Regulations and Recommendations for Appropriate Disposal of Antineoplastics

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The increase in the amount of toxic substances and the inappropriate disposal of them by institutions and health service industries are a threat to public and environmental health. In spite of federal regulations and evidence-based scientific recommendations for the appropriate disposal of chemical substances, some companies and institutions still do not implement these recommendations in the work area. Meanwhile, waste continues to pollute the land, the air, and the water, exhausting natural resources and, eventually, harming the human health (1).

Approximately 5.5 million workers are exposed to drugs and hazardous materials in Puerto Rico and in the United States (1-2). In 2005, Puerto Rico generated 22.6 million pounds of solid waste including biomedical waste and carcinogens (3-4). Some companies that manage this type of waste face ethical and financial dilemmas and, on occasion, choose to inappropriately dispose of hazardous waste. The cost of disposing a pound of hazardous waste is approximately $2.00 when it is incinerated by a company that has an incinerator certified by the Resource Conservation and Recovery Act (RCRA); but it would only cost $0.35 in a non-certified facility (5).

In 2007, a company in Puerto Rico inappropriately disposed of some biomedical waste and polluted an area of Caguas. To remedy the situation, the Environmental Quality Board hired Western Medical to appropriately dispose of this waste at a cost of approximately $3.2 million (6). This situation stresses the importance of properly disposing toxic waste.

The objective of this paper is to review the regulations and evidence-based recommendations for the appropriate disposal of antineoplastic medications and to update the reader on this important issue.

Regulations and recommendations

There are various agencies and professional organizations that are in charge of establishing controls regarding the management of hazardous waste. The Occupational Safety and Health Administration (OSHA) and the Environmental Protection Agency (EPA) are regulatory agencies that establish regulations regarding the management of antineoplastics that must be obeyed by law.

OSHA regulates the personal protective equipment used by employees, the information provided to the employee, the employee training, the workplace exposure record, the preparation area equipment, the evaluation of respirator use, and the disposal of hazardous drugs (7-8). In addition, the OSHA Technical Manual provides some recommendations about preparation, administration, manufacturing, and disposal of hazardous materials. These recommendations guide the institutions to comply with OSHA regulations (9).

The EPA focuses on the establishment of regulations for the appropriate disposal of hazardous materials. Appropriate disposal includes generation, transportation, treatment, and storage of this type of waste. The United States Congress gives this authority to the EPA by a federal law enacted in 1976 [Resource Conservation and Recovery Act (RCRA)] (10). Under this law, Congress establishes the initial guides and guidelines of the EPA for the management of hazardous waste (11).

The National Institute for Occupational Safety and Health (NIOSH)(12), the United States Pharmacopeia (USP)(13), and the American Society of Health-System Pharmacists (ASHP)(14) are organizations that make recommendations based on scientific evidence.

At the local level, a regulation signed on December 30, 2008 (Regulation #133 of the Secretary of Health and Regulation #7658 from the Department of State) establishes that the recommendations in Chapter 797 of the United States Pharmacopeia must be observed. This regulation was enacted by law 247 on September 3, 2004 (Pharmacy Law of Puerto Rico) (15).

Definitions of hazardous drugs and waste

Once a hazardous drug is going to be disposed of it is considered hazardous waste.

- NIOSH defines as hazardous drugs those agents used for the treatment of cancer (antineoplastic), antiviral drugs, hormones, bioengineered drugs, and other miscellaneous drugs (12).
- EPA defines as hazardous waste all compounds that are specified by the RCRA or that comply with at least one of the following criteria: is corrosive, toxic, reactive, or

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flammable (16). Waste that has these properties is known as *characteristic waste*.

RCRA's lists

EPA subclassifies the types of waste as either U or P. Agents in the P category are acutely toxic. Antineoplastics included in this category are listed in Table 1.

These lists have not been updated since 1976 (12, 14). After this date, many new antineoplastics have emerged and have not been included. For this reason, NIOSH and ASHP have made some recommendations about how to dispose of drugs that are not included in these lists (12, 14). A list of some antineoplastic drugs classified as hazardous by NIOSH may be found in the appendix. Each institution should create its own list of drugs considered to be hazardous. The information can be obtained from the NIOSH Alert, which offers a section that explains how to generate your own list of hazardous drugs (12).

Disposal of hazardous waste and antineoplastics

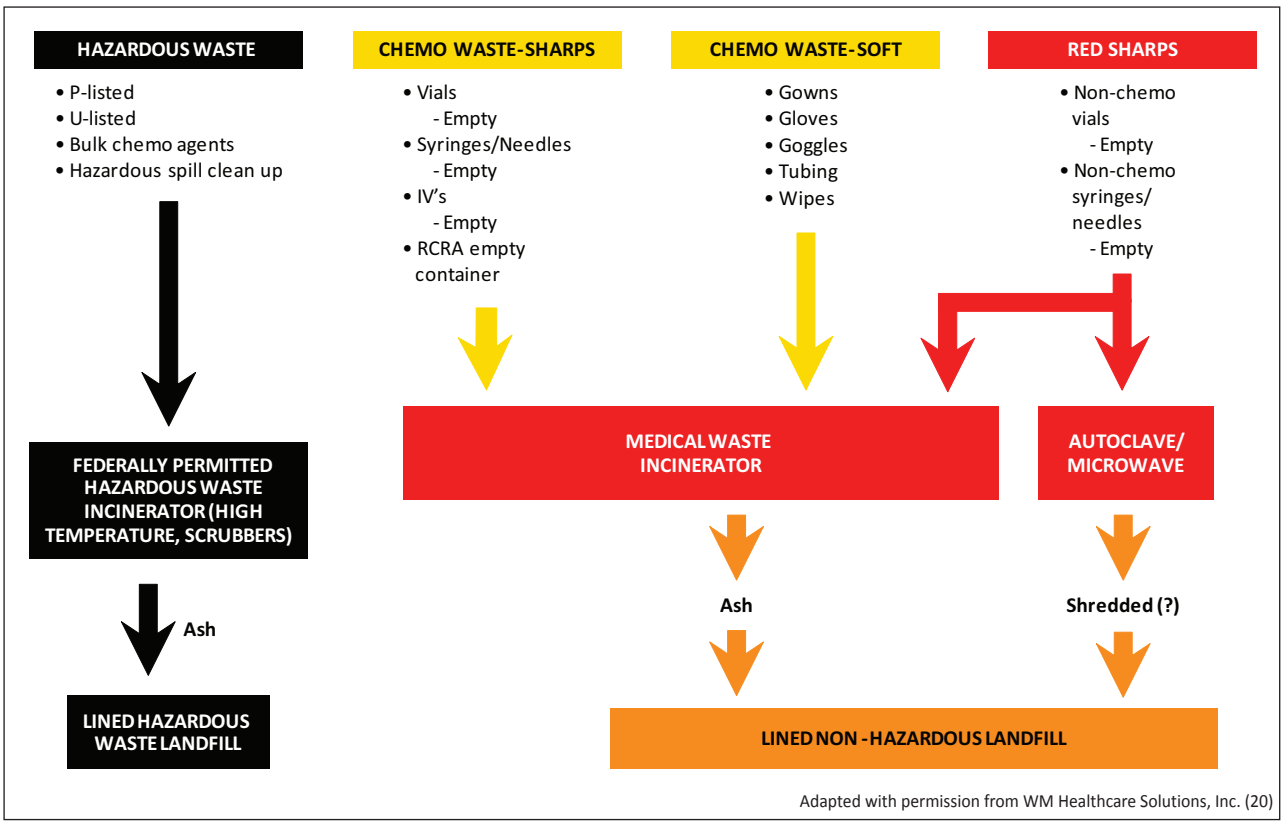
Antineoplastic waste generated by a company or institution must be disposed of separately from regular waste and infectious materials because the incineration process for antineoplastics is different from that of regular waste as a result of the regulations established by the regulatory agencies (12). The EPA specifies that *characteristic waste* must be incinerated in an RCRA incinerator which uses higher temperatures and a scrubber system (16).

OSHA and ASHP recommend that waste from hazardous drugs (including antineoplastics) that have more than *trace contamination* be disposed of in a way similar to drugs in the RCRA's list (Table 1) (9, 14). *Trace contamination* refers to a material that has been in contact with antineoplastic agents such as gloves, coats, needles, syringes, *RCRA empty containers*, empty lines, etc.

Table 1.

Antineoplastics classified as hazardous waste* (40 CFR 261.33)	List	Assigned number
Arsenic trioxide (Trisenox®)	P	P012
Cyclophosphamide (Cytoxan®)	U	U058
Chlorambucil (Leukeran®) U	U	035
Daunorubicin (Daunomycin®, Cerubidine®)	U	U059
Diethylstilbestrol	U	U089
Melphalan (Alkeran®)	U	U150
Mitomycin (Mitomycin C®, Mutamycin®)	U	U010
Streptozocin (Zanosar®, Streptozocin®)	U	U206
Uracil Mustard (Uramustine®)	U	U237

*U.S. Environmental Protection Agency (EPA) (17-18), National Archives and Records Administration (19).



Adapted with permission from WM Healthcare Solutions, Inc. (20)

Figure 1. Recommended Changes for Hazardous and Trace Chemotherapy Waste Disposal.

RCRA *empty containers* are an exception to the regulations established by the EPA for the disposal of hazardous waste. This means that some used containers do not have to be disposed of in an RCRA incinerator (14). These include:

- Containers that had a hazardous waste from list P in which the waste has been completely removed and the container has been washed 3 times.
- Containers that had a hazardous waste from list U or a substance classified as characteristic waste and that does not constitute more than 3% of the weight of the container.

Hazardous drug waste with more than *trace contamination* is called *bulk hazardous drug waste*. *Bulk hazardous drug waste* refers to waste from drugs that are in list P and U (Table 1), *characteristic waste*, any container that is not classified as an *RCRA empty container*, and materials used to clean spills (14).

In short, *RCRA hazardous waste* and bulk chemotherapy waste from drugs that have not been classified as RCRA hazardous waste after 1976 should be incinerated in a RCRA-permitted treatment, storage and disposal facility (12, 14). An example of the processing of these materials is given in Figure 1.

Facilities authorized for the treatment, storage, and disposal of hazardous drugs manage waste under RCRA's Subtitle C. These facilities need an RCRA permit for the use of duly certified incinerators; these and other requirements are available in the Code of Federal Regulations (12, 16). Before this type of waste arrives at the phase of incineration, it is important to know how companies or institutions should manage this waste. It is the responsibility of each institution to make sure that the company that they hire manages these substances adequately.

Bags and containers that are used to dispose of antineoplastics, as well as biomedical waste, must be leak proof and resistant to perforations. These vary in color, and, therefore, in use (9, 14, 16, 21).

- *Red bags or containers* - These are used for medical waste or infectious waste and must be labeled with a universal symbol to denote that they represent a biological hazard or biohazard, thus preventing the exposure of employees to infectious materials (22).
- *Yellow bags or containers* - They are used for antineoplastic waste and materials contaminated by them. Correct disposal ensures that employees are not exposed to volatile gases and aerosol particles that these toxic substances may emit (12).
- *Blue or black containers* - Some companies sell blue or black sharp containers to use for *bulk hazardous waste*, P-listed, U-listed, and materials used to clean up hazardous drug spills. In this way, they are differentiated from waste that has to be incinerated in a certified RCRA container.

It is very important that the people that manage these substances label the waste appropriately. In this way, the inappropriate disposal of toxic and infectious materials can be prevented as well as the adverse effects to the health of those that come into contact with them. Also, the appropriate management of waste contributes to environmental conservation avoiding the negative impact these products have on nature.

It is the duty of each institution to establish specific protocols that provide safety to the employees and guarantee the quality of the product. In Puerto Rico, the Environmental Quality Board verifies that institutions comply with required disposal procedures for hazardous drugs and biomedical products. A discussion of important aspects to take into consideration for the disposal of antineoplastics follows.

Important aspects to consider in the disposal of hazardous waste (that includes antineoplastics) (9, 12, 21, 23-30)

When disposing of hazardous waste, the employee should:

- Use two protective gloves to manage waste (nitrile, neoprene rubber and polyurethane).
- Use gowns with polyethylene or vinyl coatings when disposing of hazardous drugs spills or materials used during intravenous preparation of antineoplastics.
- Deposit needles and syringes, blades, and other sharp materials that have been used to manage antineoplastics in a yellow sharp container designed for this use. Needles and other sharp materials must not be covered or broken upon disposal.
- Place non-sharp hazardous waste (e.g. coats) in a yellow bag.
- Deposit antineoplastics and materials used for the preparation of antineoplastic in a strong container or yellow bag in order to be appropriately incinerated. Since infectious materials may go through an autoclave or microwave, it is important to remember not to put antineoplastics in a red bag or container because they will be disposed of as infectious material and could potentially expose those that manage these materials to the gases emitted by these substances.
- Dispose of bulk hazardous materials in the container designed to be incinerated in RCRA certified incinerators.
- Seal the bags or containers that contain hazardous materials once they are full and put them in a bag or any other container that the waste disposal company provides for this service.
- Prevent the contamination of the outside of the bag or container of hazardous waste with toxic substances that may be accidentally spilled. If the outside gets contaminated, place the bag or container in a second container to prevent the contamination of surfaces and employees.
- Dispose of all hazardous material through subcontracted companies that are duly authorized for this purpose, following the appropriate regulations.

In addition to following good practices in the composition and management of toxic substances, it is indispensable that personnel know the precautionary measures pertinent to the disposal of these substances. It is the responsibility of the pharmacist to adequately implement protocols for the management of antineoplastics and other hazardous materials. The pharmacist also has the duty of enforcing the compliance

of these protocols in their respective practice scenarios to prevent the exposure of employees to these substances and avoid other complications such as environmental pollution and long-term health problems. Given that these drugs may cause irreversible damage to human health, including cancer and fertility problems, federal regulations and NIOSH and ASHP's recommendations should be implemented in the work field.

Sample list of antineoplastics that should be handled as hazardous

Aldesleukin	Idarubicin
Alemtuzumab	Ifosfamide
Alitretinoin	Imatinib mesylate
Altretamine	Irinotecan HCl
Amsacrine	Letrozole
Anastrozole	Lomustine
Arsenic trioxide	Mechlorethamine
Asparaginase	Megestrol
Azacitidine	Melphalan
Bacillus Calmette-Guerin	Mercaptopurine
Bexarotene	Methotrexate
Bicalutamide	Mitomycin
Bleomycin	Mitotane
Busulfan	Mitoxantrone HCl
Capecitabine	Nilutamide
Carboplatin	Oxaliplatin
Carmustine	Paclitaxel
Chlorambucil	Pegaspargase
Cisplatin	Plicamycin
Cladribine	Procarbazine
Cyclophosphamide	Raltitrexed
Cytarabine	Streptozocin
Dacarbazine	Tacrolimus
Dactinomycin	Tamoxifen
Daunorubicin HCl	Temozolomide
Docetaxel	Teniposide
Doxorubicin	Testosterone
Epirubicin	Thalidomide
Estramustine	Thioguanine
Etoposide	Thiotepa
Exemestane	Topotecan
Floxuridine	Toremifene citrate
Fludarabine	Tositumomab
Fluorouracil	Tretinoin
Flutamide	Uracil mustard
Fulvestrant	Valrubicin
Gemcitabine	Vidarabine
Gemtuzumab ozogamicin	Vinblastine sulfate
Hydroxyurea	Vincristine sulfate
Ibritumomab tiuxetan	Vindesine

Adapted from National Institute for Occupational Safety and Health (NIOSH) (31-32)

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