ASHP technical assistance bulletin on handling cytotoxic drugs in hospitals

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In recent years, much concern[1,2] has arisen over the known and postulated occupational hazards associated with the routine handling of cytotoxic drugs in hospitals and clinics.[a] This Technical Assistance Bulletin summarizes the published information on these hazards as of July 1984. This information, combined with expert opinion, is the basis for the remainder of the document—recommended policies, procedures, and equipment for handling cytotoxic drugs in a safe and reasonable manner. When establishing safe handling policies and procedures, hospitals must consider any new information and the professional judgments of their staffs as well as the recommendations herein.

Cytotoxic Drug Dangers

The danger to hospital personnel from handling a cytotoxic drug is a combination of its inherent toxicity and the extent to which workers are directly exposed to the drug in the course of carrying out their duties. This exposure[b] may be through inadvertent ingestion of the drug on foodstuffs (e.g., workers' lunches), inhalation of drug dusts or droplets, or direct skin contact. The variables that determine the occupational hazard of a drug to an individual include the following:

1. The *drug's chemical properties:* Alkylating agents, for example, likely are a greater hazard than antimetabolites.
2. The *susceptibility of the individual* to the drug's toxic effects. Sexual, racial, and other genetically related factors control this variable.
3. *Cofactors* such as dietary habits, smoking, and natural or man-made environmental contaminants may alter an individual's susceptibility to the effects of the drugs.
4. The *number of exposures, magnitude of any one exposure,* or *cumulative amount of exposure.* The quantitative aspects of these variables are uncertain. It may be that critical biological changes from cytotoxic drugs will not occur unless a certain threshold level has been exceeded. This threshold can exist for single exposure situations, i.e., unless any single exposure exceeds magnitude *X*, no adverse effects result. It also could remain until enough small exposures over time add up to *X*.
5. *Type of exposure,* such as skin contact or inhalation. If the drug is not absorbed through the skin, for example, it poses a smaller hazard to the worker in cases of direct skin contact than a drug that is readily absorbed. (Except for local reactions, which can be severe.)

Of the five interrelated variables, only 4 and 5 can be controlled to any substantial degree. Variables 2 and 3 very likely are not even known to the individual or the institution. Control of variables 4 and 5 is achieved through safety procedures and equipment.

The oncogenic and teratogenic effects[c] of therapeutic doses of several chemotherapy agents are well established,[3–7] though they are unpredictable. However, the long-term effects (e.g., cancer, organ damage) of continued exposure to very small amounts of such drugs remain a questionmark.

Several studies have attempted to assess indirectly the drugs' potential cancer exposure to hospital pharmacists and nurses.[8–12] These studies examined the urine mutagenicity or evidence of chromosome damage in subjects who prepared or administered chemotherapy injections. The mutagenicity and chromosome damage that was found was thought to show exposure to and absorption of the drugs that were handled. An association may exist between

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carcinogenicity and chromosome breakage or mutagenicity. Therefore, one might conclude that handling cytotoxic drugs entails some hazard to hospital personnel. ASHP believes that these studies, though not conclusive, do support the postulated occupational risks. However, several recent reports make the situation a bit more ominous. Palmer and co-workers[13] measured chromosome damage in 10 patients receiving chlorambucil. They found that the damage was cumulative and was related both to the daily dose and the duration of therapy. Another report[14] described permanent liver damage in three nurses who had worked 6, 8, and 16 years, respectively, in an oncology ward. On the basis of histories, the investigators suggested that the liver injuries may have been related to the intensity and duration of exposure to cytotoxic compounds. The chlorambucil study involved therapeutic doses of drug, and three cases of liver damage is a small base for drawing any final conclusions. Nevertheless, this information is disturbing in view of the fact that many pharmacy and nursing staff prepare or administer hundreds or even thousands of doses of cytotoxic drug solutions during their careers. If the oncogenic or toxic threshold is a cumulative one, strict compliance with safe handling procedures becomes critical.

The use of chromosome and mutagenicity studies as indicators of the occupational hazards of cytotoxic drugs has been questioned.[15] However, several researchers have employed more direct methods of determining whether or not workers have been exposed to and absorbed cytotoxic drugs handled in the customary manner. Demonstration that absorption has occurred would be strong support for the imposition of safety measures. (The absorption of drug would be presumed to be hazardous.) A letter in *The Lancet*[16] described a study that used the presence of thioethers in the urine as an indicator of exposure to alkylating agents. The mean urinary thioether concentration (UTC) was higher in a group of 15 oncology nurses after a five-day duty spell than it was when they returned to work after a three-day leave ($p < 0.01$). There was no difference between the mean "pre-exposure" UTC and that of a group of 20 nurses who never handled cytotoxic drugs. Twelve of the study group nurses wore gloves when handling cytotoxic drugs; none wore any other form of protective apparel. Drug preparation procedures were not reported. Using gas chromatography, Hirst's group[17] found cyclophosphamide in the urine of two nurses working in a cancer clinic who took no special precautions when handling the drugs. They also demonstrated that cyclophosphamide can be absorbed through intact skin. On the other hand, another group of researchers[18] looked for (but could not detect) platinum in the urine of 10 pharmacists and nurses who frequently prepared or administered cisplatin and other chemotherapy agents. However, these subjects employed several protective measures when working with the drugs; this may have influenced the results (and demonstrated the effectiveness of the safety precautions employed). Also, the assay method may not have been sensitive enough. In a different type of approach, Neal et al.[19] detected fluorouracil in the air in a medicine preparation room (and nearby office) where it was frequently prepared. A similar study[20] showed that routine drug manipulations in a horizontal laminar airflow hood contaminated the air in an i.v. admixture preparation room. Fluorouracil and cefazolin sodium were the test drugs employed.

To our knowledge, these are the only reports published to date that provide any immediate evidence that hospital staff may be exposed to cytotoxic drugs during the course of their work. The mutagenicity studies provide additional indirect support for exposure and absorption if one believes that urine mutagenicity or chromosome breakage studies are valid indicators of drug absorption.

In theory, correct and perfect preparation technique will completely prevent drug particles or droplets from escaping from their containers while they are being manipulated or administered. Our opinion is that near perfect technique is uncommon; therefore, contamination of the workplace and worker is likely without protective equipment and other safety measures. This is particularly true, we think, in the absence of any structured training and quality assurance programs covering the proper handling of hazardous drugs. (Such programs are most likely to be found in hospitals where cytotoxic drug preparation is centralized.) Beyond problems in technique, however, contamination also will occur from inevitable spills and breakage of cytotoxic drug solutions. ASHP believes that the occupational dangers of cytotoxic drugs can be summarized as follows:

1. If (injectable) cytotoxic drugs are handled in the same way as other less hazardous substances (e.g., potassium chloride injection), contamination of the work environment is almost certain to occur.
2. The limited data available suggest that this contamination may result in exposure to and absorption of the drugs by hospital staff and others. The amount of drug absorbed by any one individual on any given day probably is very small except for rare and unusual instances of gross contamination.
3. However, if future studies indicate that cytotoxic drug damage is cumulative, individuals with job responsibilities that require them to prepare or administer large numbers of cytotoxic drug doses for long periods of time (e.g., oncology nurses, pharmacy i.v. service staff) are at risk.
4. Considering the above, the establishment of procedures, equipment, and materials that demonstrably or theoretically prevent exposure to cytotoxic drugs in the hospital workplace is necessary.

Currently, the question is what safety precautions should be employed.

Safety Precautions

Ideally, the safety precautions employed would be those whose effectiveness and cost-effectiveness have been documented. Unfortunately, very little information relevant to hospital practice is available. Hoy and Stump[21] concluded that a commercial air-venting device effectively stopped the release of drug aerosols into the air during reconstitution of drugs packaged in vials. Anderson's study[9] provides support for wearing latex gloves and preparing chemotherapy drugs in a vertical laminar airflow containment hood (more accurately, a NSF Class II biological safety cabinet) rather than a horizontal laminar airflow hood. Common sense also suggests that the airflow characteristics of containment cabinets would protect workers whereas other laminar airflow cabinets would not. Two studies[22,23] looked at the permeability of vinyl and latex gloves to antineoplastic drug solutions. These studies found that the amount of drug solutions penetrating the glove material increases with longer contact time and decreases with greater thickness. No glove material tested was impervious to all drugs. However, the investigators did establish that gloves can provide considerable protection against skin contact. This is important since many chemotherapy agents are skin irritants or even vesicants and, as Hirst[17] showed, at least one (cyclophosphamide) is absorbed through the skin. An earlier report[24] provides additional evidence for wearing gloves and gowns. To our knowledge, these are the only published reports on this topic relevant to hospital practice.

The dearth of substantive data means that the protective measures chosen by a hospital will be based to a great extent on professional judgment rather than scientifically established fact. In some situations, no "best" choice exists. For example, some might feel that externally vented safety cabinets provide better worker protection than nonvented units. But this perceived benefit carries with it substantially higher installation and operating costs. Furthermore, the unit's exhaust system must be correctly designed and installed; if not, the cabinet might provide *less* protection to both the product and the worker than a nonvented unit. Finally, if the ductwork becomes contaminated with cytotoxic drug particles—a theoretical possibility after several years of heavy use—decontamination is extremely difficult, perhaps impossible. This situation illustrates how, for the same set of circumstances, two different "experts" could provide what appear to be contradictory recommendations.

Recommended Safe Handling Methods

The balance of this article presents our suggestions for policies, procedures, and safety materials to control, prepare, administer, and dispose of cytotoxic drugs. They are given in a format that can be used either as a base for establishing safe handling methods or for evaluating existing procedures as part of a quality assurance program. Many recommendations for handling antineoplastic drugs have been published since 1981.[25-28] Those presented herein are ASHP's opinion of a "conservative but reasonable" approach to the precautions that should be taken.

Our recommendations are in the format of evaluation criteria organized into four groups. We have alluded to the importance of a quality assurance program for cytotoxic drug handling. This format should be useful in establishing a quality assurance system for all nontherapeutic aspects of cytotoxic drug use. Each group begins with a broad goal followed by a set of specific criteria and recommendations for achieving the goal. The four goals reflect the following axioms for handling cytotoxic drugs:

1. Protect and secure packages of hazardous drugs.
2. Inform and educate hospital personnel about the special nature of antineoplastic drugs and train them in the safe handling procedures relevant to their responsibilities.
3. Do not let the drugs escape from their containers when they are manipulated (i.e., dissolved, transferred, or administered).
4. Eliminate the possibility of inadvertent ingestion, inhalation, and direct skin or eye contact with the drugs.

We emphasize that the handling of cytotoxic drugs is a complex issue and the advice of legal counsel, industrial hygienists, oncologists, and others should be obtained when establishing cytotoxic drug policy.

Goal I. Accidential contamination of hospital staff and visitors and the hospital environment with cytotoxic substances is prevented by maintaining the physical integrity and security of packages of cytotoxic drugs.

1. *Access to all areas where cytotoxic drugs are stored is limited to specified autorized staff.*

2. *A method for identifying for personnel, those drugs that need special precautions (e.g., antineoplastics) should be present.* One way to accomplish this is to post a list of all drugs covered by the special handling policies and to apply appropriate warning labels (see Figure 1) to all cytotoxic drug containers and shelves and bins where they are permanently stored.

3. *Written procedures for handling damaged packages of cytotoxic drugs are maintained.* Shipping cartons of cytotoxic drugs received damaged should be opened cautiously in an isolated area, preferably in a fume hood. Protective apparel, closed front gown, double disposable latex or vinyl gloves, a disposable dust and mist respirator, and eye protection should be worn. Broken containers and contaminated packaging materials should be placed in the designated receptacles as described in this article.

4. *Facilities (shelves, carts, counters, trays, etc.) for storing*

cytotoxic drugs are designed to prevent breakage. Bins, shelves with barriers at front, or other designs that reduce the chance of drug containers falling to the floor should be used.

5. *Methods for transporting cytotoxic drugs within the hospital do not cause breakage or leakage of their containers.* Conveyances that produce severe mechanical stress on their contents (for example, pneumatic tubes) should not be used to transport cytotoxic drugs. The drugs should be securely capped or sealed and properly packaged and protected during transport in order to further reduce the chance of breakage in a public area such as a corridor (the worst place for breakage).

Goal II. The preparation[d] of cytotoxic drugs does not result in contamination of the hospital work environment or staff with cytotoxic drug powders, dusts, liquids, or mists.

1. *Written policies and standard procedures for preparing cytotoxic drugs are maintained.*
   a. They should include a method for identifying for hospital staff the particular drugs covered by these policies.
   b. Policies and procedures should be consistent with applicable governmental regulations, professional practice standards, and the recommendations of pharmaceutical manufacturers, hospital safety officers, and other knowledgeable parties.
   c. Since several hospital departments, such as pharmacy, nursing, maintenance, housekeeping, and medical staff, will be involved with some aspect of the cytotoxic issue, preparation of safe handling policies and procedures must be a collaborative effort.
   d. All personnel who handle cytotoxic agents should receive a copy of the procedures pertaining to their responsibilities. Deviations from the standard procedures must not be permitted except under defined circumstances.
2. *A method for orienting all* involved *personnel to the special nature of cytotoxic drugs and the policies and procedures that govern their preparation is present.*
   a. The orientation should include, as appropriate, a literature review, discussion of the known and potential hazards of the drugs, and explanation of all relevant policies. Training done in association with the orientation should cover all relevant techniques and procedures and the proper use of protective equipment and materials.
   b. Staff who are pregnant or breast-feeding should be transferred to comparable duties that do not involving handling cytotoxic drugs, if they so request. (Hospital legal counsel may recommend that this policy be mandatory.) A policy covering those staff who are actively trying to conceive a child should also be established.
   c. Prospective temporary and permanent employees who may be required to work with cytotoxic drugs should be so notified and should receive adequate information about the policies and procedures pertaining to their use.
   d. Students, residents, and medical staff who are not hospital employees should be informed through customary channels that they will be expected to comply with established procedures for preparing, administering, and disposing of cytotoxic drugs and their associated waste.
3. *A system for verifying and documenting acceptable staff performance of and conformance with established procedures is maintained.* This is an important part of a program for assuring that cytotoxic drugs are being handled properly. Proper technique is essential to maintain the sterility of the product being manipulated and to prevent the generation of cytotoxic contaminants. Therefore, knowledge and competence of personnel should be periodically evaluated and documented. Very likely, this will involve a combination of written examinations and direct observation of an individual's performance, perhaps using the preparation of practice solutions as an evaluative technique. As noted, the monitoring of staff performance and the control of cytotoxic drugs usually are best achieved if their storage and preparation are centralized within one area or department.
4. *Sufficient information on the safe use of those cytotoxic drugs used within the hospital is maintained.*
   a. The pharmacy should maintain a loose-leaf notebook, index card, or computerized file containing information on the toxicity, acute exposure treatment (if available), chemical inactivators, solubility, and stability of cytotoxic drugs (including investigational agents) used in the institution.
   b. Currently, a large number of investigational agents that are cytotoxic are under clinical study in hospitals. Nurses should not administer any investigational drug unless they have received adequate information and instruction about its safe and correct use.
5. *Equipment, facilities, protective apparel, and other safety materials are available and used properly and consistently.*
   a. Safety materials should meet appropriate standards (e.g., NSF, NIOSH) when applicable.
   b. General agreement exists that cytotoxic drugs should be prepared in a NSF Class II containment cabinet. (Less agreement exists on whether or not the hood should be vented to the outside.) The only exceptions to this would be facilities where cytotoxic drugs are used very rarely. The hood must be disinfected and cleaned regularly and must be used correctly if the sterility of the product is to be retained and if the worker is to be protected from cytotoxic dusts and aerosols that might be generated during its manipulation.[29]
   c. Workers should wear talc-free disposable gloves and a solid front gown with closed cuffs. Gloves should be tucked into the gown's cuffs and changed after each use, if overtly contaminated, and at least hourly. (No skin on the person's wrist or arm should be exposed.) The gown should not be worn outside of the work area.
   d. If a Class II containment cabinet is unavailable, the drug should be prepared in a quiet work space, away from heating and cooling vents and away from other personnel. Good technique is critical. Work should be done on a disposable,

plastic-backed paper liner. The liner should be changed after the preparation is completed. Contaminated liners should be disposed of as per these guidelines. Eye protection and a disposable dust and mist respirator should be worn. Hydrophobic filter venting units should be used to reconstitute cytotoxic drug vials if done in the open.

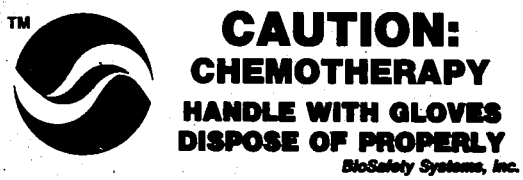
e. Syringes and i.v. sets with Luer-lock fittings should be used for preparing and administering cytotoxic drug solutions since they are less prone to separate than friction fittings. Care must be taken to assure that all connections are secure.

6. *Proper manipulative technique to maintain the sterility of the drug and to prevent the generation of cytotoxic drug contaminants is used consistently.*
   a. The contents of ampuls should be tapped down before the ampul is opened. A sterile gauze should be wrapped around the ampul neck when it is opened. The ampul should be wiped or sprayed with alcohol before opening.
   b. Substantial positive or negative deviations from atmospheric pressure within drug vials and syringes should be avoided through the use of appropriately designed venting needles or negative pressure techniques.[30]
   c. Each individual's technique should be evaluated before that person is assigned to prepare cytotoxic drugs. Thereafter, technique should be assessed periodically. This performance evaluation should be part of the facility's quality assurance program.
7. *Procedures for handling the preparation and dispensing of nonparenteral dosage forms of cytotoxic drugs are established and followed.*
   a. When preparing nonsterile liquid or powdered cytotoxic drug dosage forms (e.g., capsules), a disposable dust and mist respirator must be worn. It should be discarded after the preparation has been completed, the work shift is over, or if breathing resistance increases noticeably. These cytotoxic drug dosage forms should be compounded in a vertical airflow containment hood, glove box, or area away from drafts and traffic patterns.
   b. All items used to dispense oral or topical dosage forms of cytotoxic drugs (e.g., counting trays, spatulas) must be thoroughly cleaned after each use. Gloves should be worn.
   c. Disposal of unused or unusable oral or topical dosage forms should be the same as that for parenteral cytotoxic waste.
8. *Personnel know the procedures to be followed in case of accidental skin or eye contact with cytotoxic substances.*
   a. The hospital's medical staff should establish a first aid protocol for treating cases of direct contact with cytotoxic drugs, many of which are very irritating and can cause tissue destruction. This treatment is basically that used to treat contact with any caustic substance. A copy of the protocol should be posted wherever cytotoxic drugs are routinely handled. Medical attention should be obtained following initial first aid measures.
   b. Cytotoxic drug work areas should have a sink (ideally with an eyewash fountain) and a bottle of isotonic sodium chloride eye wash close by.
9. *All cytotoxic drugs are labeled with a warning label stating the need for special handling.* A distinctive label with the phrase "Chemotherapy—Handle with Gloves—Dispose of Properly" should be attached to all syringes and i.v. bags and bottles that contain cytotoxic drugs. All hospital personnel must be informed about the meaning of the label, i.e., that this item must be handled with special care in accordance with established procedure. An example of a suitable label is shown in Figure 1.

Goal III. Procedures for administering cytotoxic drugs prevent contamination of staff and the work environment with cytotoxic drug solutions.

1. *Standard procedures for the safe administration of cytotoxic drugs are established and followed.*
   a. Fluid administration sets and devices should be watched for leakage. A plastic-backed absorbant pad should be placed under the tubing during administration to absorb any leakage.
   b. I.V. sets should be primed (before adding the drug, if possible) into a sterile gauze pad, preferably inside a sealable plastic bag. Likewise, a sterile gauze pad should be placed close to the needle tip when air is expelled from syringes. Whether or not syringes should be recapped is a matter of individual judgment. The cap is protective; however, the recapping act is a large cause of inadvertant needle sticks.
   c. Syringes, i.v. containers (particularly the injection port), and i.v. sets should be wiped clean of any drug contamination with a sterile gauze pad. Injection ports should be sealed or capped after they are wiped.
   d. If possible, glass i.v. containers that have venting tubes should not be used. If such containers are used, a sterile gauze pad should be placed over the tube when it is inverted in order to catch any solution trapped in the tube.
   e. Personnel should wash their hands after preparing or administering cytotoxic drugs.
   f. All contaminated gauzes, syringes, i.v. bags, etc. should be disposed of properly.
   g. Gloves should be worn when urine and other excreta from patients receiving cytotoxic drugs must be handled. Contaminated garments should be changed. Skin contact and splattering should be avoided during disposal.
   h. Linen contaminated with cytotoxic drugs should be handled with gloves and treated in a manner analogous to those contaminated with infectious material. One procedure is to place them in specially marked water-soluble laundry bags. These bags should then be prewashed and the linens

Figure 1. Example of a warning label applied to packages and containers of cytotoxic drugs.



then added to other laundry for an additional wash. Items contaminated with cytotoxic drugs should *not* be autoclaved unless also contaminated with infectious material. (Cytotoxic drugs are chemical hazards, not biological hazards, and autoclaving serves no purpose.)

2. *A method for informing and training medical and nursing staff in these procedures is maintained.* (*See Goal II. 2.*)
3. *Appropriate protective apparel and other materials needed to protect the staff and work environment from contamination are readily available and used.* Supplies of disposable gloves and long-sleeve gowns, disposable plastic-backed absorbent liners, gauze pads, cytotoxic waste disposal bags, cytotoxic drug warning labels, plastic vials to contain discarded needles and ampuls, venting needle units, etc. should be conveniently located. A "Chemotherapy Administration Kit" is one way to furnish nursing and medical personnel with the materials usually needed to prepare and administer a cytotoxic drug safely.
4. *Personnel know the procedures to be followed in case of accidental skin or eye contact with cytotoxic drug solutions.* (*See Goal II. 6.*)

Goal IV. The hospital, its staff, and the outside environment are not contaminated with cytotoxic waste materials[e] produced in the course of using cytotoxic drugs.

1. *Written policies and procedures governing the containment, collection, and disposal of cytotoxic waste materials are established and maintained.* All hospital staff must be familiar with and follow the procedures established for collecting, segregating, and disposing of cytotoxic waste.
2. *Throughout the facility, cytotoxic waste materials are contained and segregated from all other hospital trash.*
   a. Cytotoxic waste should be placed in specially marked (with cytotoxic warning label) plastic bags or leakproof cartons. These receptacles should be in all areas where the drugs are commonly used. All and only cytotoxic waste should be placed in them. Receptacles used for glass fragments, needles, and syringes should be puncture proof. Cytotoxic waste should not be mixed in with any other hospital waste. Waste containers should be handled with gloves.
   b. Cytotoxic waste collected from pharmacy and patient care units should be held in a secure area in labeled, leak-proof drums or cartons until disposed of. This waste should be disposed of as hazardous waste by an appropriately licensed contractor. It should not be incinerated on-site unless the hospital has a high-temperature incinerator specifically designed for this purpose, and only if local law permits. (Cytotoxic waste incineration is an unsettled issue; see reference 31 for further information on this subject.)
3. *Materials to clean up spills of cytotoxic drugs are readily available and personnel are trained in their proper use. A standard clean-up protocol is established and followed.*
   a. "Spill Kits" containing all of the materials needed to clean up spills of cytotoxic drugs should be prepared and kept in a readily accessible location(s). The kit should include sealable plastic waste disposal bags (labeled with the cytotoxic warning label), disposable dust and mist respirator, splash goggles, absorbent sheets or powders, two pair of gloves, and a small scoop to collect glass fragments. Disposable coveralls and shoe covers should be available.
   b. Spills and breakages must be cleaned up immediately by a person trained in the proper clean-up procedures. The basic clean-up procedure will be as follows: (1) if outside the containment cabinet, identify the spill with a warning sign so that other people in the area do not touch it; (2) wearing the protective apparel (including double gloves), carefully remove any broken glass; (3) absorb the liquid or, if it is a powder, remove with damp disposable towel; (4) for spills on floors or countertops, wipe clean with detergent solution, then several times with water; for spills inside the hood, wipe clean with sterile water and then with alcohol; (5) place all clean-up materials in the cytotoxic waste disposal bags and seal. (The general clean-up procedure will vary somewhat depending on the location and volume of the spill.)
   c. The circumstances and handling of substantial spills should be documented.
4. *Cytotoxic waste is disposed of in accordance with all applicable governmental regulations.*

Other Cytotoxic Issues

Three cytotoxic drug issues that cannot be dealt with solely at the individual hospital level deserve comment. First, the hospital community should consider the advisability and feasibility of establishing a national registry of hospital personnel who prepare and administer chemotherapy agents routinely. This might provide epidemiological data that would help define the occupational health danger associated with the drugs. Second, no completely acceptable method for disposing of cytotoxic drug waste is on the horizon. High temperature incineration is fraught with technical difficulties and is easier said than done on a large scale. Disposal in hazardous chemical landfills has substantial disagreeable political and public relations overtones because of the landfills' potential environmental dangers. Hospitals could find themselves entangled in the controversy of hazardous waste disposal even through cytotoxic drug wastes are only a very small part of the overall toxic waste disposal problem. Third, many cytotoxic drugs are excreted unchanged or as equally toxic metabolites. The amount of cytotoxic drug transferred to the environment (primarily the water supply) from this source greatly exceeds that from the hospital trash pathway. No method to reduce this source of contamination likely will be found in the foreseeable future.

It is appropriate to note here that no method currently exists for routinely monitoring personnel for evidence indicative of cytotoxic drug exposure. (Chemical analysis of urine for the presence of cy-

totoxic drugs appears at present to be the monitoring method most likely to prove useful.) Therefore, the institution should have a strong quality assurance program that periodically evaluates and verifies staff adherence to and performance of the established safe handling policies and procedures. Though quality assurance programs usually are for the benefit of patients, in this case, they serve the institution's staff as well.

Though this document has dealt solely with internal hospital procedures, we also recommend that an institution's ambulatory and home-care patients be given the instruction and materials that will enable them to safely handle and dispose of any cytotoxic drugs they are taking.

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[a] A substantial number of cytotoxic drug regimens are administered in physicians' offices and other nonhospital sites. The extent to which the safe handling issue has been addressed in these settings is not known.

[b] *Exposure* means skin contact, inhalation, or inadvertent ingestion of small amounts of drug dusts, liquids, or aerosols.

[c] Additional hazards related to the strong irritant effect many of these agents exert on tissues exist as well.

[d] Preparation of cytotoxic drugs usually involves the addition or removal of a calculated volume of solution from an ampul or vial, and packaging and labeling it in a form suitable for administration (either as a filled syringe or diluted in a large or small volume parenteral fluid.)

[e] Cytotoxic waste materials: any object to be discarded that is or presumed to be contaminated with cytotoxic substances. This includes used disposable gloves and gowns, syringes, vials, ampuls, i.v. bags and bottles that held cytotoxic drugs, and materials used to clean up spills of these drugs.

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