	Cyclophosphamide	340	spill: 2ml of solution (20 mg/ml)
		5-Fluorouracil	1200	bottle was contaminated
		Etoposid	230	
		Carboplat	1530	
7/16/98	3,5	Vindesine	230	
		Etoposid	420	
		5-Fluorouracil	3000	bottle was contaminated
		Ifosfamide	5400	

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List of Manufacturers

The following list does not claim to be complete. Please tell us if you have any suggestions for improvement so that we can include them in the next updated version.

Safety cabinets

Heraeus Instruments GmbH
P.O. Box 1563
D-63405 Hanau
Germany
Telephone: +49/6181/35-300
Fax: +49/6181/355973
Internet: http://www.heraeus.de

Labconco Corporation
8811 Prospect Avenue
Kansas City, MO 64132-2696
U.S.A.
Telephone: +1/800-821-5525
Fax: +1/816-363-0130
Internet: http://www.labconco.com
E-Mail: labconco@labconco.com

NUAIRE, Inc.
2100 Fernbrook Lane
Plymouth, MN 55447-4722
U.S.A.
Telephone: +1/612-553-1270
Internet: http://www.nuaire.com
E-Mail: nuaire@nuaire.com

HEMCO
111 N. Powell Rd.
U.S.A.
Independence, MO 64056, U.S.A
Telephone: +1/816-796-2900
Fax: +1/816-796-3333

Berner International GmbH
Mühlenkamp 6
D-25337 Elmshorn
Germany
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Gloves

Regent Hospital Products
Broxbourne EN106LN, U.K.
Telephone: +44/1992451111

Paul Hartmann AG
P.O. Box 1420
D-89504 Heidenheim, Germany
Telephone: +49/7321-36-0
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Allegiance Healthcare Corporation
1430 Waukegan Rd.
McGaw Park, Illinois 60085, U.S.A.
Telephone: +1/847-689-8410
Internet: http://www.allegiance.net

SCA Hygiene Products
P.O. Box 1429
D-85732 Ismaning
Germany
Telephone: +49/8035/800
Fax: +49/8035/80412
Internet: http://www.sca.se

Berner International GmbH
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D-25337 Elmshorn, Germany
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Fax: +49/4121/4356-20

Gowns

Kimberly Clark
World Headquarters
P.O. Box 619100
Dallas, Texas 75261-9100 U.S.A.
Telephone: +1/800/742-1996
(Customer Service Department)
Internet: http://www.kimberly-clark.com

3M Medical-Surgical Division, 3M Health Care,
3M Center, Building 275-4E-01,
St. Paul, MN 55144-1000 U.S.A.
Telephone: +1/800-228-3957
Fax: +1/612-733-9596.
E-mail: healthcare@mmm.com
Internet: http://www.mmm.com

Allegiance Healthcare Corporation
1430 Waukegan Rd.
McGaw Park, IL 60085 U.S.A.
Telephone: +1/847-689-8410
Internet: http://www.allegiance.net

Sage Products Inc.
815 Tek Drive
Crystal Lake, IL 60014-9693 U.S.A.
Telephone: +1/800-323-2220
Fax: +1/815-455-5599
E-Mail: customerservice@sageproducts.com
Internet: http://www.sageproducts.com

List of Manufacturers

Goggles

Fisher Safety
1801 Gateway Blvd., Suite 101
Richardson, TX 75080-3750, U.S.A.
Tel: +1-800-955-5090
Fax: +1-800-772-7702
http://www.fisherscientific.com

Uvex Arbeitsschutz GmbH & Co. KG
Würzburger Straße 181/189
D-90766 Fürth, Germany
Telephone: +49/911/9736-0
Fax: +49/911/9736-727
Internet: http://www.uvex.com

Aearo Company
One Washington Mall - 8th Floor
Boston, MA 02108-2610, U.S.A.
Telephone +1/617-371-4200
Fax: +1/617-371-4233
E-Mail: jimgray@indy.net
Internet: http://www.aearo.com

Respirator masks

3M Occupational Health and Environmental
Safety Division
3M Center, Building 275-6W-01
P.O. Box 33010
St. Paul, MN 55133-3010, U.S.A.
Telephone: +1/800243-4630
Fax: +1/8006461655
E-mail occsafety@mmm.com
Internet: http://www.mmm.com

Fisher Safety
1801 Gateway Blvd., Suite 101
Richardson, TX 75080-3750, U.S.A.
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FAX: +1-800-772-7702
http://www.fisherscientific.com

Aearo Company
One Washington Mall - 8th Floor
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Fax: +1/617-371-4233
E-Mail: jimgray@indy.net
Internet: http://www.aearo.com

Spill Kits

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E-Mail: customerservice@sageproducts.com
Internet: http://www.sageproducts.com

Berner International GmbH
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Preparation Mats

Sage Products Inc.
815 Tek Drive
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Fax: +1/815-455-5599
E-Mail: customerservice@sageproducts.com
Internet: http://www.sageproducts.com

Berner International GmbH
Mühlenkamp 6
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Telephone: +49/4121/4356-0
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Mini-Spikes

B. Braun Melsungen AG
Carl-Braun-Straße 1
D-34212 Melsungen, Germany
Telephone: +49/5661/71-0
Internet: http://www.bbraun.com

Berner International GmbH
Mühlenkamp 6
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Disposal containers

Gebr. Otto KG
Siegener Straße 69
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Telefax: +49/2732/776200

Sulo Eisenwerk Streuber & Lohmann GmbH
Bünder Straße 85
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