Managing Pharmaceutical Waste

A 10-Step Blueprint for Healthcare Facilities In the United States

PRACTICE Greenhealth™

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Introduction

The discovery of a variety of pharmaceuticals in surface, ground, and drinking waters around the country is raising concerns about the potentially adverse environmental consequences of these contaminants. Minute concentrations of chemicals known as endocrine disruptors, some of which are pharmaceuticals, are having detrimental effects on aquatic species and possibly on human health and development.[1] The consistent increase in the use of potent pharmaceuticals, driven by both drug development and our aging population, is creating a corresponding increase in the amount of pharmaceutical waste generated.

Recent concerns regarding the documentation of drugs in drinking, ground, and surface waters have led to a rapid rise in public awareness and calls for action at the federal, state, and local level. These developments are discussed in more detail in Step 3, Considering Best Management Practices.

Pharmaceutical waste is not one single waste stream, but many distinct waste streams that reflect the complexity and diversity of the chemicals that comprise pharmaceuticals. Pharmaceutical waste is potentially generated through a wide variety of activities in a healthcare facility, including but not limited to intravenous (IV) preparation, general compounding, spills/breakage, partially used vials, syringes, and IVs, discontinued, unused preparations, unused unit dose repacks, patients' personal medications and outdated pharmaceuticals.

In hospitals, pharmaceutical waste is generally discarded down the drain or landfilled, except chemotherapy agents, which are often sent to a regulated medical waste incinerator. These practices were developed at a time when knowledge was not available about the potential adverse effects of introducing waste pharmaceuticals into the environment.

Proper pharmaceutical waste management is a highly complex new frontier in environmental management for healthcare facilities. A hospital pharmacy generally stocks between 2,000 and 4,000 different items, each of which must be evaluated against state and federal hazardous waste regulations. Pharmacists and nurses generally do not receive training on hazardous waste management during their academic studies and safety and environmental services managers may not be familiar with the active ingredients and formulations of pharmaceutical products.

Frequently used pharmaceuticals, such as physostigmine, warfarin, and nine chemotherapeutic agents, are regulated as hazardous waste under the Resource Conservation and Recovery Act (RCRA). Failure to comply with hazardous waste regulations by improperly managing and disposing of such waste can result in potentially serious violations and large penalties.

The Healthcare Environmental Resource Center (HERC) and Practice Greenhealth (formerly Hospitals for a Healthy Environment (H2E)) recommend this 10-step approach to help you

[1] Sumpter, J. and Johnson, A. Lessons from Endocrine Disruption and Their Application to Other Issues Concerning Trace Organics in the Aquatic Environment. Vol. 39, No. 12, 2005, Environmental Science and Technology.

develop and implement a comprehensive pharmaceutical hazardous waste management program – one that combines regulatory compliance and best management practices with waste minimization – to safeguard human health and the environment, while minimizing risk in a cost effective manner.

Navigating the Blueprint

The steps in this Blueprint do not necessarily have to be taken consecutively. Some steps will occur in parallel and other steps will probably be referenced throughout the development of your pharmaceutical waste management program.

Following is a summary of the 10-steps and how each can be used to develop and implement your pharmaceutical waste management program:

√ **Step1** begins with some action items that you can begin immediately.

√ **Step 2** is an overview of how the federal Resource Conservation and Recovery Act (RCRA) regulations apply to pharmaceutical waste management.

√ **Step 3** begins where the regulations leave off providing guidance on how to manage non-regulated hazardous pharmaceutical waste.

√ **Step 4** walks you through the steps necessary to perform a drug inventory review. This step can be very tedious and time consuming.

√ **Step 5** alerts you to waste minimization opportunities. It will be helpful to become familiar with the waste minimization opportunities before assessing your current practices based on the guidance provided in Step 6. Review these opportunities again upon completion of the department reviews.

√ **Step 6** discusses performing department reviews and determining your generator status.

√ **Step 7,** taking on the Communication/Labeling Challenge, is one of the most critical aspects of implementing a pharmaceutical waste management program and possibly the most challenging. How you decide to communicate pharmaceutical disposition information to the people handling the waste will depend and be dependent upon which of the management options presented in Step 8 you select.

√ **Step 8**, Considering the Management Options, introduces you to five implementation models that have worked for other hospitals. You may choose one model or a hybrid.

√ **Step 9**, Getting Ready for Implementation, assists you with vendor selection, satellite and storage accumulation, and pilot program development.

√ **Step 10**, Launching the Program, is the culmination of the first nine steps, plus the actual roll-out to the entire facility.

The following icons have been used to assist you in using the Blueprint:

Indicates additional steps where relevant information can be found.

Indicates that additional resources can be found in the Appendices

NEW! Indicates substantive changes to this revision of the Blueprint.

Applying the Precautionary Principle

This Blueprint focuses primarily on four aspects of pharmaceutical waste management:

(1) Management of regulated hazardous pharmaceutical waste;
(2) Management of non-regulated hazardous pharmaceutical waste applying best management practices;
(3) Management of non-regulated, "non-hazardous" pharmaceutical waste applying best management practices, and;
(4) Minimization of pharmaceutical waste

While your first priority has to be the proper management of hazardous pharmaceutical waste, careful consideration should be given to the management of ***all*** pharmaceutical waste. As research data accumulates on the adverse impacts of waste pharmaceuticals on human health and the environment, applying the Precautionary Principle becomes increasingly relevant:

"When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically."[2]

When in doubt, apply the Precautionary Principle.

[2] The original Precautionary Principle statement drafted in 1998 at the Wingspread Conference Center, Racine, WI, can be accessed at http://www.gdrc.org/u-gov/precaution-3.html.

Step One: Getting Started

Designing and implementing a successful pharmaceutical waste management program is a highly interdisciplinary process. It begins by obtaining support from senior management and establishing a committee of stakeholders that will meet regularly to develop and implement the program. This committee may be the current Environmental Health and Safety Committee or Environment of Care Committee but must include at minimum the managers of Pharmacy, Environmental Services, Safety, Nursing, Education, and Infection Control. Additional members for consideration are personnel from Facilities/Engineering, Administration, Laboratory and Purchasing/Materials Management.

Given the complexity of implementation and the potential budgetary impacts (e.g., purchase of pharmaceutical waste containers and potentially increased disposal costs), the newly formed committee should plan a presentation to senior management explaining the opportunities, challenges and financial implications of proper pharmaceutical waste management without getting into program specific details. A designated leader to assure that compliance requirements are met should be appointed by Administration.

> No single department owns all the responsibility and no single department can implement a pharmaceutical waste management program alone.

Step Two: Understanding the Regulations

Pharmaceutical waste management is especially challenging given the complexity of the regulations that govern this activity and the multiple regulatory agencies that are oversee it. Step 2 focuses primarily on how the federal RCRA regulations apply to hazardous pharmaceutical waste management. It is divided into five major sections to provide a broad overview of the applicable regulations and an awareness of the overlap between RCRA and other statutes.

1. Defining Hazardous Waste Categories
2. Grappling with Hazardous Waste Combinations
3. Distinguishing Between Trace and Hazardous Chemotherapy Waste
4. Understanding Hazardous Waste Management
5. The Impact of the Universal Waste Rule on Hazardous Pharmaceutical Waste

> It is important to note that the RCRA regulations were written with industrial waste generation in mind, and did not consider the impact on finished pharmaceutical dosage forms such as tablets, capsules, and injectables. Checking with federal and state regulators on areas that are open to potentially differing interpretations is highly recommended. This Blueprint offers a conservative interpretation in those situations. A conservative approach is always acceptable and offers greater environmental protection.

USEPA Region 2 has been very aggressive in inspecting and enforcing hazardous waste regulations at the 480 hospitals in New York, New Jersey, Puerto Rico and the U.S. Virgin Islands. Fines have ranged from $40,000 to almost $280,000. USEPA Region 1 has also begun a healthcare initiative and has notified 250 hospitals in New England of its intention to enforce hazardous waste laws in healthcare facilities.

State regulations may be more stringent than federal regulations and may vary by state. A number of states, including California[3], Washington, and Minnesota, have implemented more stringent hazardous waste regulations that impact pharmaceutical waste management. Be sure to check your state regulations to make sure that you understand your state-specific requirements. Two states, Michigan and Florida, have implemented Universal Waste Rules for hazardous pharmaceutical waste. USEPA is proposing to add pharmaceuticals to the federal Universal Waste rule. The proposed rulemaking is due to be published in December, 2008.
It will be available for comment and revision at that time.

There are additional resources in Appendix A: Tools and Resources that will provide you with a more complete understanding of RCRA and your organization's responsibilities.

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[3] A California version of this Blueprint is available through funding provided by the Bay Area Pollution Prevention Group, a subcommittee of the Bay Area Clean Water Agencies, under the leadership of Karin North, City of Palo Alto, Karin.North@cityofpaloalto.org,

Regulatory Bodies that Oversee Pharmaceutical Waste Management

> Environmental Protection Agency (EPA)
> Department of Transportation (DOT)
> Drug Enforcement Administration (DEA)
> Occupational Safety and Health Administration (OSHA)
> State Environmental Protection Agencies,
> State Pharmacy Boards, and
> Local Publicly Owned Treatment Works (POTW)

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1. Defining Hazardous Waste Categories

Hazardous wastes are divided into two categories: (1) listed wastes, and (2) characteristic wastes. Listed wastes appear on one of four lists of hazardous waste (F, K, P and U). Pharmaceuticals are found on two of these lists, the P and U lists which both contain commercial chemical products. Characteristic wastes are regulated because they exhibit certain hazardous properties – ignitability, corrosivity, reactivity and toxicity.

Wastes that are not listed and do not exhibit a characteristic are considered solid waste. Solid wastes should be discarded according to state and/or local regulations, including regulated medical waste requirements. Many landfills and wastewater treatment works have also established *waste acceptance criteria* that govern what can be disposed of in their landfill or down the sewer respectively, so that they may achieve compliance with state and regional requirements placed on the operation of their facilities. There may be situations where a solid waste pharmaceutical should be handled as a hazardous waste applying best management practices.

Step 3: Considering Best Management Practices for Non-Regulated Pharmaceutical Wastes provides recommendations for applying best management practices.

a. P- Listed Wastes (40 CFR Part 261.33(e))

Pharmaceuticals are chemicals first and therapeutic agents second. P-listed wastes are commercial chemical products that are categorized as acutely hazardous under RCRA.

One of the primary criteria for including a drug on the P-list as acutely hazardous is an oral lethal dose of 50 mg/kg (LD50) or less. LD50 is the amount of a material, given all at once, which causes the death of 50% of a group of test animals. Eight chemicals on the P-list are used as pharmaceuticals (see Table 1).

Constituent of Concern	Waste Code	Constituent of Concern	Waste Code
Arsenic trioxide	*P012*	Phentermine (CIV)	P046
Epinephrine base	P042	Physostigmine	P204
Nicotine	P075	Physostigmine salicylate	P188
Nitroglycerin	P081	Warfarin >0.3%	P001

Table 1: P-listed Pharmaceuticals *(Chemotherapy agents are noted in italics)*

The two most commonly generated P-listed chemicals in healthcare facilities are epinephrine and nitroglycerin. Fortunately, actions by USEPA and many state environmental protection agencies have provided exclusions for each of these. Epinephrine salts have been excluded federally as of October 15th, 2007 and weak medicinal nitroglycerin was excluded federally as of August 14th, 2001. Not all states have accepted or adopted these exclusions, so it is important to check with your state agency. More information regarding these exclusions is included below.

Identifying Waste Pharmaceuticals

Some drugs have more than one trade name. The underlying chemical name, not the trade name, is regulated under RCRA. To be sure you do not miss a chemical due to using a trade name or generic name, use the Chemical Abstracts Service registry numbers that can be obtained from the Merck Index or other chemical reference and compare them to the CAS numbers in the Code of Federal Regulations.

- Phentermine is a good example of the use of the CAS number, since it is listed in the 40 CFR 261.33 only as Benzeneethanamine, alpha, alpha-dimethyl-. By looking up phentermine in the Merck Index, its CAS number of 122-09-8 would tie to the chemical name in the P046.
- Trisenox® is the trade name for arsenic trioxide which is regulated as P012.

See Healthcare Related P- and U-Listed Wastes in Appendix A: Tools and Resources for further assistance.

i. Two Necessary Conditions (40 CFR Part 261.33)

When a drug waste containing a P-listed constituent of concern is discarded or intended to be discarded, it must be managed as hazardous waste if two conditions are satisfied: (1) the discarded drug waste contains a ***sole active ingredient*** (54 FR 31335) that appears on the P list, and (2) ***it has not been used for its intended purpose*** (54 FR 31336).

To satisfy the definition of ***sole active ingredient***, the listed chemical in the discarded drug must be the only ingredient that performs the intended function of the formulation. Ingredients that serve ancillary functions such as mobilizing or preserving the active ingredient are not considered when determining the sole active ingredient. Saline and dextrose solutions are also not considered to be active ingredients.

The phrase "***has not been used for its intended purpose***" refers to drugs and their associated containers or dispensing instruments that have not been given to a patient and need to be discarded. The portion of an IV infusion that was not given to a patient and needs to be discarded is an example of an item that has not been used for its intended purpose.

How Dermal Patches Work

In order to maintain consistent release rates, transdermal patches contain a surplus of active molecule. A stable concentration gradient is the mechanism used to maintain consistent release rates and constant serum drug levels. Most transdermal patches contain 20 times the amount of drug that will be absorbed during the time of application. Therefore, after removal, most patches contain at least 95% of the total amount of drug initially in the patch.

Nicotine is a P-listed constituent of concern (P075). Do worn nicotine patches need to be managed as RCRA hazardous waste? Nicotine is the sole active ingredient. So, the answer differs depending on whether you decide to evaluate the patch or the nicotine remaining in the patch to determine if the drug has been "used for its intended purpose." EPA has not provided any specific guidance on how to manage worn dermal patches. Best Management Practice would encourage management of the used nicotine dermal patch as hazardous pharmaceutical waste.

ii. Empty Containers of P-Listed Wastes (40 CFR Part 261.7(b)(3))

A container that has held a P-listed waste is not considered "RCRA empty" unless it has been:

(1) Triple rinsed, and

(2) The rinsate is managed as hazardous waste.

Since triple rinsing is not practical in healthcare settings, all vials, IVs, and other containers that have held a P-listed drug must be managed as hazardous waste, regardless of whether or not all of the contents have been removed. Some states have chosen to interpret "used" less stringently in the case of solid dosage forms (tablets, capsules) and are not regulating "empty" warfarin stock bottles or unit-dose packaging.

Tablets and Capsules Containing P-Listed Constituents of Concern

Are you managing the following as hazardous waste?

> The cups used to deliver P-listed pharmaceuticals such as Coumadin, containing P001 Warfarin

Minnesota does not consider the "soufflé cups" used to deliver tablets and capsules containing P-listed constituents of concern to be containers. Therefore, these cups do not have to be managed as hazardous waste in Minnesota unless they are overtly contaminated with a P-listed residue.

> The residue that is generated when tablets of drugs such as Coumadin are cut to prepare a smaller dose

> The unit dose packaging from tablets and capsules

Check with your state regulatory agency for guidance on their interpretation or apply a conservative approach and discard all containers of P-listed waste as hazardous waste.

iii. Dilute Concentrations of P-Listed Waste

There are no concentration limits or dilution exclusions for P-listed hazardous wastes. If saline or another solvent is added to a P-listed chemical, additional P-listed hazardous waste is generated.

Epinephrine Syringe Interpretation Extended to Other P and U-Listed Drugs

Excess and residue epinephrine in a syringe after the proper dose has been administered to a patient is the single pharmaceutical exception to the definition of the phrase *has not been used for its intended purpose*. This exception is based on a December 1994 EPA Hotline interpretation.[4] After the proper dose has been injected, EPA considers residues remaining in a syringe to have been used for their intended purpose.

USEPA published an interpretive letter dated April 14th, 2008, extending the exemption to other P and U-listed drugs in a used syringe.[5] The extension does not include the contents of unused

[4] RCRA Online # 13718
http://yosemite.epa.gov/osw/rcra.nsf/0c994248c239947e85256d090071175f/1c1deb3648a62a868525670f006bccd2!OpenDocument

[5] The expanded syringe interpretation may be accessed at
http://yosemite.epa.gov/osw/rcra.nsf/0c994248c239947e85256d090071175f/6a5dedf2fba24fe68525744b0045b4af!OpenDocument.

syringes. "Use" includes both patient injection and transfer of product by syringe from a vial to an IV, for example.[6]

In the interpretative guidance, a reference is made to the syringe as a dispensing instrument. The question arises regarding the regulatory status of other forms of delivery or dispensing instruments, such as an IV bag containing excess or residue epinephrine. EPA *has not* expanded the definition of a dispensing instrument to include any form of delivery other than a used syringe. *Check with your state environmental protection agency to see if they have accepted USEPA's exclusion of P-listed waste in a used syringe.*

v. Epinephrine Salts Interpretation

EPA's Office of Solid Waste sent a memorandum to all of its RCRA Division Directors on October 15, 2007 entitled: Scope of Hazardous Waste Listing P042 (Epinephrine), to clarify the scope of the hazardous waste listing for this product. The clarification was in response to inquiries as to whether the hazardous waste listing for epinephrine included epinephrine salts. EPA acknowledged that it was their understanding that most if not all of the chemical that is in use in hospitals is one of several epinephrine salts. EPA determined that the scope of the P042 listing does not (emphasis added) include epinephrine salts.[7] Until this clarification, epinephrine salts were classified and handled as RCRA hazardous wastes. Since this clarification, best management practices dictate that epinephrine salts be handled as non-hazardous pharmaceutical waste and sent to a medical waste incinerator or municipal incinerator for treatment. Not all states have accepted this decision. Minnesota, for example, considers epinephrine a hazardous waste under its Minnesota Lethal category. *Check with your state agency for their determination.*

vi. Nitroglycerin Exclusion

In 2001, a revision to the mixture and derived from rules (66 FR 27286) excluded all P- and U-listed wastes listed solely for an ignitability, reactivity and/or corrosivity characteristic (including mixtures, derived-from and as generated wastes) once they no longer exhibit a characteristic.

Nitroglycerin, P081, is listed solely for its reactivity characteristic. This action effectively removed medicinal nitroglycerin as a P-listed waste at the federal level since it is a weak, non-reactive formulation that does not exhibit the reactivity characteristic.

Nitroglycerin formulations must still be evaluated for the other characteristics. Some injectable pharmaceuticals, such as nitroglycerin 5 mg/ml in some formulations, fail the ignitability characteristic, which is discussed later in this Step.

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[6] Email guidance provided by Lisa Lauer, USEPA, to Charlotte Smith, PharmEcology, on May 21, 2008.

[7] Hale, Matt, Scope of Hazardous Waste Listing P042 (Epinephrine) Memorandum, United States Environmental Protection Agency, Office of Solid Waste, October 15, 2007. May be accessed at http://yosemite.epa.gov/osw/rcra.nsf/0c994248c239947e85256d090071175f/6a5dedf2fba24fe68525744b0045b4af!OpenDocument

Status of Nitroglycerin Exclusion in Your State

All states except Iowa and Alaska must adopt the revised Mixture and Derived From Rule before weak non-reactive nitroglycerin is excluded. Hazardous waste regulations are enforced by USEPA in Iowa and Alaska, therefore this provision was effective immediately in those states.

Until your state has adopted this provision, nitroglycerin must be managed as a P081 waste and therefore is still subject to Land Disposal Restrictions, which are discussed later this Step Two.

Some states, such as Michigan, have chosen to be more stringent and not adopt this revision. Check with your state regulatory agency to determine the status of medicinal nitroglycerin in your state.

b. U-Listed Wastes (40 CFR Part 261.33(f))

i. Two Necessary Conditions

There are 21 drugs on the U-list (see Table 2: U-Listed Pharmaceuticals). These chemicals are listed primarily for their toxicity. Similar to a P-listed waste, when a drug waste containing one of these chemicals is discarded, it must be managed as hazardous waste if two conditions are satisfied:

(1) The discarded drug waste contains a ***sole active ingredient*** that appears on the U list, and

(2) ***It has not been used for its intended purpose***.

As with P-listed wastes, there is no concentration limit or dilution exclusion.

Constituent of Concern	Waste Code	Constituent of Concern	Waste Code
Chloral hydrate (CIV)	U034	Paraldehyde (CIV)	U182
Chlorambucil	U035	Phenol	U188
Cyclophosphamide	U058	Reserpine	U200
Daunomycin	U059	Resorcinol	U201
Dichlorodifluoromethane	U075	Saccharin	U202
Diethylstilbestrol	U089	Selenium sulfide	U205
Hexachlorophene	U132	*Streptozotocin*	U206
Lindane	U129	Trichloromonofluromethane	U121
Melphalan	U150	*Uracil mustard*	U237
Mercury	U151	Warfarin <0.3%	U248
Mitomycin C	U010		

Table 2: U-Listed Pharmaceuticals (*Chemotherapy agents are noted in italics*)

ii. Empty Containers of U-Listed Wastes (40 CFR Part 261.7(b)(1))
A container that has held a U-listed waste is considered "RCRA empty" if two conditions are met:

(1) All the contents have been removed that can be removed using normal means[8], such as drawing liquid out with a syringe

AND,

(2) No more than 3% by weight remains.

If both of these criteria are not met, the container must be managed as hazardous waste. Any residues removed from the empty container must be managed as hazardous waste.

c. Characteristic Hazardous Waste (40 CFR Parts 261.21 – 261.24)

In addition to the P- and U- listed wastes, a waste is considered hazardous under RCRA if it possesses at least one of four unique and measurable properties or characteristics:

(1) Ignitability,

(2) Corrosivity,

(3) Reactivity, or

(4) Toxicity.

As the generator, you are responsible for determining whether a drug formulation that is intended for discard exhibits one of the four characteristics through testing or through knowledge of the drug formulation. Once a characteristic waste no longer exhibits any of these properties, it is no longer considered a hazardous waste. However, RCRA places certain restrictions on the manner in which a waste can be treated (See What is Treatment? below).

i. Ignitability: D001 (40 CFR 261.21)
The objective of the ignitability characteristic is to identify wastes that either present a fire hazard under routine storage, disposal, and transportation or are capable of exacerbating a fire once it has started. There are several ways that a drug formulation can exhibit the ignitability characteristic.

[8] Normal means are practices commonly employed industry-wide to remove the material from that type of container, such as pouring, pumping, aspirating, and draining (40 CFR Part 261.7(b)(1)(i))

> Aqueous drug formulations containing 24 percent or more alcohol by volume and having a flashpoint of less than 140 degrees F or 60 degrees C must be managed as ignitable hazardous waste. Aqueous refers to a solution containing at least 50 percent water by weight. Since flashpoint data is somewhat hard to obtain, you should consider managing all waste formulations containing 24% or more alcohol as ignitable hazardous waste. Many drugs are relatively insoluble in water and require alcohol to keep them in solution.

> Liquid drug formulations, other than aqueous solutions containing less than 24 percent alcohol, with a flashpoint of less than 140 degrees F or 60 degrees C must be managed as ignitable hazardous waste. Being a non-aqueous solution, the flashpoint is used to make the hazardous waste determination. Acetone and flexible collodion are examples of non-aqueous liquids used in drug formulations.

> Oxidizers or materials that readily supply oxygen to a reaction in the absence of air as defined by the DOT[9] must be managed as hazardous waste.

> Flammable aerosol propellants meeting the DOT definition of compressed gas must be managed as hazardous waste.

[9] Reference 40 CFR 264 Appendix V Examples of Potentially Incompatible Waste Group 6-A Oxidizers

What is Treatment?

- Diluting an ignitable solution containing greater than 24% alcohol during the normal course of usage, as in the preparation of an IV solution, is **not** considered treatment. Any resulting waste would **not** be ignitable hazardous waste.
- Diluting an ignitable alcoholic solution containing over 24% alcohol for the purposes of rendering it non-ignitable is considered treatment. As a hazardous waste generator, you are not permitted to treat hazardous waste. A treatment, storage and disposal facility permit, which is inappropriate for hospitals, is required. (Some states may allow some form of treatment in this manner, but it is not recommended for pharmaceutical waste.)

Ignitable Properties	Resources	Ignitable Drug Formulations
Aqueous drug formulation containing 24 % or more alcohol by volume and having a flashpoint of less than 140 ° F or 60 ° C (261.21(a)(1))	> Material Safety Data Sheet > Common pharmacy references such as Facts and Comparisons or their on-line database, E-Facts	> Erythromycin Gel 2% > Texacort Solution 1% > Taxol Injection
Liquid drug formulations, other than aqueous solutions containing less than 24 % alcohol, with a flashpoint of less than 140 ° F or 60 ° C	> MSDS > Standard laboratory test procedure for measuring flashpoint	> Flexible collodion used as a base in wart removers is not an aqueous solution and has a flashpoint = 45 degrees C
Oxidizers or materials that readily supply oxygen to a reaction in the absence of air as defined by the DOT	> 40 CFR 264 Appendix V Examples of Potentially Incompatible Waste Group 6-A Oxidizers > Possible ORM-D Consumer Commodity exclusion in 49 CFR 173.151 for small packages	> Bulk chemicals found in the compounding section of the pharmacy such as potassium permanganate
Flammable aerosol propellants meeting the DOT definition of compressed gas (261.21(a)(3))	> Possible ORM-D Consumer Commodity exclusion in 49 CFR 173.306	> Primatene aerosol [10]

Table 3: Pharmaceuticals with Ignitability Characteristics

ii. Corrosivity: D002 (40 CFR Part 261.22)

Any waste which has a pH of less than or equal to 2 (highly acidic) or greater than or equal to 12.5 (highly basic) exhibits the characteristic of corrosivity and must be managed as a hazardous waste. Generation of corrosive pharmaceutical wastes is generally limited to compounding chemicals in the pharmacy. Compounding chemicals include strong acids, such as glacial acetic acid and strong bases, such as sodium hydroxide.

Step 9: Locating Your Satellite Accumulation Area includes a discussion on managing corrosive pharmaceutical waste.

[10] Primatene aerosol contains epinephrine as a salt, so the P042 waste code no longer applies.

iii. Reactivity: D003 (40 CFR Part 261.23)
Reactive wastes are unstable under "normal" conditions. They can cause explosions, toxic fumes, gases, or vapors when heated, compressed, or mixed with water. Nitroglycerin is the only drug that is potentially reactive. Refer to the section above, entitled Nitroglycerin Exclusion, for an understanding of the regulatory status of medicinal nitroglycerin.

iv. Toxicity: Multiple D Codes (40 CFR Part 261.24)
Forty chemicals have been included in RCRA as a concern in a solid waste landfill environment above certain concentrations. Table 4 provides a subset of that list and examples of drug formulations containing these chemicals and heavy metals. Wastes that exceed these concentrations must be managed as hazardous waste. The test that determines the ability of these chemicals and heavy metals to leach in a landfill environment is called the Toxicity Characteristic Leaching Procedure, or TCLP. If the concentration determined by the TCLP exceeds the stated limits, the waste must be managed as hazardous waste.

Ingredient	Waste Code	Regulatory Level (mg/l)	Drugs Formulations Containing These Ingredients
Arsenic	D004	5.0	Arsenic trioxide (also P-listed)
Barium	D005	100.0	Barium sulfate (used in radiology)
Cadmium	D006	1.0	Multiple mineral preparations
Chloroform	D022	6.0	No longer commonly used
Chromium	D007	5.0	Multiple mineral preparations
Lindane	D013	0.4	Treatment of lice, scabies (also U-listed)
M-cresol	D024	200.0	Preservative in human insulins
Mercury	D009	0.2	Vaccines with thimerosal, eye, ear preparations
Selenium	D010	1.0	Dandruff shampoo, multiple mineral preparations
Silver	D011	5.0	Silver sulfadiazine cream

Table 4: D-listed Chemicals Used in Drug Formulations

Appendix B contains sample Toxicity Characteristic calculations.

v. Empty Containers of Characteristic Wastes (40 CFR 261.7)
A container that has held a characteristic waste is defined as empty in the same manner as a U-listed waste: if all of the contents have been removed that can be removed through normal means[11] ***and*** no more than 3% by weight remains.

[11] Normal means are practices commonly employed industry-wide to remove the material from that type of container, such as pouring, pumping, aspirating, and draining (40 CFR Part 261.7(b)(1)(i))

2. Grappling with Hazardous Waste Combinations

This section provides guidance on how to manage combinations of hazardous waste and:
> Personal Protective Equipment (PPE) and spill materials
> Regulated Medical Waste (RMW),
> Sharps, and
> Controlled substances

a. Contaminated Personal Protective Equipment and Spill Materials

i. Listed Waste
PPE worn to protect employees from exposure to hazardous chemicals, materials used to perform routine cleaning or decontamination of Biological Safety Cabinets and glove boxes, and spill clean up materials may become contaminated with hazardous waste.

According to EPA's contained-in policy[12], the resulting waste has the same regulatory status as the original listed component. For example, personal protective equipment such as gloves and gowns that are known to be or suspected of having been contaminated with P- or U-listed hazardous waste must be managed as hazardous waste. If PPE is routinely worn but does not appear to have come into contact with listed waste, it is acceptable for it to be discarded either as trace chemotherapy waste, if its use involved chemotherapy agents, or in the trash as solid waste.

Any materials used to clean up a hazardous waste spill, such as the contents of an IV bag of Cytoxan (cyclophosphamide), must be managed as hazardous waste and cannot be discarded in a trace chemotherapy or solid waste container.

Refer to the section below, Distinguishing Between Trace and Hazardous Chemotherapy Waste, for further discussion of PPE and spill materials contaminated with chemotherapy agents.

ii. Characteristic Waste
The contained-in policy applies differently to characteristic hazardous wastes. PPE and spill materials contaminated with characteristic wastes are hazardous only if the PPE and spill material exhibit a characteristic. However, it is best to be conservative and manage PPE that has been contaminated with a flammable waste or a highly corrosive waste as hazardous waste.

[12] EPA's contained in policy is explained in the following letters: (1) Marcia Williams to Gary Dietrich (2/9/1987); (2) Sylvia Lowrance to Timothy Fields, Jr. (1/3/1989; RCRA Online #11387; http://yosemite.epa.gov/osw/rcra.nsf/0c994248c239947e85256d090071175f/ae8507395dc469558525670f006bdce8!OpenDocument); and, (3) Devereaux Barnes to Norm Niedergang (2/17/1995; RCRA Online #13732; http://yosemite.epa.gov/osw/rcra.nsf/0c994248c239947e85256d090071175f/34dd8e7f201f99da8525670f006c23c3!OpenDocument).

Contaminated Personal Protective Equipment

Indications of contaminated PPE include, but are not limited to:
> Shiny sheen,
> Change in color,
> Change in texture or feel, and/or
> Visual evidence such as seeing the contaminant on the PPE.

b. Regulated Medical Waste (Biohazardous)

Before beginning this discussion, it is important to clarify the usage of the term "biohazardous." In this document and in common usage throughout most healthcare facilities, the term "biohazardous" refers to infectious, or potentially infectious, waste and is often termed "Regulated Medical Waste." It usually includes unused sharps, although that definition varies by state. In pharmacy circles, "biohazardous" has sometimes been erroneously used to describe chemotherapy waste, based on the premise that chemotherapy is hazardous to living systems. This usage causes untold confusion and has even resulted in the availability of commercial labels with both "chemotherapy" and "biohazardous" on them. The term "biohazardous" should ONLY be used as defined by your state's regulations. Having said that, there will be situations where a combination waste that is both infectious Regulated Medical Waste (RMW) and hazardous waste must be managed by a limited number of vendors that are permitted to handle ***both*** waste streams. We will refer to this combined waste stream as "dual waste." The type of dispensing instrument used and the type of drug being administered both play an important role in determining how the resulting waste must be managed.

If, for example, bloody tubing or sharps are not disconnected from an IV bag that contains a partially used P- or U-listed chemical or from one that no longer contains a P-listed chemical, the waste must be managed as ***both*** RMW and hazardous waste. Fortunately, in many cases, luer-lock fittings enable the safe disconnection of the tubing or sharps from the IV bag. Disconnecting the tubing or sharps from the IV bag avoids the generation of a waste that is ***both*** RMW and hazardous waste and instead enables the management of the tubing or sharps and IV bag individually as RMW and hazardous waste, respectively.

c. Sharps

Often partially used syringes, vials or ampules containing P- or U-listed hazardous chemicals or characteristic hazardous wastes are erroneously discarded in RMW sharps containers. Generally speaking, most vendors that manage sharps are not legally permitted to manage RCRA

hazardous waste. These vendors are permitted to treat ***only*** infectious waste. As the generator, it is your responsibility to train staff that these distinct types of waste are managed differently and must be segregated (e.g., not to discard hazardous waste or waste that is both RMW and hazardous waste in sharps containers unless the containers are specially marked as both infectious and hazardous waste). If hazardous waste is improperly placed in a sharps container, the container should be relabeled as RMW and hazardous waste and managed by a vendor that is permitted to handle both waste streams. Shipment of needles, for example, in a hazardous waste container could result in the entire container being rejected at the treatment, storage, and disposal facility, unless it was appropriately labeled and the receiving company was appropriately permitted.

Arsenic trioxide and physostigmine are drugs that may be prepared or administered by needle and syringe and as a result needle/syringe may need to be managed as ***both*** hazardous waste and RMW. Check with your state environmental protection agency to see if they have accepted USEPA's exclusion of P-listed waste in a used syringe, as discussed above.

d. Controlled Substances (21 CFR Parts 1300 to 1399)

Controlled substances are those drugs regulated by the Drug Enforcement Administration. They are divided into five schedules based on their potential for abuse.

Controlled Substance Schedules

- Schedule I includes drugs that have no accepted medical use, such as heroin.
- Schedule II drugs are used medically but have high abuse potential, such as morphine, and their purchase, storage, and use requirements are very strictly monitored.
- Schedules III through V are drugs with decreasing abuse potential, all the way from sedatives to cough suppressants, such as codeine.

Controlled substances must be destroyed so that they are beyond reclamation and two healthcare professionals must document the destruction. Since hospitals no longer generally have ready access to incinerators in which to burn the drugs, the next most efficient way to accomplish this is through drain disposal. This method is increasingly discouraged by USEPA, state regulatory agencies, and publicly owned treatment plants.

There are three controlled substances that are on Schedule IV due to their moderate abuse potential that are also RCRA listed constituents of concern: (1) Chloral hydrate (U034), (2) Paraldehyde (U182), and (3) Phentermine (P046)**.** Other controlled substances may be state

listed hazardous waste, as is the case in Minnesota. Be sure to check with your state regulatory agency.

These hazardous controlled substance wastes can be transferred to a limited number of hazardous waste vendors that are also DEA registrants or, possibly sewered. You need to request written permission from your wastewater treatment plant to sewer small amounts of hazardous controlled substances. Sewering of controlled substances may be prohibited in your state or municipality. The hazardous waste regulations pertaining to sewering are described in more detail below in the section entitled, Drain Disposal. Larger volumes of controlled substances, such as 50 mL. IV bags of morphine, can also be transferred to reverse distributors.

Companies are working to develop containment devices that would render the controlled substances "non-recoverable" as required by the Drug Enforcement Administration (DEA). This is a disposal challenge that still needs a good solution.

Step 5: Minimizing Pharmaceutical Waste provides examples of controlled substances that are routinely wasted and alternatives that will minimize generation of this waste stream.

Step 9: Selecting the Right Vendor(s) contains requirements for hazardous waste vendors that are also DEA registrants.

Appendix A: Tools and Resources provides additional information on controlled substances and DEA requirements.

3. Distinguishing Between Trace and Hazardous Chemotherapy Waste

a. Terminology

There is a great deal of confusion among the terms chemotherapeutic, antineoplastic, and cytotoxic. Technically, chemotherapy is therapeutic chemical treatment. While most commonly used to describe cancer treatment, it was originally used as an anti-infective term in reference to the use of mercury and arsenic before the advent of antibiotics. Some journals still refer to antimicrobial chemotherapy. The term antineoplastic refers specifically to inhibiting or preventing the growth or development of malignant cells, and is the most specific. The term cytotoxic is a very general term referring to any chemical that is toxic to cells. It again has taken on the common meaning of cancer chemotherapy. To confuse matters more, the pharmaceutical profession tends to equate the term biohazardous with cytotoxic. Some manufacturers put both words "Chemotherapy" and "Manage as Biohazardous Waste" on the same label. These labels create confusion as the term "biohazardous" waste should be restricted to the commonly accepted definition of infectious waste in state blood-borne pathogens regulations, which are typically items contaminated with pourable, drippable, flakable or squeezable blood, used or unused sharps, and lancing devices.

Although the term "chemotherapy" technically refers to any type of drug treatment, it will be used to describe highly toxic cancer therapy agents in this document.

b. Trace Chemotherapy Waste

The federal RCRA regulations do not address trace chemotherapy waste. There is no recognized distinction between bulk and trace chemotherapy contamination for P- and U-listed hazardous wastes since there isn't a lower concentration limit under which these wastes can exit the regulatory system.

Most state regulated medical waste regulations are either silent or not specific on the definition of trace chemotherapy waste. The original reference to segregating trace chemotherapy waste is found in an article written in 1984 by pharmacy personnel at the National Institutes of Health who pioneered applying the RCRA regulations to antineoplastic wastes.[13] California's Medical Waste Management Act and Wisconsin's Medical Waste Rules identify trace chemotherapy waste and require incineration at a regulated medical waste facility or other approved treatment method.

Refer to Appendix A: Tools and Resources for information on how to access the California Medical Waste Management Act and the Wisconsin Medical Waste Rules.

All chemotherapy paraphernalia should be managed as ***trace*** chemotherapy waste if there has been the potential for exposure to chemotherapy contamination. Items that are appropriate for management as trace chemotherapy waste include:

> "RCRA empty" vials, syringes, IV bags, and tubing;

> Gowns, gloves, wipes and other paraphernalia associated with routine handling, preparation, and administration of chemotherapy; and,

> Wipes and other materials used during routine cleaning and decontamination of a Biological Safety Cabinet or glove box (unless alcohols, phenols or other hazardous materials are used).

c. Hazardous Chemotherapy Waste

One chemotherapy agent is a P-listed constituent of concern and eight chemotherapy agents are U-listed (See Table 5). Trace chemotherapy containers have long been used to discard listed chemotherapy drug waste that should be managed as hazardous waste. This is not only illegal

[13] Vaccari, P; Tonat, K; DeChristoforo, R; GTallelli, J, Simmerman, P. Disposal of antineoplastic wastes at the National Institutes of Health, AJHP Vol 41 Jan 1984, pp. 87 – 93.

but also inappropriate since trace chemotherapy waste is incinerated at an RMW incinerator, not a hazardous waste incinerator. RMW incinerators have less restrictive emissions limits and permit requirements. Discarding "bulk" P- or U- listed chemotherapy agents as trace chemotherapy waste has been the cause of substantial enforcement actions and fines and should be one of the first changes you implement in your pharmaceutical waste management program.

> The term "**bulk chemotherapy**" is not a regulatory term but is used to differentiate chemotherapy containers that are not "RCRA empty."

Constituent of Concern	Product Name	Waste Code
Arsenic Trioxide	Trisenox	P012
Chlorambucil	Leukeran	U035
Cyclophosphamide	Cytoxan, Neosar	U058
Daunomycin	Daunorubicin, Cerubidin, DaunoXome, Rubidomycin	U059
Diethystilbestrol	DES, Stilphostrol	U089
Melphalan	Alkeran, L-PAM	U150
Mitomycin C	Mitomycin, Mutamycin	U010
Streptozotocin	Streptozocin, Zanosar	U206
Uracil Mustard	No longer in active use	U237

Table 5: P- and U-Listed Chemotherapy Agents

Over 100 chemotherapy agents have been introduced into the market since the RCRA regulations were written. Bulk quantities of these agents should be managed as hazardous waste as a best management practice. This topic is addressed more completely in Step 3, Considering Best Management Practices.

i. Combination Hazardous Chemotherapy and Regulated Medical Wastes

The Oncology Nursing Society strongly discourages unhooking an IV set unless it has been designed to protect employees from exposure. When a chemotherapy waste that is both RMW and hazardous waste is generated, it must be managed by a limited number of vendors that are permitted to handle both waste streams (See the section above on Regulated Medical Waste for information on combination wastes).

ii. Spill and Decontamination Materials

Any materials used to clean up a hazardous waste spill, such as the contents of a used chemotherapy spill kit, must be managed as hazardous waste. This material cannot be discarded in a trace chemotherapy waste container. If overt contamination of the Biological Safety Cabinet or glove box surfaces is known or suspected, all cleaning materials should be discarded as hazardous waste. It is always permissible to manage a waste up to the next hazard class. When making this decision, you should use good judgment based on how often the Biological Safety

Cabinet or glove box is used and decontaminated. Unless a closed transfer system such as PhaSeal is being utilized, it is safe to assume that some chemotherapy contamination occurs with each transfer.

Minimizing Employee Exposure

> Contamination of Biological Safety Cabinets can be greatly minimized through the use of a closed transfer system such as PhaSeal at all stages of preparation, transfer, and administration. The M.D. Anderson Cancer Center in Houston, Texas has done extensive studies to demonstrate the importance of good work practices in minimizing employee exposure.

> NIOSH and ASHP studies have shown that trace chemotherapy contamination poses a threat to exposed workers, especially if autoclaved. It is very important to incinerate rather than autoclave any material that has the potential of being contaminated with chemotherapy agents.

Step 3: Considering Best Management Practices for Non-Regulated Pharmaceutical Wastes contains a discussion of best management practices for the over 100 non-regulated chemotherapy wastes.

Step 6 provides opportunities to minimize chemotherapy waste.

Appendix A: Tools and Resources contains additional resources on managing chemotherapy wastes and insuring employee safety.

4. Understanding Hazardous Waste Management

a. Generator Status[14]

Organizations that generate RCRA hazardous waste are regulated as one of the following:

> Large Quantity Generators (LQGs), facilities that generate greater than or equal to 1,000 kg of hazardous waste per calendar month (approximately 2,200 lbs) **or** greater than 1 kg of acutely hazardous waste per calendar month (approximately 2.2 lbs).

> Small Quantity Generators (SQGs), facilities that generate between 100 kg (approximately 220 lbs) and 1,000 kg of hazardous waste per calendar month **and** accumulate less than 6,000 kg (approximately 13,200 lbs) of hazardous waste at any time. Please note that SQGs must also generate 1 kg or less of acutely hazardous wastes per calendar month.

[14] USEPA Office of Solid Waste has developed a document entitled "Hazardous Waste Generator Regulations" which summarizes all of the generator requirements and can be accessed at http://www.epa.gov/epaoswer/osw/gen_trans/tool.pdf.

> Conditionally Exempt Small Quantity Generators (CESQGs), facilities that generate less than or equal to 100 kg of hazardous waste per calendar month **or** less than or equal to 1 kg of acutely hazardous waste per calendar month.

Whether the wastes that you generate are U-listed or P-listed can affect your generator status. Any amount greater than 1 kilogram, or 2.2 pounds, of P-listed waste generated in a calendar month will cause your facility to become an LQG. These limits are based on how much is generated in a calendar month and not the amount placed into a container or shipped off site during that month.

When the amount of P-listed pharmaceutical waste that you generate has been accurately taken into account, it is possible that you may become an LQG. To provide some perspective, 1 liter of water weighs 2.2 pounds. Now that epinephrine salts are no longer considered P-listed waste federally, warfarin containers may be the primary source of P-listed waste. This assumes that your state has accepted both the epinephrine salt and nitroglycerin exclusions. Be sure to check with your state on their requirements.

LQGs have additional requirements related to proper waste management, time and storage limits, training, prevention and preparedness, contingency plans, and reporting to local, state, and federal agencies (40 CFR Part 262).

Refer to Appendix A for resources on generator requirements.

Confirm Your Generator Status

Many hospitals currently classify themselves as CESQGs or SQGs. However, the identification, segregation, documentation and proper disposal of hazardous pharmaceutical waste have not yet occurred in many of these facilities.

If your state has accepted the epinephrine salt and nitroglycerin exclusions, it is likely that your facility will be a SQG or CESQG. Be sure to document all P-listed waste generated per calendar month. Check with your state to see if warfarin containers and wrappers have been excluded. If not, your generator status may be LQG.

Refer to Step 6: Assessing Current Practices for suggestions on how to confirm your generator status.

b. Drain Disposal (40 CFR 403.12 (p))

According to the Clean Water Act's General Pretreatment Regulations, sewering of 15 kg (33 lbs) or more of U-listed and characteristic wastes and any amount of P-listed waste in a calendar month requires notification to the local POTW, the state environmental protection agency, and the regional EPA waste management division director. Notification of P-listed wastes includes certification that you have a program in place to reduce the volume and toxicity of hazardous wastes generated to the degree it has determined to be economically practical. The drain disposal of these hazardous wastes is allowable under RCRA as RCRA regulations (40 CFR 261.4(a)(1)(ii)) provide an exclusion to industrial hazardous waste discharged to publicly owned treatment works via a general use sewer system. This exclusion, which is known as the "domestic sewage exclusion," relies generally on the CWA's pretreatment standards as well as any applicable local limits, but no review or approval is required under RCRA. The exclusion is self-implementing, as long as the disposal to the sewer system meets the RCRA requirements. The domestic sewage exclusion requires that the hazardous waste mix with sanitary wastes prior to its arrival at the publicly owned treatment works. Therefore, if the hazardous waste arrives at the publicly owned treatment works via a dedicated pipeline (i.e., a pipeline connected directly from a facility to a POTW such that any hazardous waste does not mix with domestic sewage), truck or rail, the exclusion does not apply. In addition, the domestic sewage exclusion does not apply if the mixture of hazardous waste and sanitary waste leak from the sewer line prior to its arrival at the publicly owned treatment works. Because this exclusion does not apply to any hazardous waste before it enters the sewer system, all RCRA requirements for hazardous waste generation, storage and treatment still apply prior to drain disposal. However, as previously noted, EPA, as well as best management practices, strongly discourage the drain disposal of any waste pharmaceuticals, with special emphasis on those that are hazardous. In addition, as states' waste regulations may be more stringent or broader in scope than the federal rules, not all local environmental regulations will include the domestic sewage exclusion.

Step 3: Considering Best Management Practices for Non-Regulated Pharmaceutical Wastes contains a discussion of this best management practice.

c. Incineration

The Land Disposal Restrictions (LDR) regulations require the *treatment* of all hazardous pharmaceutical waste, most commonly by hazardous waste incineration, before it can be discarded in a hazardous waste landfill. The required technology for each waste category or Best Demonstrated Available Technology (BDAT) is listed in 40 CFR Parts 268.40 and 268.48. The resulting ash is tested and eventually disposed in a lined hazardous waste landfill.

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Step 9: Getting Ready for Implementation provides a discussion of the paperwork requirement.

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Aerosol Cans: Things to Consider

Non-Hazardous Aerosol Cans

> There are many pharmaceuticals that come in aerosol cans that do not contain propellants that exhibit the ignitability characteristic. You need to determine how you are going to manage this waste stream. Managing them with hazardous aerosol cans is often the simplest approach.

Hazardous Aerosol Cans

> Aerosol cans with flammable propellants that meet the DOT definition of compressed gas should be managed as hazardous waste under the ignitable waste code of D001.

5. The Impact of Including Pharmaceuticals in the Universal Waste Rule

The USEPA has announced its intention of proposing to amend the federal universal waste regulations to include pharmaceuticals.[15] Two states, Michigan[16] and Florida[17], have already included pharmaceuticals in their universal waste regulations. It is important to note that the universal waste rule is a subset of hazardous waste regulations.[18]

> **What is Universal Waste?**
>
> "The universal waste regulations streamline collection requirements for certain hazardous wastes in the following categories: batteries, pesticides, mercury-containing equipment (e.g., thermostats) and lamps (e.g., fluorescent bulbs). The rule is designed to reduce hazardous waste in the municipal solid waste (MSW) stream by making it easier for universal waste handlers to collect these items and send them for recycling or proper disposal."
>
> http://www.epa.gov/epaoswer/hazwaste/id/univwast/index.htm

If finalized, this means that only those drugs that designate as RCRA hazardous waste, between 4% and 5% of pharmaceuticals on the market, would be directly impacted.[19] The importance of the rule is related to the impact on generator status. As universal waste, hazardous pharmaceutical wastes would no longer need to be counted towards generator status. Recent changes in the categorization of epinephrine salts (See v. Epinephrine Salts Interpretation) have made it more likely that a hospital will be a small quantity or conditionally exempt small quantity generator. However, currently under the RCRA subtitle C regulations, a small quantity or conditionally exempt small quantity generator facility must still document its hazardous waste generation monthly, a cumbersome burden. In addition, some states have not adopted the epinephrine exclusion or even the earlier nitroglycerin exclusion. Moving hazardous pharmaceutical wastes into the Universal Waste system will alleviate these concerns. Once the rule is finalized, each EPA authorized state will need to adopt it. (All states except Iowa and

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[15] See the original posting on April 30, 2007 on page 23281 in the Federal Register accessed at http://www.epa.gov/fedrgstr/EPA-GENERAL/2007/April/Day-30/g01422.pdf and slight modifications published on the EPA website in the fall of 2007 at http://yosemite1.epa.gov/opei/Smallbus.nsf/04b7c5966aaff14285257015004717 9e/273617ce3ab52bbb852572ec006af28c!OpenDocument

[16] Information regarding Michigan's Universal Waste Rule can be accessed at http://www.deq.state.mi.us/documents/deq-ead-tas-univwaste.pdf and at R299.9228 Universal wastes at http://www.deq.state.mi.us/documents/deq-wmd-hwp-Part111Rules00.pdf

[17] Information regarding Florida's Universal Waste Rule can be accessed at rule number 62.730.186 at http://www.dep.state.fl.us/waste/quick_topics/rules/documents/62-730.pdf.

[18] Additional information on universal waste can be accessed at http://www.epa.gov/epaoswer/hazwaste/id/univwast/index.htm.

[19] USEPA would encourage the management of RCRA non-hazardous pharmaceutical waste as universal waste.

Alaska have EPA-authorized RCRA programs.) It is important to note that this rule will be less stringent than the current hazardous waste standards. Therefore, authorized states would not be required to modify their programs by adding hazardous pharmaceutical wastes to their universal waste programs. Finally, if finalized, the rule will not be mandatory; thus a hospital can choose to manage their hazardous pharmaceutical waste under the Universal Waste rule or to continue to operate under the current RCRA subtitle C regulations.

Adding hazardous pharmaceutical wastes to the Universal Waste system will also make it easier for consumer take-back programs to operate in states where the household exemption for hazardous waste does not apply to centralized collection facilities.

Since it is expected that only 5% or so of pharmaceuticals will be addressed by the Universal Waste Rule, the remaining 95% of pharmaceuticals in the marketplace will still remain unregulated at the federal level, even though USEPA will encourage facilities to manage all pharmaceutical wastes as universal wastes. While environmentally sound, it is unlikely hospitals will choose to pay the premium price required for this level of disposal, since universal waste must be disposed at a RCRA treatment, storage, and disposal facility (TSDF), the highest and most expensive mode of incineration. It will remain up to the state agencies and the regulated community to adopt best management practices for the environmentally sound management of the majority of pharmaceutical waste generated.

The next section discusses the Best Management Practices hospitals are encouraged to follow for the unregulated portion of waste pharmaceuticals.

Step 3: Considering Best Management Practices for Non-Regulated Pharmaceutical Wastes

Many drugs of concern to EPA and the Center for Disease Control and Prevention (CDC), including hormones, antibiotics, antidepressants, antihypertensives, and other potent drugs, are not caught by the current hazardous waste regulations. The RCRA hazardous waste regulations have not been substantially updated since their inception in 1976 and as a result have not kept pace with drug development. In addition, these regulations were not developed with a hospital setting in mind. As a result, approximately 10% of the drugs that are not technically subject to the hazardous waste regulations are equally hazardous under RCRA criteria. Considering that only 5% of drugs are regulated under RCRA, the remaining 95% of drugs may be "hazardous" using both traditional toxicity measures and newer criteria, such as antibiotic resistance, endocrine disruption, and developmental disruption due to prenatal or early postnatal exposure. Therefore, pharmaceuticals that are not technically RCRA hazardous waste when discarded should be analyzed for their potential to cause harm to human health and the environment. Best management practices encourage managing drugs that are equally harmful as hazardous waste when discarded and managing all other drug waste through incineration rather than drain disposal and landfilling. Following best management practices is also good risk management.

Recent activity by the EPA Office of Water has indicated their growing concern with drugs entering the ecosystem. In October, 2007, EPA published its Preliminary 2008 Effluent Program Guidelines Plan for public comment.[20] At the time of this publication, a voluntary survey of drug disposal practices is being conducted by EPA among healthcare facilities, long term care facilities, and veterinary practices. That report will be forthcoming.

Between March 10th, and March 12th, 2008, the Associated Press ran a series of research articles documenting drugs in drinking water across the nation.[21] The concerns expressed in the articles and the public reactions to them spurred Senators Barbara Boxer and Frank Lautenberg to conduct a hearing on April 15th, 2008 in which a number of interested parties including EPA were asked to testify.[22] It is expected that the level of interest in this topic will continue to increase with possibly more articles and hearings. All of this attention should encourage healthcare facilities to move to best management practices for pharmaceutical waste disposal.

The criteria outlined in this step can be used as a guideline in making best management practice determinations. Drugs that satisfy any of these criteria are sufficiently hazardous to warrant being treated in the same manner as drugs that are identified as RCRA hazardous waste. It is always appropriate to manage drug waste at a higher level of care than required by regulation. Drugs that do not meet these criteria should be managed at a lower level of incineration, such as regulated medical waste or municipal waste-to-energy plants, to avoid drain disposal and landfilling of any drugs. States such as California have already mandated these practices.[23]

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[20] The announcement can be accessed at http://www.epa.gov/guide/304m/2007/index.html#summary.
[21] Drug Traces Common in Tap Water, March 10, Drugs in Water Causing Troubling Problems to Fish, Wildlife, March 11, Little Done to Test, Limit Contaminated Water, March 12.
[22] Information on the Senate hearing may be accessed at http://a.abcnews.com/Health/wireStory?id=4660381.
[23] http://www.cdph.ca.gov/certlic/medicalwaste/Pages/default.aspx

Appendix A: Tools and Resources contains additional information on the best management practices described in this step.

Incinerate as Hazardous Waste

- Formulations With a Listed Active Ingredient That is Not the Sole Active Ingredient
- All Chemotherapeutic Agents
- Drugs Meeting NIOSH Hazardous Drug Criteria
- Drugs Listed in Appendix VI of OSHA Technical Manual
- Drugs with LD50s Less Than or Equal to 50 mg/kg
- Carcinogenic Drugs
- Combination Vitamin/Mineral Preparations with Heavy Metals
- Endocrine Disruptors

1. Formulations With a Listed Active Ingredient That is Not the Sole Active Ingredient

From a regulatory perspective, in order for a formulation to meet the scope of a P- or U-listing in 40 CFR 261.33, the formulation must contain only one active ingredient. As a result, there are a number of drug formulations that do not have to be managed as hazardous waste because they contain more than one listed constituent of concern or other non-listed active ingredients. There also are formulations where there are differing regulatory interpretations. To simplify implementation, assure environmental protection and preclude second-guessing by a regulator who may not be familiar with the difference between active pharmaceutical ingredients and inactive excipients, vehicles, and diluents, best management practices encourage managing all drugs that contain any P- or U-listed constituents as hazardous waste, regardless of whether or not the listed constituent is the sole active ingredient.

Examples of Formulations with More Than One Listed Ingredient

- Fluori-methane, a drug formulation containing 15% dichlorodifluoromethane (U075) and 85% trichloromonofluoromethane (U121) does not have to be managed as a hazardous waste. It contains two listed constituents that both perform the same intended function so neither one of the listed chemicals is the sole active ingredient.
- When diluent with .05% saccharin (U202) is discarded in the pharmacy in its original form, it must be managed as a hazardous waste due to the presence of saccharin as the sole active ingredient. However, saccharin may no longer be the sole active ingredient and, therefore, no longer a U-listed waste when diluent with .05% saccharin is used for compounding oral liquid preparations.

2. All Chemotherapeutic Agents

Only 9 chemotherapy drugs are either P- or U- listed chemicals (See Table 4 in Step 2). These are the drugs that were in use in 1976 or, in the case of arsenic trioxide, were listed as chemicals before they were used as drugs. Therefore, over 100 equally hazardous chemotherapy drugs currently in use today are not identified federally as hazardous waste and are not subject to the RCRA Subtitle C requirements. Examples of these chemotherapy drugs are methotrexate, vinblastine, vincristine, and 5-fluorouracil.

Best management practice recommends the handling of all chemotherapy agents greater than trace amounts as hazardous waste even if the waste doesn't meet the definition of a P- or U-listed chemical or exhibit any of the characteristics of hazardous waste. By managing all bulk chemotherapy waste as hazardous waste, the potential liability for improper handling of chemotherapy waste streams is greatly reduced.

EPA Region 2 actively encourages managing all bulk chemotherapeutic agents as hazardous waste. This management practice is also consistent with (1) the state of Minnesota which requires all chemotherapy drugs to be managed as hazardous waste[24], (2) the intent of the National Institute of Occupational Safety and Health (NIOSH) Hazardous Drug Alert[25] regarding the proper handling and management of these materials due to the danger for employee exposure, and (3) the American Society of Health-System Pharmacists (ASHP) Guidelines on Handling Hazardous Drugs[26].

The statutory definition of hazardous waste provides sound reasoning for broadening the universe of chemotherapeutic drugs that should be managed as hazardous waste. The statute defines the term "hazardous waste" to mean a solid waste, or combination of solid wastes that because of its quantity, concentration, physical, chemical, or infectious characteristics may: (1) cause, or significantly contribute to an increase in mortality or an increase in serious irreversible, or incapacitating reversible, illness; or, (2) pose a substantial present or potential hazard to human health or the environment when improperly treated, stored, transported, or disposed of, or otherwise managed. Chemotherapy agents, if managed improperly, meet this definition of hazardous waste, which is much broader than the regulatory definition. If discarded improperly, chemotherapy drugs also could be subject to the imminent and substantial endangerment provisions of RCRA Section 7003, 42 U.S.C. 6973.

> It is important to know and understand the properties of each chemotherapeutic agent to determine the proper waste management practice. For example, some chemotherapy agents, such as BCG Intravesical, fit the criteria of a biohazardous or infectious waste, being a live attenuated mycobacterium.

[24] http://www.pca.state.mn.us/publications/w-hw4-03.pdf
[25] http://www.cdc.gov/niosh/docs/2004-165/
[26] http://www.ashp.org/s_ashp/bin.asp?CID=6&DID=5420&DOC=FILE.PDF

3. Drugs Meeting NIOSH Hazardous Drug Criteria

The criteria for hazardous drugs as listed in the NIOSH Hazardous Drug Alert include:

> Mutagenicity,
> Carcinogenicity,
> Teratogenicity or other developmental toxicity,
> Reproductive toxicity,
> Organ toxicity at low doses,
> Genotoxicity, and
> Structure and toxicity of new drugs that mimic existing drugs determined hazardous by previous criteria.

OSHA [1999], NIOSH [2004], and the American Society of Health-System Pharmacists (ASHP) [1990, 2006] recommend that hazardous drug waste be disposed of in a manner similar to that required for RCRA-listed hazardous waste. This recommendation encourages applying the RCRA regulations to newer hazardous drugs, addressing the concern that RCRA is outdated with respect to new drug development.

4. Drugs Listed in Appendix VI of OSHA Technical Manual

The hazardous drug list in the OSHA Technical Manual Section 6, Chapter 2, Appendix VI: 2-1 was developed in the early 1990's by surveying several prestigious healthcare organizations and combining their hazardous drug lists. The NIOSH Hazardous Drug Alert Appendix A list is more comprehensive. However, the appendix in the OSHA Technical Manual does still serve as a primary reference for identifying drugs that should be managed as hazardous waste. While the manual itself is not a regulation, the fact that it is made available by OSHA adds considerable weight to the recommendations, under the General Duty Clause Section 5(a)1.

5. Carcinogenic Drugs

The U.S. Department of Health and Human Services National Toxicology Program's Report on Carcinogens (11th Edition)[27] provides information about substances that are known or appear likely to cause cancer. Section 301(b)(4) of the Public Health Services Act, as amended, requires that the Secretary of the Department of Health and Human Services (DHHS) publish a biennial report that contains, among other items, the following information: A) a list of all substances (1) which either are known to be human carcinogens or may reasonably be anticipated to be human carcinogens and (2) to which a significant number of persons residing in the United States are exposed; and, B) information concerning the nature of such exposure and the estimated number of persons exposed to such substances. In addition to chemotherapy agents such as cyclophosphamide and diethylstilbestrol, which are U-listed constituents of concern, and tamoxifen, which is on the NIOSH Hazardous Drug Alert list, the drug methoxsalen, used for

[27] The 11th edition of the Report on Carcinogens can be accessed at http://ntp.niehs.nih.gov/?objectid=035E5806-F735-FE81-FF769DFE5509AF0A.

skin conditions, is listed in Part A as a known carcinogen and is not caught elsewhere. Drugs listed in Part B are reasonably anticipated to be human carcinogens.

6. Drugs with LD50s Less Than or Equal to 50 mg/kg

One of the primary criteria for including a drug on the P-list as acutely hazardous is an oral lethal dose of 50 mg/kg (LD50) or less. Certain drugs, such as colchicine, meet this but are not included as constituents of concern on the P-list. You should evaluate the LD50s of highly toxic drugs to determine if they should be managed as a hazardous waste. LD50 data is often available on the MSDS or on the drug package insert.

7. Combination Vitamin/Mineral Preparations with Heavy Metals

If a pharmaceutical waste contains a heavy metal, such as chromium, cadmium, or selenium, a Toxicity Characteristic Leaching Procedure (TCLP) calculation can be performed using a 20 times dilution for a solid dosage form and the stated concentration for a liquid dosage form. If the concentration of the heavy metal fails the toxicity characteristic level for that metal, it must be managed as a hazardous waste. There are vitamin and mineral preparations, however, with inadequate data on the specific concentrations of chromium, selenium, or cadmium. These preparations may fail the toxicity characteristic. In the absence of definitive data, it is prudent to manage these preparations as hazardous waste.

Appendix B contains sample Toxicity Characteristic calculations.

PPE and Other Potentially Contaminated Items

Contaminated PPE should also be managed as hazardous waste under best management practices. This includes items such as gloves and gowns, drip pads, other materials overtly contaminated in the preparation or administration of chemotherapy drugs, and other hazardous materials that are known or suspected of having been overtly contaminated with a drug that is being managed as a best management practice hazardous waste. “Trace” contaminated chemotherapy materials should be incinerated as regulated medical waste.

8. Endocrine Disruptors

Endocrine disruptors are chemicals that interfere with an organism’s master glands, such as the thyroid, adrenal, and reproductive glands, and their hormones. These potent chemicals mimic a hormone, block the hormone, or in some other way enhance or disrupt normal hormone activity. Endocrine disruptors are active at extremely low concentrations, such as parts per billion or even

parts per trillion, especially in developing embryos, including humans, and in juvenile amphibians and other aquatic species. Increasing concern is being expressed among toxicologists and water research experts regarding the impact of endocrine disruptors on aquatic organisms, particularly those downstream from wastewater treatment plants. Environmental studies have demonstrated feminization of fish populations due to the presence of estrogenic substances, the female hormone. Laboratory studies have shown interferences with sex determination and other vital developmental processes when organisms have been exposed to minute amounts of drugs, both individually and in combinations. The Faroes Statement[28] was released May 27th, 2007, and documents a phenomenon coined "fetal programming" in which sensitive genes are turned on or off inappropriately due to exposure to endocrine disruptors and other toxins during prenatal and early postnatal development. These malfunctioning genes can affect the organism throughout its life and may lead to medical conditions such as genital deformities, diabetes, obesity, cancer, and other chronic illnesses.

It makes prudent environmental sense not to deliberately introduce these potent chemicals into water systems. Therefore, consider eliminating the drain disposal of endocrine disruptors and managing these wastes either as hazardous waste or at least incinerate them at a municipal incinerator or a regulated medical waste incinerator.

Which Pharmaceuticals Are Endocrine Disruptors?

There is no complete list of endocrine disruptors. Many common endocrine disruptors, such as estrogens, testosterone, progesterone, androgens, contraceptives, and oxytocics are listed in the NIOSH Hazardous Drug Alert. Additional endocrine disrupting drugs, such as the anti-fungal ketoconazole, can be found at www.ourstolenfuture.org.

9. <u>All Other Drugs</u>

a. Incinerate

While your hospital's first priority has to be identifying, segregating and properly managing hazardous pharmaceutical waste, the precautionary principle should be applied and all other drugs can be collected in a separate container for incineration at either a regulated medical waste or municipal solid waste incinerator permitted to handle non-hazardous pharmaceutical waste. Thermal destruction of all discarded drugs would provide the highest level of best management practice available at this time. Future technologies, such as plasma arc units, may eventually provide an even more environmentally sound option.

[28] The Faroes Statement can be accessed at http://www.blackwell-synergy.com/doi/pdf/10.1111/j.1742-7843.2007.00114.x?cookieSet=1.

California and Washington require non-RCRA drugs to be incinerated either in a regulated medical waste incinerator or municipal incinerator based on the specifications and permit of the incinerator. Other states, such as Minnesota, strongly encourage incineration of these "non-hazardous" drugs.

b. Eliminate Drain Disposal

Many hospitals currently dispose of excess material in syringes and IV bags down drains that pass into sewer systems. The two largest sources of pharmaceuticals entering the sewer systems are believed to be from hospitals and households. Wastewater treatment plants are designed to remove conventional pollutants such as suspended solids and biodegradable organic material, but they are not designed to remove low concentrations of synthetic pollutants such as pharmaceuticals. The removal efficiencies of pharmaceuticals appear to be chemical-specific. Limited testing suggests that certain types of treatment substantially remove some pharmaceuticals. However, many synthetic compounds are designed to be resistant to biological degradation and there doesn't appear to be a single wastewater treatment technology that will remove all of the pharmaceuticals. Careful consideration should be given to eliminating drain disposal of unused IVs and other drugs.

States, such as California and Washington, have already prohibited the sewering of virtually any drugs. You should work with your local wastewater treatment plant to determine what wastes are appropriate for discharge to the sewer system. Most POTWs (Publicly Owned Treatment Works) do not have a problem with the sewering of solutions in IV bags that only contain saline, lactate, nutrients, vitamins, potassium and other electrolytes.

c. Avoid Landfilling

For states where landfilling of non-hazardous drugs is legal, the landfills generally require MSDSs for each pharmaceutical that is to be landfilled so they can assure themselves it is not a RCRA hazardous waste and they are permitted to accept it. Landfilling non-hazardous pharmaceutical waste should be avoided, however, both for environmental and security reasons. Drugs added to a landfill will eventually leach into groundwater or be deliberately sewered by the landfill from its leaching beds. Unless immediately rendered non-recoverable in some way, drugs brought to a landfill are also subject to diversion.

Use Non-PVC IV Sets

Many pharmaceutical products are prepared and dispensed in PVC-containing IV bags and tubing. Polyvinyl chloride (PVC) manufacture and disposal, when incinerated, contribute to dioxin formation. Because some dioxins are carcinogens and endocrine disrupting chemicals, minimizing their production and release to the environment is protective of public health. The use of non-PVC IV sets for all chemotherapy drugs will reduce the adverse environmental and public health impacts of treating the waste in a regulated medical waste incinerator. Non-PVC bags are a little more expensive but compared to the cost of the drug the increased expense is insignificant. To the extent possible, all pharmaceutical waste being incinerated should be administered in PVC-free IV sets.

Step 4: Performing a Drug Inventory Review

Now that you have gained an understanding of the regulations in Step 2 and determined which best management practices you will adopt from Step 3, the next step is to perform a drug inventory review. Depending on your time, background and resources, you may decide to hire a commercial service to perform this function (see Employing Alternative Approaches below).

Most hospital pharmacies stock 2,000 to 4,000 drugs in their inventory. Approximately 4% to 5% or 100 to 200 of the drugs in a typical pharmacy inventory are subject to the RCRA hazardous waste regulations and an additional 10% should be managed as hazardous waste based on best management practices. It is important to understand that the percentage of drugs in the inventory will not necessarily correlate with the percentage of hazardous drug waste generated at your facility (See Conducting a Frequency Analysis in Step 5 for a detailed explanation).

RCRA places the burden of proof for making a hazardous waste determination on the generator. Therefore, as the generator, your next step is to go through all of the individual drugs that are administered at your facility and determine which ones must be managed as hazardous waste.

As you review every drug product to determine which drugs are RCRA hazardous and which drugs will be handled as hazardous waste based on best management practices, be sure to document your research, calculations, and waste stream determinations. Include all of the waste codes and the reason for managing a non-RCRA drug as hazardous waste. This information will be invaluable if you are ever audited and asked to support your waste management policies and procedures.

1. Gathering Drug Specific Data

The vast array of different drugs available within a therapeutic category makes it necessary for the pharmacy to maintain a formulary to limit the number of drugs stocked, avoiding costly additions for therapeutic equivalents. The hospital's formulary is a list of drugs approved by the Pharmacy and Therapeutics Committee that can be prescribed for patients by attending physicians. Special circumstances may require purchases of drugs not listed in the formulary to meet a therapeutic need or because of shortages in the industry.

Since drugs not listed in the formulary may be ordered and administered, drug-purchasing records will provide a more complete list of what the pharmacy has in stock than the approved formulary. Therefore, an initial review begins by obtaining a 12-month summary of purchasing records from your drug wholesaler.

To perform the inventory review you will need the following information for all of the drugs administered at your facility:

- National Drug Code;
- Brand name;
- Generic name;
- Manufacturer;

- Strength;
- Dosage form; and
- Package size.

It's Preferable to Obtain Purchasing Data from Your Drug Wholesaler

Manufacturers will sometimes modify drug formulations. When a formulation is modified, the manufacturer assigns a new national drug code (NDC) to the new formulation. Sometimes the formulation is modified to make it non-hazardous, as in the case of removing mercury as a preservative in vaccines and nasal sprays. Therefore, the waste determination for one specific NDC may be different from another NDC of a drug with the same therapeutic function. However, your hospital may use one National Drug Code (NDC) to represent multiple drug manufacturers. If your hospital's NDC list is not current, modifications of drugs may not be identified making waste evaluations inaccurate. Working with the purchase history will eliminate this problem.

Next you will need to identify all of the ingredients found in each drug formulation, including preservatives, heavy metals, and alcohol, using common pharmaceutical references such as Facts and Comparisons® and eFacts®. Drug formulations containing preservatives may require additional effort to determine the composition of the preservative. Thimerosal and phenylmercuric acetate are the two preservatives containing mercury. Their presence will cause the item to fail the TCLP. Some manufacturers list the amount of mercury per dose (e.g. Fluzone), while others, simply list the concentration of the preservative thimerosal (e.g. multi-dose Haemophilus b Conjugate Vaccine). M-cresol, D024, commonly found in human insulin, is the other preservative which can cause a formulation to fail the TCLP, but not in all formulations, depending on concentration.

a. Compounded Items and Re-formulations

It is essential to consider all compounded items as well as re-formulations and IV admixtures to determine their hazardous waste designation, as the characteristic waste designation for the re-formulation or IV admixture may not be the same as for the original formulation. In particular, a pharmaceutical may exhibit the characteristic of ignitability when it is purchased by the pharmacy but no longer exhibit it after being compounded or prepared for administration in the pharmacy. The reverse situation also can occur. If a raw chemical is formulated into an alcoholic preparation, the resulting product may exhibit the characteristic of ignitability (see examples in Table 6).

Drug Prepared for Administration	Waste Designation of Prepared Drug	Original Ingredients	Waste Designation of Original Ingredients
Paclitaxel (Taxol®; BMS), valrubicin, etoposide, or teniposide diluted in an IV containing less than 24% alcohol	> Used IV managed as trace chemotherapy waste > Unused IV managed as hazardous chemotherapy waste according to BMP (See Step 3)	Original vials contain 30 - 50% alcohol	Ignitable Hazardous Waste
Compounded wart remover with salicylic acid and other ingredients compounded in a base of flexible collodion	Ignitable Hazardous Waste	Salicylic acid and flexible collodion	> Salicylic acid is a non-hazardous waste > Flexible collodion is an ignitable hazardous waste

Table 6: Effects of Compounding and Reformulations

2. Making RCRA Hazardous Waste Determinations

Once you have obtained drug specific information, you are ready to gather the data necessary for making hazardous waste and best management practice determinations.

You may find that a formulation is both ignitable and contains a P- or U- listed chemical. It is important to identify all of the applicable waste codes for each drug in your inventory. This information will be valuable when you are designing your program, selecting your vendor and eventually when you are manifesting your pharmaceutical wastes.

Selecting the Right Vendor(s) in Step 9 and Hazardous Waste Manifest in Step 10 provide more information on managing drug formulations with more than one waste code.

a. Toxicity

Determining which drug formulations exhibit the characteristic of toxicity is the most challenging waste determination. Table 3 in Step 2 contains a list of the D-listed chemicals and the concentrations at which they become a hazardous waste. Identify all formulations that contain any of these chemicals using Facts and Comparisons®, EFacts®, or a similar reference.

Appendix A: Tools and Resources has information on accessing Facts and Comparisons®, and EFacts®

Appendix B contains sample Toxicity Characteristic calculations for both liquids and solids.

Alternatively, you can send the formulation to a laboratory for analysis using the TCLP. The laboratory will determine whether or not the formulation exhibits the toxicity characteristic. The expense of performing the TCLP may outweigh applying a conservative approach by managing tablets and capsules, such as vitamin/mineral preparations containing Toxicity Characteristic chemicals and heavy metals, as hazardous waste.

Step 3: Considering Best Management Practices for Non-Regulated Pharmaceutical Waste discusses this approach as a best management practice for vitamin/mineral preparations with heavy metals.

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Thimerosal

> All drugs containing thimerosal fail the TCLP for mercury.
> Therefore, manage all drugs containing thimerosal as D009.
> Wherever possible, minimize hazardous waste by purchasing alternative products that do not contain thimerosal.

b. Best Management Practices

While you are reviewing your inventory to determine which drugs should be managed as hazardous waste, you also will want to apply the criteria for making best management determinations outlined in Step 3 to the inventory. Drugs that satisfy any of these criteria are sufficiently hazardous to warrant being treated in the same manner as drugs that are identified as RCRA hazardous waste.

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1. <u>Documenting Your Decisions</u>

As you review every drug product to determine which drugs are RCRA hazardous and which drugs will be handled as hazardous waste based on best management practices, be sure to document your research, calculations, and waste stream determinations. Include all of the waste codes and the reason for managing a non-RCRA drug as hazardous waste. This information will be invaluable if you are ever audited and asked to support your waste management policies and procedures.

2. <u>Keeping the Review Current</u>

Once you have performed an initial review of all of the drugs in the inventory, systems must be established to keep this list updated at least quarterly to capture new drugs that are added to the formulary and other non-formulary drug purchases on a regular basis, to appropriately manage outdated physician's samples, and personal medications that are left behind by patients.

Each hospital is responsible for maintaining and updating its OSHA hazardous drug list as new drugs enter the facility. As you evaluate new drugs proposed for the formulary, you are required by OSHA to make a hazardous drug determination with respect to employee exposure. This would be the time to also evaluate the drug for hazardous waste status. In addition to making hazardous waste determinations during the inventory/formulary review process, a system must also be set up to include determinations for off-formulary drugs purchased by pharmacy and other departments, such as radiology. Either set a trigger within the receiving software that requires this determination or change printed policies and procedures to inform appropriate personnel of the need to make the waste determination. It is likely that receiving personnel will need to notify a specific pharmacist or safety person of those drugs needing review, as this is a highly technical function.

Summary of Inventory Review Process

- Obtain Drug Specific Data from Drug Wholesaler (e.g., National Drug Code (NDC), brand name, generic name, manufacturer, strength, dosage form and package size)
- Identify Ingredients using Facts and Comparisons®, eFacts®, or MSDS
- Determine RCRA Hazardous Waste Code using Code of Federal Regulations, Merck Index, Periodic Table
- Make Best Management Practice Determinations
- Keep Review Current

3. Employing Alternative Approaches

The number of drugs stocked in a hospital pharmacy and the multiple national drug codes (NDCs) that may be stocked for a specific drug name make the initial review of all of the drugs administered at your facility an extremely time-consuming task. If you decide that manually determining the hazardous waste status of all of these drugs is too time-consuming given the pressure on current staffing levels, there are commercial services available. Subscription on-line web search engines can be used to look up all of the drugs in the inventory. Using an on-line web search engine to review your inventory is still a labor-intensive process, but depending on your familiarity with pharmaceuticals and the hazardous waste regulations and your time constraints, it may be more efficient than a manual review. Alternatively, you can utilize a commercial service to perform a review of all drugs purchased within the past 12 months. Once again, depending on your particular circumstances, this may be a cost-effective method for establishing an initial list of drugs, their NDCs and their hazardous waste status.

Step 5: Minimizing Pharmaceutical Waste

As you design and implement your pharmaceutical waste management program, it is important to ask what pharmaceuticals are being "wasted," why they are being wasted and how wasting can be minimized. There are inherent limitations on the substitution of a less hazardous drug since the hazardous nature of the chemical often provides the therapeutic effect. In addition to being the most environmentally preferable alternative to waste management, source reduction practices can minimize compliance hassles, reduce costs and ultimately reduce the liability. The following section provides a number of minimization opportunities to consider and explore.[29]

1. Considering Lifecycle Impacts in the Purchasing Process

Implement a purchasing policy that includes restrictions and preferable purchasing practices. Examples include but are not limited to:

> Specifying that you will not accept any drugs with less than one year dating unless they are only available with shorter expiration dates.

> Selecting products with less packaging. This is particularly relevant if the drug contains a P-listed constituent of concern. Packaging that comes in contact with drugs that contain P-listed chemicals must be managed as hazardous waste in many, but not all, states.

> Selecting products without preservatives whenever possible. Drugs such as some multi-dose vaccines, and eye and ear preparations, may contain the preservatives thimerosal or phenylmercuric acetate. Manufacturers are moving away from these controversial mercury-based chemicals to less toxic alternatives. Always check your references, such as eFacts®, manufacturers' websites, and your group purchasing organization (GPO) to see if mercury-free alternatives are available.

> Consider single dose containers, which do not need a preservative.

> Communicating your views through your GPO to see if formulation changes can be made in the future. Human insulin is often preserved with m-cresol, a D-listed chemical that causes some of these products to exhibit the characteristic of toxicity. At this time there are no alternatives for this specific product.

2. Maximizing the Use of Opened Chemotherapy Vials

Sometimes opened chemotherapy vials are retained for possible use in oncology pharmacies until they expire. However, this is not always the case especially in lower volume pharmacies. Consider possible ways to maximize usage of these partial vials to minimize waste and save money.

3. Implementing a Samples Policy

[29] See also the Practice GreenHealth Webinar "Pharmaceutical Waste Prevention" March 28, 2008, accessed at http://cms.h2e-online.org/teleconferences/calendar/details/406

Controlling physicians' samples is often an emotionally charged topic. The ability of the pharmacy to control sampling within the organization is often based on the political realities of the organization, who controls the medical staff, and who owns the associated clinics. The fact that samples are outdated and need to be discarded indicates that pharmaceutical representatives are over-supplying samples, physicians' offices are not rotating sample inventory, physicians are not providing samples to patients, or drug usage patterns have changed for particular drugs. Whatever the cause, the organization is incurring added costs and liabilities managing waste drug samples and should adopt a policy that addresses the acceptance and end-of-life management of samples.

A good initial step is to document the amount and frequency of outdated sample generation per out-patient clinic or medical practice area. Determine the cost of handling and disposing of the samples, being sure to check for hazardous drug waste. Be sure to include staff time to review sample dating, transport samples, and manage their waste segregation and disposal. At a minimum, present the estimated costs to the physicians involved in the sample generation as well as waste minimization opportunities. Ideally, outdated sample management costs should be transferred to these medical practices, which encourages opening up the dialog. Also, consider asking the manufacturers to cover the disposal costs that they are imposing on the facility's budget. This should be their cost of doing business, not the responsibility of the hospital.

Many integrated delivery networks have implemented a variety of controls on physician sampling, moving from the least restrictive to the most restrictive, the allowance of no sampling whatsoever. Trial medications can still be managed for patients either through introductory vouchers from manufacturers or through small initial trial prescriptions with larger refills. Patients will need to pay the co-pay, which is a disincentive for the smaller prescription.

Less restrictive strategies include requiring pharmaceutical representatives to package outdated samples for return to the manufacturer. Under the Food and Drug Administration's Prescription Drug Marketing Act (PDMA), manufacturers' representatives are not allowed to physically remove samples from the physicians' offices, but can facilitate their shipment back for disposal. Another approach is to limit sampling to the top six drugs prescribed in each clinic or practice or to those drugs listed in the Formulary. If personal use by physicians is an issue, allow physicians to receive samples but require them to store them personally off-site.

4. Labeling Drugs for Home Use

Many single patient items, such as aerosols, ointments, and sometimes insulin, are only used for a few days during the hospital stay. These patient-specific medications are returned to the pharmacy for destruction when the patient is discharged or are discarded in the trash or in needleboxes in the nursing units. They cannot be legally dispensed to the patient without a discharge prescription from the doctor and proper outpatient labeling. In the current system, these procedures would cause delays in the discharge process that would be unacceptable to the patient. Consider how the system could be changed to include pre-authorized discharge orders for maintenance medications and possible label production in the units. This would reduce waste and save money for both the healthcare system and the patient. Smaller hospitals in particular

should consider relabeling for home use. This is more difficult logistically in large facilities, and patients often will not wait for the new orders to be communicated to the pharmacy and new labels attached. A number of rural hospitals in northern Minnesota have pre-labeled these items for home use with much success.

5. Priming and Flushing IV Lines with Saline Solution

Pharmacies should prime all chemotherapy IVs with saline prior to dispensing and nurses should flush the tubing after administration. These practices not only insure the patient receives the full dosage but also reduces the opportunity for employee exposure and enables IV tubing and bags to be managed as trace chemotherapy waste.

6. Examining the Size of Containers Relative to Use

Certain medications are routinely administered in doses that result in waste or in dispensing devices. Explore purchasing containers that are designed to be lighter and use less materials or purchase dosages in sizes more appropriate to your usage. Consider conducting a survey of all drugs routinely wasted in your facility due to the prepared product being too large for complete administration. Through an on-site review, one hospital found that Lopressor was purchased in 100 mg tablets but only 50 mg tablets were routinely administered. Therefore, 50 mg of Lopressor were routinely wasted. Lopressor is available in 50 mg tablets and the generic version, metoprolol, is available in 50 mg or 25 mg tablets. Changes in your purchasing patterns can save your hospital money by reducing the amount of pharmaceutical waste that you generate.

If you can't find the product size that meets your needs, share this information with your group purchasing organization (GPO) so they may provide feedback to the pharmaceutical distributors and manufacturers to encourage more appropriate packaging sizes. Encourage your GPO to conduct a broad-based study to determine the total universe of drug formulations that are routinely wasted due to package size.

There are variations in the weight of dispensing instruments. For example, consider using two-part polyolefin IV devices to administer antibiotics (e.g. *Duplex*) that weigh one-third less than traditional glass vial/PVC IV bag alternatives.

> In a small rural hospital, a doctor wanted three 250 cc IV bags of dilute epinephrine available for shoulder surgeries, but routinely only used one. The pharmacist agreed to be available to formulate additional IV bags immediately, if needed. After six months, the system is running smoothly and the amount of waste generated has decreased.

7. Replacing Prepackaged Unit Dose Liquids with Patient-Specific Oral Syringes

To avoid having to routinely waste the remaining contents of 5 ml and 10 ml prepackaged unit dose liquids, consider moving to patient-specific oral syringes, especially in the neonatal and pediatrics units where doses are very customized and patient-specific. This practice is especially

useful for drugs like chloral hydrate, which is also a controlled substance. Eliminating waste also saves nursing time while preventing the usual drain disposal of a hazardous waste.

Review all Emergency Department multi-dose vials to determine the optimum dosage unit to stock based on usage frequency and consider moving to single dose syringes when possible to avoid possible mercury preservatives and to minimize partial use. For example, the single dose syringe, Decavac[30] (Diphtheria and Tetanus Toxoids, Combined; Aventis-Pasteur) can replace the 5 ml multi-dose vial that contained a mercury preservative, thimerosal. The 5 ml multi-dose vials often need to be discarded and the level of mercury causes the wasted product to be managed as a hazardous waste.

If patient-specific insulin vials are used, re-evaluate the necessity of this practice since most are discarded with significant drug remaining. Multiple patient use of an insulin vial reduces waste since patient-specific vials are destroyed at the time the patient leaves the hospital regardless of the remaining volume. Insulin pens are another consideration as they represent a smaller total volume than a vial (3 ml vs. 10 ml) and can be relabeled when the patient is discharged. Human insulin contains m-cresol as a preservative, requiring management as a hazardous waste. Each organization has its own philosophy regarding infection control and medication management.

8. Controlled Substances

Due to the difficulty in disposing of a controlled substance that is also a hazardous waste and the desire to avoid the drain disposal of all pharmaceutical wastes, it is best to try to eliminate the generation of these wastes to the degree possible. Minimizing the wastage of controlled substances will also save the staff time of the two nurses required to witness their destruction. Chloral Hydrate is an example of a controlled substance that is routinely wasted when it is administered in a 5 ml unit dose cup to children. If it is purchased as bulk syrup, the exact dose can be dispensed in an oral syringe, eliminating any routine wastage.

9. Delivering Chemotherapy Drugs

Deliver chemotherapy in ziplock bags to the nursing units in hard plastic trays or closed "coolers." This will provide greater spill and leak protection during transport.

10. Monitoring Dating on Emergency Syringes

Generally, hospitals replace epinephrine and nitroglycerin syringes and vials on general crash carts when they are within three months or less of their expiration date. These products can be moved from general crash carts to the Emergency Department or ICU/CCU three months prior to outdate to avoid discarding them.

[30] Facts and Comparisons indicates the Decavac contains up to .3mcg. of mercury/dose due to the manufacturing process, or 0.6mcg/ml which exceeds the 0.2mcg/ml limit for the TCLP. However, there should not be a reason to discard the Decavac since the entire dose should be used during administration.

11. <u>Reviewing Inventory Controls to Minimize Outdates</u>

Create a tighter inventory control program to limit the amount of original manufacturers' containers and repacks that expire before use. Resources spent on the management of expired products are resources lost. More and more hospitals are implementing automated pharmacy shelving and inventory systems and experiencing cost savings through waste reduction.

NEW! Appendix C: Pharmaceutical Waste Minimization: Two Case Studies presents first-ever documentation of pharmaceutical waste minimization and significant cost savings.

Step 6: Assessing Current Practices

1. Performing Department Reviews

Gathering current waste generation and disposal practice information, including estimated volumes and weights, will assist you in designing your program, establishing a baseline to estimate waste management costs and track progress over time, and identifying ideas for reducing your pharmaceutical waste stream.

Documenting quantitative volumes of drug waste currently being generated is challenging and involves either creating a detailed log of all drug waste being discarded within the pharmacy and nursing units by pharmacy and nursing personnel during a specified timeframe, or manually sorting and documenting the waste. The first option is time consuming for professional staff. The second option, a traditional waste audit or assessment, raises safety concerns for those involved.

The most efficient way to gather this information is through an informal but well documented interview process throughout the organization to determine current medication disposal practices. Informal interviews should be undertaken in the pharmacy, all nursing units, and outpatient clinics for which the hospital has waste management responsibilities. If time or resources are limited, interviews should be conducted in the pharmacy, inpatient and outpatient oncology areas, cardiac care unit, emergency department, and operating room, including anesthesia.

Learning what the current practice is will provide valuable guidance as to what practices need to be modified and what level of consistency is present throughout the organization, especially where stated policies and procedures have been developed. This exercise will also inform staff that attention is now being focused on pharmaceutical waste management.

Basic questions should focus on what drugs are being discarded and how pharmacy, nursing, and medical staff are routinely discarding them: in sharps containers, red bags, down the drain, or other options. It also is valuable to gain an understanding of how drugs are administered in your facility to provide a sense of which drugs may need to be managed as both hazardous waste and RMW. In addition, this is a good time to ask for assistance in identifying waste minimization opportunities. Care should be taken to emphasize the fact-finding nature of this process and that there are no right or wrong answers.

The basic interview process can be completed within one or two 8-hour days or longer, depending on the size and complexity of the organization. All departments that will be visited should be notified in advance and a schedule set up if at all possible to assure availability of both the supervisor and designated staff. Do not rely on managers reporting in a meeting setting. As many staff should be queried as possible to obtain an accurate picture. It is paramount that nursing management is heavily involved and supportive of this effort.

Data generated from automated drug dispensing cabinet systems can be used to supplement the information that you collect through your on-site interviews. Automated cabinet systems are

designed to electronically record and track actions related to the disposition of drugs dispensed from them. This data can be downloaded onto a spreadsheet and analyzed for the frequency, location and amount of drug wastage. Pharmacy information systems and medication management systems may also be a source of data regarding where RCRA drugs are used.

2. Conducting a Frequency Analysis

It is very helpful to perform an analysis on which drugs are dispensed to each unit and in what quantities over a specific time frame, such as 30 days. If the dispensing software has a function to sort data by unit and order, this should be a relatively simple task. Billing records might also be a source of this information. If hard data are not readily available, review with pharmacy staff their impressions of which units receive the 5% of drugs that are RCRA hazardous waste. These should already be identified by this time. In addition to the oncology inpatient and outpatient areas, find out what other units receive chemotherapy drugs for other purposes, such as treatment of autoimmune diseases. The data from this analysis can be presented by department or by drug. This will provide a better understanding of which units within your facility have the potential to generate significant amounts of hazardous waste. It will also indicate which drugs you can expect to manage as hazardous waste most frequently.

While there is no documented percentage of drug waste per drug dispensed available at this time, it is reasonable to assume that areas administering higher volumes of potentially hazardous waste will generate more hazardous waste. Knowing which units have the potential to generate significant amounts of hazardous waste will help you identify which departments to visit during your on-site review and prioritize the roll-out of your program. Knowing the frequency with which hazardous drugs are administered by department also will help you target the questions that you ask staff in order to better understand their current waste generation and disposition practices

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Pharmaceutical Waste Generation

For the following reasons, the percentage of hazardous drugs in your inventory does not correlate with the percentage of hazardous drug waste that will be generated at your facility.

> A particular P-listed drug,.such as physostigmine, may be discarded on a regular basis, due to the nature of its use, while another P-listed drug, like warfarin, which is a tablet, may be discarded less often.
> The frequency of use will vary among drugs, resulting in fewer opportunities for waste generation for some compared to others.
> U-listed drugs are not managed as hazardous waste if the containers are RCRA empty. (See Step 2, U-Listed Wastes, for a definition of RCRA empty.)
> Contaminated PPE and spill materials will increase the amount of hazardous waste generated

3. Confirming Your Generator Status

Hazardous pharmaceutical waste is generated from numerous activities and events including preparing IVs, general compounding, cleaning up of spills and breakage, and discarding partially used vials, IVs, discontinued medications such as ointments and inhalers, unused unit-dose repacks, patients' personal medications, outdated pharmaceuticals, and contaminated PPE.

If you are not convinced that you are a LQG, have the pharmacy and nursing staffs document the weight of all P-listed waste discarded in a calendar month to confirm your generator status. The reason for doing this is that only 1 Kg. of P-listed waste, including empty containers, causes your facility to become a large quantity generator. Alternatively, you can include questions in an on-site review that will help you to qualitatively determine your generator status.

Logs are particularly helpful in defending your CESQG or SQG status. An inspector will look at your manifests and then compare them with your logs. The log becomes the record of the P-listed wastes generated and not the manifest. If you don't log your wastes as you generate them, you cannot prove the volume generated in a calendar month. If you are a LQG, there is no need to document how much P-listed waste is generated in a given month.

The weight of the P-listed waste includes the weight of the container regardless of the amount of the drug remaining.[31] In states where nitroglycerin has not been excluded from regulation as a P-listed waste, the heavy glass bottles will also contribute greatly to large quantity generator status. Not all states have accepted the USEPA decision that epinephrine salts are not regulated as P-listed waste. If either of these situations exist in your state, it is likely you are a LQG.

If P-listed wastes are in their original packaging and combined with other materials, the weight of the entire container does not have to be included in determining if the facility is a LQG as long as: the exact weight of each P-listed waste in the container is documented; the P waste remains in its original container; and the P-listed waste is not mixed with the other waste. Essentially, the original package is considered primary containment and the outer storage bucket is secondary containment.

[31] RCRA Online #12946, http://yosemite.epa.gov/osw/rcra.nsf/0c994248c239947e85256d090071175f/a84d28e4c573528e8525670f006c1bcc!OpenDocument

Step 7: Taking On the Communication/Labeling Challenge

Once the pharmaceuticals in your inventory have been classified as to their hazardous waste status, the next challenge is to choose a method for communicating that information to pharmacy and nursing staff as they generate pharmaceutical waste during the course of their everyday activities. You may need two systems: one for drugs discarded in the pharmacy and the other for drugs discarded in the nursing units. How you choose to communicate this information will be influenced by variables unique to your organization, such as facility size, pharmacy complexity, dispensing software, and internal expertise or resources available to procure expertise. You may decide to adopt one approach to labeling initially while you develop a more sophisticated approach over time. Regardless of which approach you choose, be sure to include a process of integrating new drugs into the labeling system.

1. Automating the Labeling Process

a. Incorporating Disposition Data in Dispensing Software

Automated labeling of drugs that are administered to patients involves entering hazardous waste disposition information for every drug in the inventory that designates as a hazardous waste into the pharmaceutical dispensing software. This will enable waste segregation information to be indicated on the patient label. If your NDC file is continually updated, that is the most desirable level to integrate the hazardous waste data. If this is not possible, use the generic name of the drug.

Consider all of the possible ways that drugs are labeled in your organization, including unit-dose items, items prepared for robotic dispensing, items dispensed from automated dispensing machines, and compounded and reformulated items such as ointments and IVs, to insure that no segment of drug distribution is missed.

Automated cabinet systems securely store and dispense controlled substances and other commonly used medications. These systems have the automated capability to identify proper pharmaceutical waste disposition practices and create accountability to better ensure regulatory compliance. When developing a labeling system for the drugs dispensed through the pharmacy, these “de-centralized pharmacies” should not be overlooked. You may decide to apply the same approach that you select for the drugs that are dispensed from the pharmacy or these systems can be customized to include appropriate disposition information as a way for the end user to make this determination.

Within the pharmacy, shelf stickers can provide pharmacy staff with information on how to dispose of drugs pulled directly from inventory for IV preparation or other compounding activities as well as provide information on spill clean up.

b. Inserting Disposition Data on Barcodes

Using bar codes also eliminates the need to label items individually. If the hospital has implemented bedside bar coding for ensuring patient safety, messages can also be inserted into the administration software, notifying nurses of disposition requirements. A hospital must be totally bar-coded at the bedside to implement this system. Between 20% and 5% of hospitals are currently at that level, but adoption of bedside bar coding is expected to escalate in the next few years.

An automated waste-sorting machine, similar to a reverse dispensing device, is now available. This device will enable nursing personnel to scan the bar code at the bedside and a door will open for the appropriate waste stream. A waste determination can be made once and then transferred to data systems that then provide a failsafe segregation system, facilitating compliance.

2. <u>Manually Labeling in the Pharmacy</u>

If your current dispensing software does not enable an additional field to be accessed or printed, you can use the hazardous waste designations in the inventory review to manually label drugs that will be administered to patients. A sticker can be placed on all orders that are prepared for patient administration. The pharmacy staff can quickly reference shelf stickers, to save time and avoid errors. Shelf stickers cue the pharmacy personnel to dispose of these drugs appropriately in the pharmacy preparation areas as well as to apply appropriate labels to each drug as it is dispensed to the nursing unit. A sticker must be placed on all orders that require special disposal as they are prepared for the nursing units. This requires strict attention to detail and continuous quality assurance. While this is a manual process that requires constant vigilance, virtually any pharmacy can implement it regardless of their software or technology level. Migrate to an automated system as soon as possible.

3. <u>Providing Guidance on the Nursing Units</u>

Place stickers on hazardous waste containers on the floor and/or display guidance posters near the containers. This approach is often used to educate users of solid waste recycling programs.

4. <u>Selecting a Message for the Label</u>

A code name or word should be chosen which is easy for staff to remember but that does not alarm the patient. There are two pieces of information that should be conveyed through this message, the discard location and how the container is managed. The message can be a color-code, text or a combination of color-code and text. The table below provides some suggested abbreviations for text messages. For P-listed drugs, such as physostigmine, the cue should include the terms “empty or full,” since the container is also considered to be hazardous waste. In addition, simply a color-coded strip or Blue Bin 1 or 2 can be used. There is no regulatory

requirement, so pick acronyms or color-coding that makes sense to your organization (see examples in Table 7).

Sample Text Label Message	Type of Waste
HW-I	Ignitable Hazardous Waste (if you decide to manage ignitable hazardous waste separately)
HW-T, empty = trace	Hazardous Chemotherapy Waste
HW-T even if empty or empty or full	P-Listed Hazardous Waste
HW-T unless empty	U-Listed Hazardous Waste
HW-P	P-Listed Hazardous Waste (if you wish to segregate P-listed drugs for documentation purposes)

Table 7: Sample Messages for Labeling

Step 8: Considering the Management Options

Your program goals (e.g., ensuring compliance and simplicity) and facility constraints (e.g., space, technology and resources) will drive the design of your pharmaceutical management program. Five models for managing pharmaceutical wastes are presented: 1) an automated bar-code driven sorting device; 2) electronic labeling in the nursing units; 3) manual labeling in the nursing units; 4) segregating waste at the central storage accumulation area; and 5) managing all drug waste as hazardous waste. All five models involve satellite accumulation (described in Step 9) and four of the five options require drug segregation within the facility. Selecting an option should proceed in parallel with Step 9: Getting Ready for Implementation, since some approaches involve more vendor participation than others, and cost estimates from vendors may also impact the approach.

1. Models 1, 2, and 3: Segregating at the Point of Generation

Ideally, hazardous pharmaceutical waste will be segregated at the point of generation and discarded in hazardous pharmaceutical waste containers that are located as conveniently as practical to the point of generation. Personnel that are trained to handle hazardous waste transfer the containers from the satellite accumulation areas at the point of generation to the central storage area (described in Step 9) where they are picked up by a permitted hazardous waste vendor.

You will need to consider purchasing containers. The container market for hazardous pharmaceutical waste is still evolving, but to date the most common containers available are black, meet DOT Packing Group II, and are labeled "Hazardous Waste." Toxic and ignitable labels are also provided. Different container sizes and configurations are now available, including trolleys to insure stability.

Management of "non-hazardous" pharmaceutical waste is discussed below in Step 9 Getting Ready for Implementation. Using Best Management Practice, these items should be segregated and incinerated at either a regulated medical waste incinerator or a municipal incinerator permitted to accept non-hazardous pharmaceutical waste. Containers for non-hazardous pharmaceuticals should be labeled: INCINERATE ONLY. Several containers for these wastes are available including white with a blue top[32] and cream with a purple top.[33]

The most common waste streams used for point of generation pharmaceutical waste segregation are included below in Table 8.

[32] Contact Mike Liscio, Director of Marketing Sharp Safety Division, (508) 261-8493, mike.liscio@covidien.com for more information.
[33] Contact David Skinner, Vice President, Daniels Sharpsmart Inc., (805) 907-1160, DSkinnner@danielsinternational.com.

Type of Waste	Description of Waste	Description of Container	Type of Treatment
Hazardous Toxic and BMP Toxic	P, U and toxic D wastes All bulk non-listed chemotherapy drugs Non-listed toxic drugs PPE with visible contamination	Black	Incineration at RCRA hazardous waste facility
Hazardous Ignitable	D001 wastes	Black	Incineration at RCRA hazardous waste facility
Hazardous and Infectious	Hazardous toxic wastes and BMP toxic wastes combined with RMW Entire contents of sharps containers if P-listed hazardous waste was properly or improperly discarded in container (NOTE: Recent expansion of the epinephrine syringe exemption should reduce this waste to a minimum if accepted by states.)	Black hazardous waste container in needlebox configuration with RMW label applied	Incineration at a facility permitted to handle RCRA hazardous waste and RMW
Trace Chemotherapy	"RCRA" empty vials of chemotherapy agents, syringes/needles, IVs, PPE used to prepare or administer chemotherapy without visible contamination	Yellow	Incineration at RMW facility
Drain Disposal	Controlled substances, NaCl, dextrose, vitamins, electrolytes	Sewer NOTE: An increasing number of states and municipalities are restricting drain disposal of drugs, including controlled substances.	Local POTW (permission required)
BMP Non-Regulated	All other drugs	White with blue top or cream with purple top	Incineration at RMW or municipal solid waste (MSW) facility

Table 8. Pharmaceutical waste streams

Should Ignitable Wastes Be Managed Separately?

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Consider the following:

- Waste compatibility
- Vendor's requirements
- Quantity of ignitable waste generated
- Potential cost savings from managing ignitable waste separately
- Feasibility of combining pharmaceutical ignitable waste with other ignitable waste
- Local and national fire code requirements

2. Model 4: Centralized Segregation

In centralized segregation, **all** drug waste is discarded in hazardous waste containers that are located at the point of generation. The nursing and pharmacy staffs are not required to make decisions regarding the final destination of the drug waste. However, bulk chemotherapy and trace chemotherapy waste are an exception, as these wastes should be segregated in the patient care areas to avoid employee exposure. Overall, this option minimizes the number of containers that must be maintained at the point of generation. Ultimately, the containers are moved to a central storage accumulation area and either hospital personnel that have received hazardous waste training or a hazardous waste vendor manually sort the waste into appropriate containers. Hospitals that are implementing this approach experience inappropriate waste segregation of regulated medical waste and trace chemotherapy. In other words, nursing and pharmacy staffs are discarding wastes that are not pharmaceutical waste in hazardous pharmaceutical waste containers. Therefore, containers for all types of waste generated at the facility should be available in the manual sorting area. The requirements for a hazardous waste storage accumulation area apply to the sorting location.

It is still necessary to determine which drugs become hazardous waste when discarded (Step 7: Taking On the Labeling Challenge). Pre-labeling may be more time efficient for segregation personnel as lists are difficult to maintain and use in this environment. However, generally speaking, hospitals that are currently implementing this approach are using an easily accessible list identifying the appropriate bin for all of the drugs and drug containers generated by the facility. This list must be updated on a regular basis to reflect changes that are made to the inventory.

Centralized segregation may be easier to implement initially but it is harder and often more costly to operate. There are also several drawbacks to this system. If any hazardous waste leaks in the container, it could potentially contaminate other items and render all of the contents hazardous. Infectious waste can render the entire contents a combination hazardous waste and RMW waste that must be managed by a limited number of vendors that are permitted to manage both waste streams. There also is a real risk of encountering sharps and infectious waste.

If hospital employees are sorting the waste, they need to receive extensive training in hazardous material and waste handling and management requirements and must be provided with appropriate personal protective equipment. Given the employee exposure risks involved, it is strongly suggested that external hazardous waste vendor personnel be used to accomplish the sort. These technicians usually have extensive hazardous materials and hazardous waste training, including Hazardous Waste Operations and Emergency Response (HAZWOPER).

If a hazardous waste vendor is utilized, labor costs should be carefully evaluated and compared with the upfront costs of developing automated hazardous waste identification systems and the labor costs associated with manual hazardous waste identification. Experience will provide the best data for an accurate cost analysis.

In states where pharmaceutical waste is defined as medical waste, such as California, it is illegal to re-sort the waste. This model is therefore not appropriate in such states and sorting must be done at the point of generation.

Step 9: Getting Ready for Implementation describes the requirement for a hazardous waste storage accumulation area in more detail.

Appendix A: Tools and Resources provides references for additional information on the Hazardous Waste Operations and Emergency Response Standard under OSHA.

3. Model 5: Managing All Drug Waste as Hazardous

To avoid the expense of labeling and training staff to determine which drugs are RCRA hazardous waste, some hospitals have chosen to manage all pharmaceutical waste as RCRA hazardous waste.

In small facilities with fewer than 50 beds, this may be the simplest and most economical solution in the long run. For large facilities, pilot programs have documented this approach could result in added hazardous waste costs of in excess of $1,000,000 annually. Analysis should provide the best answer as to whether this approach is a viable alternative. Careful cost modeling or a pilot program may be the only way to make this determination.

Step 9: Getting Ready for Implementation

1. Locating Your Satellite Accumulation Area

Collecting hazardous waste in the immediate area in which it is generated is called "satellite accumulation." Specific federal regulations apply to this activity and state requirements may be more stringent.

All of the program design options presented in Step 8 involve satellite accumulation. It is not realistic for nursing and pharmacy staff to go to a central storage accumulation area each and every time hazardous waste is generated. Therefore, you will need to evaluate where waste containers will be placed, consulting with pharmacy and nursing staff in the process.

To maximize compliance, satellite accumulation sites should be conveniently located as near as possible to where drug waste is generated. In the pharmacy, consider locating hazardous waste containers in the sterile products clean room and in the main pharmacy. On the nursing units, the soiled utility rooms, medication rooms, or near medication carts in a secure area have worked well. Containers cannot be stored near a working sink or open floor drain without secondary containment. A locked wall unit that can be placed in the patient's room is now available. This is often a choice for the medication room due to its small size and convenient wall-mount.

Each container must be spill-proof, leak-proof, compatible with the waste to be contained, labeled as hazardous waste and the appropriate waste stream noted (toxic and/or ignitable). The containers must be kept closed when active addition is not occurring. This can be a challenging requirement but one that needs to be taken seriously. During the administration of chemotherapy drugs, for example, the containers may be open, as active addition will be occurring. However, these containers must not be left open when they will not be added to for a period of time (e.g., lunch breaks, over night, when the satellite operator/nurse is not present). Violations of this requirement are often cited during compliance inspections. The simplest way to insure timely and consistent container closure is the use of wire frame trolleys or hard plastic carriers that are opened with a foot pedal, leaving the hands free and closing automatically.

While there is no time limit on the length of satellite accumulation federally, some states do have limits, usually one year. There is, however, a quantity limit. No more than 55 gallons of combined U and characteristic waste can be accumulated and not more than **1 quart** of P-listed waste. Once a quart of P-listed waste has been stored, the container must be sealed and moved to the storage accumulation area within 3 days. Some states do not allow the three days, so check your state regulations and design monitoring systems accordingly.

For states that have accepted EPA's exclusion of nitroglycerin and of epinephrine salts, the one quart rule should not be a problem. If that is not the case, the 1-quart limit is a major concern regarding the generation of waste IV nitroglycerin in the ICU and epinephrine in the pharmacy, ICU and Surgical Suites, especially if orthopedic surgery is routinely performed. Another surgical area to check for epinephrine is ophthalmic surgery, as it is often used as flush with partial IV bags remaining after the procedure.

It is important to remember that wastes should be kept in their original closed containers when discarded, not squirted or drained into the waste container. If there is any free liquid designated as P waste within the container then all of the content that is contaminated with the free liquid is a hazardous waste mixture and therefore the P-listing applies to the entire contents within the container.

a. Corrosive Waste

It is not necessary to set up a separate container for corrosive hazardous waste in the pharmacy, since it will not be generated on a day-to-day basis. All compounding chemicals should be reviewed annually and disposed of as lab packs by your hazardous waste vendor if no longer in use. Under the requirements of the United States Pharmacopeia Chapter 797 (USP 797), all chemicals used in sterile compounding must also be dated upon receipt and discarded after one year unless the manufacturer has included an expiration date.

b. "Non-hazardous" Pharmaceutical Waste

Best management practices discussed in Step 3 encourage you to collect "non-hazardous" pharmaceutical waste and dispose of it through either regulated medical waste incineration or waste-to-energy municipal incineration. Containers are available from several sources for this waste stream which should be placed near the hazardous waste containers at the satellite accumulation site for staff convenience. These should NOT be stored with your hazardous waste, although you may receive permission to store them in the same area as long as they are segregated in an obvious manner. If you will be using your RMW waste disposal company to incinerate them, you may choose to store them with the Regulated Medical Waste, which should always be in a locked containment area. Security is very important, due to the street value of even non-controlled substances.

2. <u>Evaluating Your Hazardous Waste Storage Accumulation Area</u>

When hazardous drug waste containers are removed from satellite accumulation areas in the pharmacy, nursing units, and clinics, they must be transferred to and stored in an area known as a hazardous waste storage accumulation area. You will need to review the state and federal requirements of a hazardous waste storage accumulation area to insure compliance with RCRA regulations for your generator size, especially if management of pharmaceutical waste moves you from SQG to LQG status. There are very specific requirements for setting up and maintaining a hazardous waste storage accumulation area that can be found in 40 CFR Part 262.34.

It is likely that your organization already has established a central storage accumulation area for other hazardous wastes such as xylene. However, it is possible the area may need to be enlarged, a second storage accumulation area established, or your hazardous waste vendor will need to schedule more frequent pick-ups to handle the new pharmaceutical hazardous waste stream. A pilot program can provide valuable data concerning the volume and frequency of hazardous

waste containers being generated and any logistical challenges associated with the location of the existing storage area.

A discussion on how to conduct a pilot program is provided in Step 10: Launching the Program.

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3. Selecting the Right Vendor(s)

First and foremost, you are looking for a vendor that is licensed by EPA to transport hazardous waste to a permitted treatment, storage, and disposal facility (TSDF). Your organization may already have a contract with a hazardous waste vendor for laboratory chemical waste or may utilize their services on an as needed basis. It is very important to insure that your current vendor is permitted to handle P, U and toxic D waste. For example, some vendors are fuel blenders and can handle ignitable wastes but are not permitted to manage the pharmaceutical wastes that you will be generating. You also may need a vendor that can provide specialty services such as being able to handle combinations of hazardous and infectious wastes or being registered with the Drug Enforcement Administration (DEA) to take possession of waste controlled substances.

Hazardous Controlled Substance Waste

A vendor that can handle controlled substances that are also hazardous waste will have a registration with the DEA. You are required by DEA regulations to have a copy of this registration for your files. It will indicate which schedules, 1 through 5, the vendor is registered to handle. Schedules 2 through 5 are applicable to healthcare facilities. When the vendor picks up the controlled substances, you are transferring these items to them in a very formal manner which must include either a Form 222, (issued from the vendor to you) if you are transferring Schedule II drugs such as morphine, or a detailed inventory list (from you to the vendor) if the drugs are in Schedules III through V. The pharmacy department should be actively involved in this process since they work with this same procedure when controlled substances are sent through reverse distribution. The vendor is taking on two areas of liability: accountability to the DEA for security and documentation and to the EPA for proper disposal and documentation. The persons responsible for this transaction should be completely familiar with DEA regulations as they pertain to a transfer between registrants.

Some vendors that operate RCRA permitted hazardous waste incinerators also provide on-site pick-up services. Availability depends on your geographical location. You will want to evaluate regional brokers as well as final disposers. Regional brokers are usually permitted as 10-day transfer stations and often take all forms of hazardous waste, including universal wastes such as

fluorescent bulbs and batteries. It is important to know all of the vendors that the broker uses for actual disposal or recycling and require the broker to alert you to all changes.

To determine your best service options, have all available vendors in your area submit detailed price quotes with line items that can be compared across vendors as well as documentation on permits, violations over the past three years, and recommendations from other hospital customers. As the generator, your facility is liable for improper management of your waste. Before you finalize your vendor selection, check with your local regulator and EPA for the vendor's compliance status. Be sure you have a solid contract with your vendor including indemnification against such liability. Hazardous waste vendors should also agree to take title to the waste as soon as they take custody of it. Remember that you can contract out your responsibility but can never escape your liability as a hazardous waste generator.

Vendor selection can proceed in parallel with Step 8: Considering the Management Option since some approaches involve more vendor participation than others.

a. **Reverse Distributors Are Not Waste Management Services**

Reverse distribution of pharmaceuticals primarily involves the return of unused, outdated pharmaceuticals to the manufacturer for credit. The reverse distribution industry emerged in the early 1990's to maintain an ever-changing database of manufacturers' return policies and to provide hospitals with the labor-intensive service of inventorying all of their unused, outdated items and comparing them to this database.

Two interpretative letters from EPA (RCRA Online #11606 Returned Pharmaceutical Products and RCRA Online #11102 Applicability of 261.33 to Discarded Products) indicate that given the underlying assumption that returned items might potentially be recycled, EPA would not consider these items a waste until they reach the destination where the decision to discard them is made. This decision allows these items to be sent through interstate commerce as products, rather than as wastes, and does not require the pharmacy to make a hazardous waste determination.

If the drugs are not returnable to the manufacturer as determined by the reverse distributor, the reverse distributor becomes the generator and must make a *hazardous waste determination* and manage the waste accordingly.

EPA did not intend for you to use reverse distribution to relieve you of your responsibility as a generator for making hazardous waste determinations. Reverse distributors cannot be used as waste management services.

The following items should **never** be returned to a reverse distributor since they are **never** creditable:

> Unused compounded IVs,
> Partial or empty vials,

> Used ointments,
> Bulk chemicals or materials,
> Outdated samples,
> Outdated unit-dose items,

Waste controlled substances unless the reverse distributor has a solid waste permit and the technical ability to report the transaction to ARCOS.[34]

Stay Abreast of Reverse Distribution Developments

In some EPA regions and in an increasing number of states, regulators are prohibiting the reverse distribution of outdated drugs that have become hazardous waste if they have a history of not being recycled or reused. These prohibitions may apply even if the drug is eligible for credit from the manufacturer.

It is important for you to be aware of how the drugs that you send to your reverse distributor are being managed and to modify your reverse distribution program accordingly.

You should monitor your state environmental protection agency and EPA region and adjust your return policies periodically. Selecting a competent and reliable reverse distributor that knows and abides by state and federal hazardous waste regulations will assist you in this effort.

4. Conducting a Pilot Program

The three highest profile areas, the pharmacy, in-patient oncology units, and outpatient oncology clinics, should be considered for an initial pilot program. Not only are they easier to control than some units, these are the areas regulatory agents will be sure to examine. There is no more certain way to generate a notice of violation than by the absence of a hazardous waste container in an area where bulk chemotherapy waste may be generated.

During the pilot program, you should be evaluating how you label the drugs for pharmacy and nursing personnel. You will need to perform training, and can therefore estimate the time and costs involved in training three shifts of personnel. Feedback from pharmacy, nursing, environmental services and safety will be extremely important. An easel with a flip chart can be posted in the department to capture staff input. This allows staff to write in direct, timely feedback to the project and gives the committee valuable information for decision-making. The

[34] Automation of Reports and Consolidated Orders System (ARCOS) is a reporting system managed by DEA. All manufacturers, distributors, and reverse distributors are required to report all schedule II and narcotic schedule III transactions to ARCOS on a monthly or quarterly basis.

logistics of number and size of container, frequency of change out, volume to be stored in storage accumulation, and costs of disposal are all areas that can be clarified by the pilot. Perhaps most importantly, if you have made decisions that just don't work for your organization, you can back away from them citing the experimental nature of pilot programs. You should have all the "bugs" worked out before you set up your full house rollout schedule.

5. Putting It All Together: Pharmaceutical Waste Management Policies and Procedures

After conducting a pilot and before rolling out the program to the entire facility, new policies and procedures for pharmaceutical waste management need to be drafted. Involve safety, nursing, pharmacy, and environmental services management in the drafting of these new policies and procedures. All aspects of your pharmaceutical waste management and minimization program should be incorporated into existing policies and procedures or if necessary new ones should be created. In addition, it is helpful to set up a specific manual of pharmaceutical waste management and minimization policies and procedures to have all of the steps documented in one location. This overarching operating manual can reference other appropriate policies and procedures, such as chemotherapy preparation, administration, and disposal or general hazardous waste management.

Policies and Procedures

At a minimum pharmaceutical waste management policies and procedures should be developed to detail the organization's approach to:

- Identifying drugs that must be managed as hazardous waste;
- Determining which non-regulated drugs will be managed as hazardous waste;
- Maintaining a system to add new drugs;
- Labeling drugs to facilitate segregation of hazardous waste;
- Segregating waste streams;
- Training staff (e.g., which staff, what information and how often);
- Managing spills;
- Contacting emergency coordinators;
- Setting up and managing satellite accumulation and storage accumulation areas;
- Preparing and maintaining hazardous waste manifests;
- Determining their hazardous waste generation status;
- What criteria are used for hazardous waste selection;
- Scheduling regular program reviews;
- Keeping management informed; and
- Using pharmaceutical waste management as a stepping-stone to a facility-wide Environmental Management System (EMS).

6. Preparing for Spills

Your organization may already have a well-developed spill management plan. Oncology nurses receive chemotherapy spill clean-up training during their annual re-certification process. Pharmacists and pharmacy technicians involved with chemotherapy preparation also usually have spill clean-up awareness and experience. Since you are now identifying other pharmaceuticals that will be discarded as hazardous waste, it is important to re-evaluate general spill management procedures and be certain that all employees, particularly nursing, pharmacy, and environmental services personnel, are trained upon hire and annually on proper spill clean-up procedures.

Determine a maximum amount of material that can be safely cleaned up by immediate personnel. Once you have made that determination, photograph a spill of that amount. It is often hard for people to visualize what 5 mLs, 15 mLs, or 30 mLs looks like when spilled. Be sure the appropriate spill kits are available to handle that maximum amount. Personnel must either be trained to determine if the spill is a hazardous waste or must call the hazardous materials team to make that determination.

If not already in place, develop a hazardous materials team for the second level of emergency spill response comprised of managers from safety, environmental services, nursing and pharmacy. These individuals should receive additional HAZWOPER training and a more complete spill cart should be kept in a central location for quick access. At least one HAZMAT team member should be on duty at all times. HAZMAT team members must be trained to determine if the spilled material is a hazardous waste and how to properly dispose of it and the spill clean up materials. Again, determine the maximum spill to be handled by this team before the Fire Department hazardous materials unit is called. If an internal spill team is not an option, contract with an outside firm that provides emergency spill response.

There are several different acronyms hospitals have used to describe the process. You might

Spill Acronyms

EAR
Evacuate the immediate area
Alert the spill response team, dial the emergency #
Remain by the phone outside affected area, keep people from going into area, and communicate with spill team.

CLEAN
Contain the spill
Leave the area
Emergency medical treatment (seek)
Access the MSDS
Notify

already have one in place that serves your organization well. Putting a laminated summary on a card that is attached to the employees ID badge is a good way to insure they have the reference with them at all times.

Step 10: Launching the Program

1. Educating and Training Staff

Once all policies and procedures are drafted, and the knowledge gained from the pilot program has been applied to refining the approach, conduct just-in-time training sessions for all pharmacy personnel and nursing personnel in the selected units on all shifts. Having a PowerPoint presentation with an accompanying waste sorting exercise is an effective method, which can then be used to orient new employees.

A successful waste pharmaceutical management program depends on the participation of all employees. Active promotion is the best way to help employees understand the program and encourage their participation. Take advantage of any Safety Fairs, Nursing Education Expos, or other hospital-wide events to do a general introduction to the topic of pharmaceutical waste management. Involve nurse educators heavily in your efforts. Consider including information in an orientation for new employees, on signs and posters and in newsletters and email updates. If environmental services personnel are to be involved in transporting hazardous waste containers, they must receive appropriate hazard training based on their responsibilities and the hazardous waste generator status of the organization.

2. Staging the Roll-Out

The most successful implementation programs have involved carefully staged roll-outs, developed with the input of all parties involved, especially nursing. Just-in-time training of all three shifts should be held the week prior to the roll-out for a particular unit. All containers, spill response items, and appropriate signage should be in place prior to the start date. Pharmacy must be ready to identify those items that will be managed as hazardous waste if the labeling approach requires their participation. In the newer automated dispensing machines, messages can be "turned on" by unit, as the rollout proceeds around the hospital.

Most of the research is done prior to launch. You do not want to have to re-visit policies and procedures or re-train anymore than is absolutely necessary. While some tweaks will be inevitable, most major hurdles should be overcome during the planning and pilot stages. A successful implementation will insure greater compliance and enthusiasm for the program.

3. Filling out the Forms

a. Hazardous Waste Manifest (40 CFR Parts 262.20 – 262.27)

The hazardous waste manifest is a form which has both EPA and DOT components. It is designed to provide documentation for cradle to grave tracking of hazardous waste from the generator through the transporter to the final disposer and to provide emergency response information should there be a spill in transit. Completing a hazardous waste manifest properly requires knowledge of the contents of each container of waste and specific DOT training to insure proper shipping names.

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There are two approaches to manifesting hazardous waste: profiling and lab-packing. In most states, hospitals can provide their vendor with a list of all P, U, and D waste codes being generated and the vendor can pre-certify the list and create a waste profile and certified waste stream. All possible waste codes will be listed on the profile for a particular waste stream. This is the simpler, more time efficient approach. Otherwise, the nursing and pharmacy staffs need to document what is discarded in each container to be able to document all the appropriate waste codes. This is considered lab packing. Please note that hazard classes such as ignitable and toxic may be mixed when waste profiling is done, but they cannot be mixed in lab packs. Mixing of hazard classes is dependent on compatibility and the capabilities of your vendor. The Uniform Hazardous Waste Manifest, which went into effect September 5th, 2006, requires only six hazardous waste codes, which should include the most frequently generated hazardous wastes.[35] A number of vendors are currently working with DOT to insure a safe but simple system for segregation, labeling, and manifesting of hazardous pharmaceutical waste.

Hazardous waste vendors can provide assistance in this area, but you shouldn't depend solely on the vendor's expertise. Ultimately, you as the generator are legally responsible for proper waste management including manifesting. If your vendor provides services in multiple states with differing requirements, you need to ensure that the appropriate state requirements are followed.

> If a compliance audit is conducted by EPA or by your state regulatory agency, the lack of hazardous pharmaceutical waste on your hazardous waste manifests is clear evidence that you are not disposing of hazardous pharmaceutical waste appropriately and may not have accurately determined your generator status.

Appendix A: Tools and Resources provides more information on hazardous waste manifests, waste profiling, and lab packs.

[35] For more information on the Uniform Hazardous Waste Manifest, access http://www.epa.gov/epaoswer/hazwaste/gener/manifest/.

b. Land Disposal Restrictions Form (40 CFR Part 268.7)

A Land Disposal Restrictions[36] form must accompany your manifest. This document indicates what wastes you are disposing and how they will be treated prior to application on the land to assure compliance with RCRA. Your hazardous waste vendor can prepare this for you.

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Step 2: Understanding the Regulations provides additional information on Land Disposal Restrictions

Appendix A: Tools and Resources provides references for further information on Land Disposal Restrictions.

4. <u>Tracking, Measuring and Recording Progress</u>

As you implement your pharmaceutical waste management program, it is important to establish a process to track and measure your progress. This can be done at each step of the process.

> Identification: Maintain complete records on how waste categorization was done initially and how new drugs are being evaluated when they enter the system. Some facilities have conducted before and after surveys to determine baseline practices and degree of implementation.

> Labeling: Document how consistent your labeling efforts are, especially if you are relying on manual stickers being placed on labels going to the nursing units. As other medication management procedures evolve, re-evaluate these procedures at least annually to determine if a more sophisticated, less labor-intensive model can be adopted, such as electronic labeling (a function of pharmacy software), or the use of a sorting device (a function of bedside bar coding capabilities).

> Compliance: Perform periodic surveys of pharmacy and nursing staff to determine if the procedures are understood and followed. Perform periodic checks of the waste containers themselves to determine if the appropriate drugs are being discarded in them. Be sure to wear appropriate personal protective equipment to perform this function.

> Quantity: Track the number, size, and weight of hazardous waste containers being generated. Adjust sizes and pick up times to maximize efficiency and minimize costs. This information is also needed for state and federal reporting purposes.

[36] For more information on Land Disposal Restrictions, access http://www.epa.gov/epaoswer/general/orientat/rom36.pdf.

> Costs: Track all costs involved with the development and set up of the program. Once fully operational, track all hard costs involved with containment, storage and disposal. Once a base line is established, consider all waste minimization opportunities to begin reducing costs.

> Joint Commission Performance Improvement Initiative: Document the entire process to be used in your next Joint Commission Survey as a Performance Improvement Initiative.

> Practice GreenHealth Award Opportunity: Identify goals and action plans detailing how your facility will achieve your goals. Submit your efforts for annual recognition as a Practice GreenHealth Partner for Change Award winner.[37]

> EPA Regional Awards and State Environmental Awards: Check with your EPA region and state to see if environmental recognition is available. Many regions and states have annual awards for which you may qualify due to this initiative.

[37] Please note that H2E is now a part of Practice Greenhealth, a non-profit initially composed of three healthcare-related non-profit organizations.

Next Steps

Overcoming the challenges unique to pharmaceutical waste management that assure compliance with RCRA and implementation of best management and waste minimization practices will require the combined and innovative efforts of the regulators, the regulated community and the supply chain. Following are recommendations for next steps to facilitate environmentally sound pharmaceutical waste management in healthcare facilities.

1. Provide Additional Pharmaceutical Waste Management Assistance to Hospitals

Given the number of hospitals that are currently out of RCRA compliance and the difficulty of implementing a pharmaceutical waste management program, it would be valuable for USEPA and state environmental protection agencies to provide training based on this Blueprint to a broad audience, including pharmacists, nurses, environmental services, and hospital-based safety professionals.

There are a number of existing pharmaceutical waste management tools that should be shared (e.g., training presentations, guidance posters for segregating pharmaceutical waste) and new tools that need to be developed (e.g., spreadsheet for performing a manual inventory review, on-site review checklist, purchasing policy) that would facilitate the development and implementation of a pharmaceutical waste management program.

2. RCRA Hazardous Waste Regulations: Clarify, Reconsider and Expand

The RCRA regulations have not been updated significantly since their inception in 1976 and as a result have not kept up with drug development. There are toxic chemotherapeutic agents, endocrine disruptors, antihypertensives, antidepressants, anticholesteremics, antibiotics, and other potent drugs that can legally be sewered or landfilled under the current regulations. Based on an increasing body of research, it is apparent that continuous introduction of these agents into aquatic environments may have negative consequences on fish and other aquatic species.

Step 3 of this Blueprint outlines criteria for identifying drugs that should be managed as hazardous waste when discarded. These criteria can be used as a starting point to assist EPA in increasing the number of hazardous drugs that are regulated as hazardous waste. For example EPA could add the drugs listed in Appendix A of the NIOSH Hazardous Drug Alert. In addition, Minnesota has developed a scheme for evaluating drugs based on risk that could be evaluated. At the same time that EPA is adding additional P- and U-listed drugs, it would be prudent to review the appropriateness of the existing listed constituents of concern.

In the meantime, there is sufficient confusion on several regulatory issues to warrant uniform clarification from EPA headquarters on aspects of the existing regulations. For example, must unit dose wrappers of warfarin and warfarin bottles be managed as hazardous waste, and how should worn nicotine patches be managed? It is also important to review the appropriateness and practicality of the regulations to pharmaceutical waste management.

In the long term, EPA should consider adapting the regulations to take a practical and holistic approach to pharmaceutical waste management that achieves a more favorable environmental outcome for this significant source of contamination. Recent interpretive guidance and the anticipated draft of regulations adding pharmaceutical hazardous waste to the Universal Waste Rules are steps in the right direction.

3. Eliminate Drain Disposal

Wastewater treatment plants are designed to remove conventional pollutants such as suspended solids and biodegradable organic material, not other pollutants such as pharmaceuticals. It is important to work with DEA to allow alternative methods to drain disposal to render controlled substances non-recoverable.

4. Making the Hazardous Waste Determination: A Communications Challenge

The initial hazardous waste determinations and communicating the hazardous waste disposition information to the nursing and pharmacy staffs are very complex and resource intensive aspects of implementing a pharmaceutical waste management program. A hospital's ability to make these determinations accurately and to communicate them effectively impacts their ability to comply with RCRA.

There are several ways that hazardous waste determinations can be made and that disposition information can be conveyed. Hazardous waste determinations can be performed manually or there are commercial services available to provide hospitals with assistance. Performing hazardous waste determinations manually is an arduous process as there are as many as 4,000 drugs that must be initially reviewed. Each determination requires research, calculations or knowledge of the drug. Generally, the MSDS does not provide sufficient disposition information to make a hazardous waste determination.

Once the hazardous waste determination has been made, the information must be communicated to the pharmacy and nursing staffs. It can be integrated into the pharmacy dispensing software, or included in the barcodes that FDA has required be placed on pharmaceuticals by manufacturers.

There is a need for a national stakeholder forum to bring these issues to the attention of the health care industry as well as the supply chain, encouraging all to come up with innovative win-win solutions that economically and environmentally benefit pharmaceutical waste management. The results of such a forum will also benefit the advancement of proper pharmaceutical management at the consumer level.

5. Broaden National Knowledge Base of Pharmaceutical Waste Generation

There is no documented percentage of drug waste per drug dispensed or per hospital bed available at this time. The percentage of hazardous drugs in the inventory does not correlate with the percentage of hazardous drug waste generated at a hospital for several reasons: 1) some drugs may be discarded on a regular basis while others may be discarded less often; 2) frequency of use varies among drugs, resulting in fewer opportunities for waste generation for some compared to others; 3) containers of U-listed drugs and characteristic hazardous wastes are not managed as hazardous waste if the containers are RCRA empty; and, 4) contaminated PPE and spill materials will increase the amount of hazardous waste generated. It is reasonable to assume that areas administering higher volumes of potentially hazardous waste will generate more waste. Determining the actual percentages of specific hazardous waste generated provides an excellent research opportunity.

6. Waste Minimization

In Step 5, various waste minimization opportunities are identified. Additional research and work involving multiple stakeholders is necessary to efficiently implement some of the practices identified. The following are examples of potential national projects that would move these waste minimization practices forward.

a. Routinely Wasted Drugs

Work with hospitals, GPOs, pharmaceutical distributors, and pharmaceutical manufacturers to conduct a broad based study to determine the universe of drug formulations that are routinely wasted due to package size and to facilitate change.

In some instances, a drug's expiration date is an overly conservative estimate of the true activity life. Work with GPOs and pharmaceutical manufacturers to ensure that the expiration dates accurately reflect safety and efficacy, thereby enabling a longer shelf life.

Generally, hospitals replace epinephrine syringes and nitroglycerin bottles and vials on general crash carts when they are within three months or less of their expiration date. Refer to Appendix C for an example of a study which moved products from general crash carts to the Emergency Department or ICC/CCU three months prior to outdate to avoid discarding them.

b. Lightweighting

There are variations in the weight of dispensing instruments. Work with the pharmaceutical supply chain to identify lightweighting opportunities. For example, a two-part polyolefin IV device used to administer antibiotics (e.g. *Duplex*) weighs one-third less than traditional glass vial/PVC IV bag alternatives.

Summary

Pharmaceutical waste continues to be a new frontier in environmental management for healthcare facilities. The compliant, cost-effective management of waste pharmaceuticals is a complex challenge. It is interdisciplinary in nature, involving pharmacy, nursing, environment services, safety, infection control, quality assurance, risk management, education, administration, and purchasing, and requiring the implementation of new systems to insure proper waste management. Aware of the need to develop new systems, professionals within state and federal environmental protection agencies are beginning to assist the regulated community in developing practical compliance models. It will take the involvement of the entire supply chain, from manufacturers through distributors to hospitals, to develop more user-friendly systems to insure protection of human health and the environment. This Blueprint is intended to provide detailed guidance to hospitals today while stimulating the broader research and solutions needed for tomorrow.

Appendix A: Tools and Resources

Step One: Getting Started

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- EPA Pharmaceutical Industry Sector Notebook http://www.epa.gov/compliance/resources/publications/assistance/sectors/notebooks/pharmaceutical.html
- Cradle-to-Cradle Stewardship of Drugs for Minimizing Their Environmental Disposition While Promoting Human Health Parts 1 and 2 can be accessed at: http://www.epa.gov/nerlesd1/bios/daughton/green1.pdf and http://www.epa.gov/nerlesd1/bios/daughton/green2.pdf
- Minnesota Pollution Control Agency Healthcare Waste Fact Sheets can be accessed at: http://www.pca.state mn.us/industry/healthcare.html
- USEPA Region 2 Guidance on Healthcare Hazardous Wastes, including pharmaceuticals can be accessed at: http://www.epa.gov/region2/healthcare
- Health Facilities Management Magazine, March 2006, Waste Watch: A Model for Managing Discarded Pharmaceuticals can be accessed at: http://www.hfmmagazine.com/hfmmagazine/hospitalconnect/search/article.jsp?dcrpath=HFMMAGAZINE/PubsNewsArticleGen/data/2006March/0603HFM_DEPT_EnvirSer&domain=HFMMAGAZINE
- Pharmaceutical Wastes in Healthcare Facilities can be accessed at http://www.hercenter.org/hazmat/pharma.cfm

Step Two: Understanding and Applying the Regulations

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General

- The RCRA Orientation Manual can be accessed at: http://www.epa.gov/epaoswer/general/orientat/
- RCRA hazardous waste regulations can be accessed at 40 CFR on e-CFR at: http://ecfr.gpoaccess.gov

Hazardous Waste Identification

- RCRA Online # 13718: Epinephrine Residue In A Syringe Is Not P042 (December 1994) can be accessed at: http://yosemite.epa.gov/osw/rcra.nsf/0c994248c239947e85256d090071175f/1c1deb3648a62a868525670f006bccd2!OpenDocument
- The expansion of the epinephrine syringe exclusion to other P- and U-listed drugs can be accessed at http://yosemite.epa.gov/osw/rcra.nsf/0c994248c239947e85256d090071175f/6a5dedf2fba24fe68525744b0045b4af!OpenDocument
- The exclusion of epinephrine salts from P042 can be accessed at http://yosemite.epa.gov/osw/rcra.nsf/0c994248c239947e85256d090071175f/6a5dedf2fba24fe68525744b0045b4af!OpenDocument
- Nitroglycerin Exclusion 66 FR 27286 Hazardous Waste Identification Rule (HWIR): Revisions to the Mixture and Derived-From Rules can be accessed at: http://www.epa.gov/EPA-WASTE/2001/May/Day-16/f11411.htm

- Healthcare-Related P -and U-Listed Wastes can be accessed at: http://www h2e-online.org/pubs/Healthcare_P_U_Wastes.pdf (Note: This is a 2005 publication which does not contain the newer interpretations.)
- Wilkosz, M and Bogner, R. (2003) Transdermal Drug Delivery can be accessed at: http://www.uspharmacist.com/index.asp?show=article&page=8_1061 htm
- Flynn GL. (1996) Cutaneous and transdermal delivery: Processes and systems of delivery. In: Banker GS, Rhodes CT, eds. Modern Pharmaceutics. New York, NY: Marcel Dekker; p.239-299.
- The California version of the H2E Blueprint can be obtained by contacting Karin North, City of Palo Alto, (650) 494-7629 and (650) 494-7629.

Chemotherapy Waste

- H2E March 11, 2005 Teleconference Presentation – Managing Waste Chemotherapeutic Agents: What to Know and What to Find Out can be accessed at: http://www.h2e-online.org/pubs/Rev_%20H2E_Chemo_Teleconference_Presentation.ppt
- California Medical Waste Management Act can be accessed at: http://www.dhs.ca.gov/ps/ddwem/environmental/Med_Waste/LawRegs/default.htm
- Recommendations for Chemotherapy Spill Response detailed in the OSHA Technical Manual C.5 can be accessed at: http://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html#5
- Recommendations for Respirator Protection detailed in the OSHA Technical Manual B.6.c can be accessed at: http://www.osha.gov/dts/osta/otm/otm_viii/otm_viii_2.html
- FAQ Chemotherapy spills on carpet can be accessed at: http://www.des.nh.gov/nhppp/Healthcare_P2/default.asp?link=faq6
- Wisconsin's Medical Waste Rules NR 526.03 (3) and 526.055 can be accessed at: http://www.legis.state.wi.us/rsb/code/nr/nr526.pdf
- Draft Questions and Answers Regarding the Management of Waste Chemotherapy (Antineoplastic) Drugs can be accessed at: http://www.h2e-online.org/pubs/R2_Waste_Chemo_QA_DRAFT.pdf
- The American Society of Health-System Pharmacists (ASHP) Guidelines on Handling Hazardous Drugs can be accessed at: http://www.ashp.org/s_ashp/bin.asp?CID=6&DID=5420&DOC=FILE.PDF
- The NIOSH Hazardous Drug Alert can be accessed at: http://www.cdc.gov/niosh/docs/2004-165/
- Spivey S. and Connor T.H. (2003) Determining sources of workplace contamination with antineoplastic drugs and comparing conventional IV drug preparation with a closed system. Hospital Pharmacy. 38: 135-139
- Information on Phaseal can be accessed at: http://www.phaseal.com/

Controlled Substances

- Controlled substance schedules can be accessed at: http://www.deadiversion.usdoj.gov/schedules/index html
- The DEA's Diversion website can be accessed at: http://www.deadiversion.usdoj.gov/new.htm
- The regulations applying to controlled substances, 21 CFR 1300 to 1399, can be accessed at: http://www.deadiversion.usdoj.gov/21cfr/cfr/index html

- The Pharmacist's Manual, a summary of the DEA disposal requirements can be accessed at: http://www.deadiversion.usdoj.gov/pubs/manuals/pharm2/index htm

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Generator Status

- Minnesota Pollution Control Agency's Evaluate Waste – Determine Generator Size can be accessed at: http://www.pca.state.mn.us/publications/w-hw1-01.pdf
- Small and large quantity generators must register with EPA for an Identification Number. Registration forms and instructions for small and large quantity generator identification numbers can be accessed at: http://www.epa.gov/epaoswer/hazwaste/data/form8700/forms htm#waste

Drain Disposal

- Sewer Disposal of Pharmaceutical Waste, September 5, 2003, Jack McGurk, Chief, Environmental Management Branch, Department of Public Health can be accessed at: http://www.cdph.ca.gov/certlic/medicalwaste/Documents/MedicalWaste/pharms_out_sewers_v3_090503.pdf
- Tri-TAC Memo to POTW Pretreatment Coordinators and Managers, September 23, 2003, can be accessed at http://www.ciwmb.ca.gov/WPIE/HealthCare/TriTACMemAtt.pdf

Aerosol Cans

- RCRA Online #11782: Regulatory Status Of Used Residential And Commercial/Industrial Aerosol Cans (October 1993) can be accessed at: http://yosemite.epa.gov/osw/rcra.nsf/ea6e50dc6214725285256bf00063269d/0c95b3d30e33cdb68525670f006bece7!OpenDocument
- State of North Carolina "Management of Aerosol Cans for Businesses and Industries" can be accessed at: http://www.p2pays.org/ref/01/00007.htm
- Minnesota Pollution Control Agency's fact sheet, Managing Waste Aerosols, can be accessed at: www.pca.state.mn.us/waste/pubs/4_00.pdf

Pharmaceuticals as Universal Waste

- EPA's original announcement in the Federal Register on April 30th, 2007 can be accessed on page 23281 at http://www.epa.gov/fedrgstr/EPA-GENERAL/2007/April/Day-30/g01422.pdf. A revised announcement of the amendment of the Universal Waste Rule to include pharmaceuticals was published in the fall of 2007 and can be accessed at http://yosemite1.epa.gov/opei/Smallbus.nsf/04b7c5966aaff142852570150047179e/273617ce3ab52bbb852572ec006af28c!OpenDocument
- Information regarding Michigan's Universal Waste Rule can be accessed at http://www.deq.state.mi.us/documents/deq-ead-tas-univwaste.pdf and at R299.9228 Universal wastes at http://www.deq.state mi.us/documents/deq-wmd-hwp-Part111Rules00.pdf
- Information regarding Florida's Universal Waste Rule can be accessed at rule number 62.730.186 at http://www.dep.state fl.us/waste/quick_topics/rules/documents/62-730.pdf.
- Additional information on universal waste can be accessed at http://www.epa.gov/epaoswer/hazwaste/id/univwast/index.htm.

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Step Three: Considering Best Management Practices for Non-Regulated Wastes

- The NIOSH Hazardous Drug Alert can be accessed at: http://www.cdc.gov/niosh/docs/2004-165/
- Environmentally Classified Pharmaceuticals, a brochure with a list of 159 active substances classified on their PBT potential, can be accessed at: http://www.noharm.org/details.cfm?ID=1027&type=document. at http://www.sll.se/upload/Milj%C3%B6/A4.1.klassific.pdf, and at http://www.janusinfo.org/imcms/GetDoc?meta_id=7238
- The Occupational Safety and Health Administration (OSHA) Technical Manual Section 6, Chapter 2, Appendix VI: 2-1 Some Common Drugs That Are Considered Hazardous can be accessed at http://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2 html#app_vi:2_1
- Minnesota Pollution Control Agency's fact sheet, Alternative Method to Evaluate Pharmaceutical Waste for the Lethality Characteristic, can be accessed at: http://www.pca.state mn.us/publications/w-hw4-45b.pdf
- The Toxicology Program's Report on Carcinogens (11th Edition) can be accessed at: http://ntp.niehs.nih.gov/ntp/roc/toc11.html
- The original Precautionary Principle statement drafted in 1998 at the Wingspread Conference Center, Racine, WI, can be accessed at http://www.gdrc.org/u-gov/precaution-3 html
- Health Care Without Harm's Alternatives to PVC and DEHP can be accessed at: http://www.noharm.org/details.cfm?type=document&id=591
- Practice GreenHealth Webinar: Pharmaceutical Waste – Learn Best Management Practices and How to Be In Compliance with RCRA, May 12, 2006, can be accessed at http://cms.h2e-online.org/teleconferences/calendar/details/249
- Practice GreenHealth Webinar: Pharmaceutical Waste Management - Case Study – Abbott Northwestern Hospital, Minneapolis, MN, January 12, 2007, can be accessed at http://cms h2e-online.org/teleconferences/calendar/details/298

Step Four: Performing a Review of Your Drug Inventory

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- Sample Toxicity Characteristic Calculations can be found in Appendix B
- Information on purchasing Facts and Comparisons and Efacts can be accessed at http://www.factsandcomparisons.com/

Step Five: Minimizing Pharmaceutical Waste

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- Practice GreenHealth Webinar: Operations Series – Pharmaceutical Waste Prevention, March 28, 2008, can be accessed at http://cms h2e-online.org/teleconferences/calendar/details/406.
- Refer to Appendix C: Pharmaceutical Wastes Minimization: Two Case Studies.

Step Eight: Considering the Management Options

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- Frequently asked questions about the OSHA Hazardous Waste Operations and Emergency Response Standard can be accessed at http://www.osha.gov/html/faq-hazwoper.html

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Step Nine: Getting Ready for Implementation

Locating Your Satellite Accumulation Areas

- USEPA's Frequently Asked Questions about Satellite Accumulation Areas, March 17, 2004, can be accessed at http://www.epa.gov/osw/specials/labwaste/memo-saa.htm

Selecting the Right Vendor(s)

- Licensed hazardous waste transport, storage, and disposal facilities nationwide can be accessed at: http://www.epa.gov/enviro/html/rcris/rcris_query_java html
- Information on compliance inspections, violations, and/or enforcement actions regarding hazardous waste generators and TSDFs nationwide can be accessed at http://www.epa-echo.gov/echo/

Reverse Distribution

- RCRA Online # 11012 Applicability of 261.33 to Discarded Products http://yosemite.epa.gov/osw/rcra.nsf/0c994248c239947e85256d090071175f/b630cd51dc85edc58525670f006bce84!OpenDocument
- RCRA Online # 11606 Returned Pharmaceutical Products http://yosemite.epa.gov/osw/rcra.nsf/ea6e50dc6214725285256bf00063269d/a3a7a7a8f297438b8525670f006be5d8!OpenDocument

Pharmaceutical Waste Management Policies and Procedures

- Healthcare Guidance to Pollution Prevention Implementation through Environmental Management Systems can be accessed at http://www.epa.gov/region2/ems

Step 10: Launching the Program

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Filling out the Forms

- Information about hazardous waste manifests can be accessed at http://www.epa.gov/epaoswer/hazwaste/gener/manifest/
- 40 CFR 173.24 contains general requirements for packaging and packages
- 40 CFR 173.24(a) for additional requirements for non-bulk packaging and packages.
- 49 CFR 173.12 (b)(2)(iii) has exceptions for shipments of waste materials
- Information on the 40 CFR Part 268 Land Disposal Restrictions can be accessed at http://www.epa.gov/epaoswer/general/orientat/rom36.pdf.

Case Studies

- Practice GreenHealth Webinar Pharmaceutical Waste Management Case Study – Abbott Northwestern Hospital, Minneapolis, MN January 12, 2007 can be accessed at http://cms h2e-online.org/teleconferences/calendar/details/298

Appendix B: Sample Toxicity Characteristic Calculations For Liquids and Solids

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Liquids

Evaluation of Thimerosal Toxicity
per *Merck Index, Twelfth Edition:*
Thimerosal ($C_9H_9HgNaO_2S$) molecular weight = 404.82
C 26.70%
H 2.24%
Hg 49.55%
Na5.68%
O 7.90%
S7.92%

1:1000 Solution

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Thimerosal may be used as a preservative in a concentration of 1:1000, which means, by definition, 1 gram in 1000ml of solution.
Since thimerosal is 49.55% mercury:
1g thimerosal x 49.55% = 0.4955 g mercury.
1g thimerosal/1000ml = 0.4955 g Hg/1000ml = 495.5 mg Hg/1000 ml = 495.5 mg Hg/liter
The regulatory limit for mercury is 0.2mg per liter

1:10,000 Solution

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Thimerosal may also be used as a preservative in a concentration of 1:10,000, which means, by definition, 1 gram in 10,000ml of solution.
1 g/10,000 ml_= 0.1 g/1000ml
Since thimerosal is 49.55% mercury:
0.1g thimerosal x 49.55% = 0.04955g mercury.
0.1 g thimerosal/1000ml = 0.04955 g Hg/1000ml = 49.55 mg Hg/1000 ml = 49.55 mg Hg/liter
The regulatory limit for mercury is 0.2mg/liter.
Therefore, products containing thimerosal as a preservative at either 1:1,000 or 1:10,000 exceed the regulatory limit for mercury and exhibit the toxicity characteristic.

Evaluation of Phenylmercuric Acetate Toxicity
per *Merck Index, Twelfth Edition:*
Phenylmercuric Acetate ($C_8H_8HgO_2$) molecular weight = 336.74
C 28.53%
H 2.39%
Hg 59.57%
O 9.50%
Most nasal sprays contain phenylmercuric acetate 0.002% (of total solution) as preservative.
0.002% = 0.002 g/100ml = 0.02 g/1000 ml

Since phenylmercuric acetate is 59.57% mercury:
0.02g phenylmercuric acetate x 59.57% = 0.0119g mercury
0.02g phenylmercuric acetate = 0.0119g Hg/1000 ml = 11.9 mg Hg/1000ml = 11.9 mg Hg/liter
The regulatory limit for mercury is 0.2mg/liter.
Therefore, products containing phenylmercuric acetate as a preservative exceed the regulatory limit for mercury and exhibit the toxicity characteristic of a RCRA hazardous waste.

Evaluation of m-Cresol Toxicity
Some insulins use m-cresol as a preservative. For example, Humalog 75/25 contains 1.76 mg/ml of m-cresol:
1.76 mg/ml = 1760 mg/1000 ml = 1760 mg/liter
The Toxicity Characteristic limit for m-cresol is 200mg/liter.
Therefore, the Humalog 75/25 would meet the criteria for the toxicity characteristic when discarded.

Evaluation of Barium Sulfate in Barium Enemas and Suspensions
The following calculations document why barium sulfate used in barium enemas and suspensions may exhibit the Toxicity Characteristic.

Barium Sulfate
Per Merck Index, Twelfth Edition:
Barium sulfate ($BaSO_4$) molecular weight 233.39:
Ba 58.84%
S 13.74%
O 27.42%

Preparations of barium sulfate for radiographic examination of the GI tract come in varying concentrations, one of the lowest being 1.2% (Readi-CAT Suspension by E-Z-EM):
1.2% = 1.2gm /100 ml = 12 gm/1000ml
Since barium is 58.84% of barium sulfate, 12 gm x .5884 = 7.06 gm of barium
7.06 gm/1000 ml = 7060 mg/liter
The Toxicity Characteristic for barium is 100mg/l, therefore even dilute solutions of barium sulfate exceed the toxicity characteristic for barium.

Some hospitals have sent their specific solutions to laboratories and the results have passed the TCLP. During an inspection, EPA has indicated it may conduct its own TCLP to verify these results. If a TCLP is not performed, manage waste barium sulfate as a hazardous waste under the toxicity characteristic.

Solids

For solid dosage forms such as creams, tablets or capsules, a dilution ratio of 20 times can be used, which is an accepted standard for determining the theoretical leaching concentration for solids. You will need to weigh the tablet or capsule to determine the starting percentage of the listed chemical in the dosage form. For creams, you can use the percentage of original drug in the base as given by the manufacturer. If the chemical itself is not listed in the Merck Index, determine the percentage of the element or chemical by taking the molecular weight, looking up the atomic weight of each element in the Periodic Table of the Elements, and determining the appropriate percentage. This can then be applied to the formulation. When you have determined the mg/Kg concentration, divide by 20 to simulate dilution in a leach bed and convert to mg/L. The following is an example of a solid calculation for silver sulfadiazine cream:

Evaluation of Silver Sulfadiazine Cream (SSD, Silvadene, Thermazene)

Molecular formula: $C_{10}H_9AgN_4O_2$ S

Element	Atomic Weight	Number of Molecules	Atomic Weight in Compound	Percentage
Carbon (C)	12	10	120	30.5
Hydrogen (H)	1	9	9	2.3
Silver (Ag)	108	1	108	27.5
Sodium (Na)	23	4	92	23
Oxygen (O)	16	2	32	8
Sulfur	32	1	32	8.1
Totals			393	99.4%

The commercial products containing silver sulfadiazine list the concentration as 10 mg/gm. The concentration of silver in silver sulfadiazine is approximately 27.5%.

10mg/gm x .275 = 2.75mg/Gm. This must be converted to kg to be comparable to liters, the unit given in the concentration limits in the regulations.

2.75mg/gm x 1000 = 2750mg/kg. To simulate a 20x dilution, which is assumed in landfill operations, divide by 20.

2750mg/kg divided by 20 = 173.5 mg/kg which would convert to 173.5mg/l in liquid measure. The regulatory limit for silver as D011 hazardous waste is 5.0mg/l. Therefore, silver sulfadazine cream fails the Toxicity Characteristic Leaching Procedure (TCLP) and must be managed as hazardous waste.

Using a Total Constituent Analysis Instead of a TCLP Analysis

Section 1.2 of the TCLP Method 1311 allows for a total constituent analysis in lieu of the TCLP extraction. If a waste is 100% solid, as defined by the TCLP method, then the results of the total constituent analysis may be divided by 20 to convert the total results into the maximum leachable concentration. This factor is derived from the 20:1 liquid-to-solid ratio employed in the TCLP. If a waste has filterable liquid, then the concentration of the analyte in each phase (liquid and solid) must be determined. The following equation may be used to calculate this value:

$$[[A \times B] + [C \times D]] \div [B + [20\ (l/kg) \times D]] = E$$

Where:

A = Concentration of the analyte in liquid portion of the sample (mg/l)
B = Volume of the liquid portion of the sample (l).
C = Concentration of the analyte in solid portion of the sample (mg/kg)
D = Weight of the solid portion of the sample (kg)
E = Maximum theoretical concentration in leachate (mg/l)

The value obtained (E) can be used to show that the maximum theoretical concentration in a leachate from the waste could not exceed the concentration specified in the toxicity characteristic (TC) (40 CFR 261.24). In addition, if the total constituent analysis results themselves are below the TC limits without dividing by 20, then the same argument holds true, i.e., the maximum theoretical concentration in the leachate could not exceed the TC limits.

The full Test Method 1311 TCLP can be accessed at http://www.epa.gov/sw-846/pdfs/1311.pdf and Test Methods, TCLP Questions can be accessed at: See http://www.epa.gov/sw-846/faqs_tclp htm#Total

Appendix C: Pharmaceutical Waste Minimization: Two Case Studies

The following case studies are the result of a Minnesota Technical Assistance Program (MnTAP) intern project. © 2008 MnTAP. Reprint only with permission from MnTAP. Available in alternative formats upon request. For more information, contact MnTAP at 612-624-1300. Ms. Catherine Zimmer, Education and Healthcare Specialist with MnTAP and Project Manager, may be contacted at (612) 624-4635 or zimme053@umn.edu. Reprinted with permission. [38]

Case Study #1: HCMC Reduces Pharmaceutical Waste

Company Overview
Hennepin County Medical Center (HCMC), a public teaching hospital in Minneapolis, Minnesota, is a nationally-recognized level one trauma center and the third largest hospital in the Twin Cities. HCMC has over 356,000 patient visits annually.

Waste Reduction Project
In 2006, HCMC returned over 900 different outdated pharmaceuticals, most in multiple quantities, through the reverse distribution process. The total cost to purchase was $146,411. Of this amount, only 202 items were credited for a total of $75,657. Therefore, a waste reduction project was conducted at HCMC that focused on reducing pharmaceutical waste from the reverse distribution process at the inpatient pharmacy. Waste reduction resulted in over $80,000 in cost savings and 378 lbs of pharmaceutical waste.

Crash boxes
Crash boxes, similar to crash carts, were found to be a significant source of waste. These boxes contain emergency medicine needed to revive someone in the event of a cardiac event. Waste occurs when boxes contain drugs that are not used by their expiration date. When this occurred in the past, the pharmacy exchanged the box and updated all the drugs so they are good for about one year. Outdated and nearly outdated drugs were sent for reverse distribution.

In investigating the crash boxes, it was determined that many of the drugs found in the boxes are regularly used in other locations in the hospital. It was recommended the pharmacy bring back the crash boxes three months prior to expiration and move the drugs to locations where they are used more frequently, potentially using them prior to expiration.

Other recommendations for the crash box drugs included:

[38] See also the Practice GreenHealth Webinar "Pharmaceutical Waste Prevention" March 28, 2008, accessed at http://cms.h2e-online.org/teleconferences/calendar/details/406

- Replacing the specialty Epinephrine Intracardiac Syringe that was rarely used. It expired and was returned 98% of the time. Use of a more commonly used epinephrine syringe and an 18 gauge, 3 inch needle banded to the epinephrine box was recommended.
- Changing the dosage of Glutose Gel from the 45 gram dosage type, much of which was wasted. In most cases, a 30 gram dose of glucose is used. A recommendation was made to lower the dosage carried from 45 gram to 15 gram for the drug to be used in more applications.
- Lowering the size of the nitroglycerin bottle from 100-count to 25-count and switching to a generic form from a brand name.

Other reverse distribution drugs

Review of reverse distribution manifests helped identify the most common and costly drugs returned. HCMC also found they were returning 4% of their inventory, which is 2% above the average as determined by the American Society of Health-System Pharmacists. The top ten of these were:

1. Crash box epinephrine
2. Epinephrine
3. Glucagon
4. Glutose gel
5. Nitrostat
6. Hydralazine
7. Lidocaine
8. Amiodarone
9. Adenosine
10. Naloxone

It was recommended that HCMC review par usage reports for the top ten returns and adjust inventory quantities accordingly. Doing so would save at least $80,000 and eliminate 210 pounds of pharmaceutical waste.

Results

HCMC implemented all the recommendations. It is estimated they are saving $80,000 annually and have eliminated 378 pounds of drug waste.

Case Study #2: Falls Memorial Hospital Reduces Drug Inventory and Pharmaceutical Waste

Falls Memorial Hospital (FMH), a 25-bed facility, is a charitable, not-for-profit Critical Access Hospital located in International Falls, Minnesota.

Inventory Reduction Project

Prior to undergoing the inventory reduction project, FMH was checking for outdated drugs every other month, stock was not rotated regularly and par usage reports were not available.

In 2006, a staff pharmacist noticed many drugs on site were outdated and the facility was stocking too many extra medications. Because par usage reports had not been used previously, FMH, at that point, did not know how many drugs were required for the facility. Due to these factors, the facility began to look at ways to reduce inventory, save money and decrease pharmaceutical waste.

Chemotherapy Drugs

Looking closely into quantities ordered and costs, FMH realized that chemotherapy drugs were the largest expense for the facility. They were being ordered monthly and in December 2007, the facility spent over $90,000. Because of the long holding time for some of the chemotherapeutics, they were outdating on the shelf. FMH also realized, through facility-wide research that some chemotherapy drugs were very high cost and came in multiple strengths. FMH changed their ordering for chemotherapeutic drugs from once per month to once a week.

Routine Stock on Floors

FMH utilizes AcuDose, an automated dispensing machine, to supply most of their stock of drugs. AcuDose machines were stationed in the emergency room, medical/surgical area, operating room, and intensive care unit. As part of the inventory reduction project, the pharmacist noted that the AcuDose machine in the intensive care unit was rarely used because most of the pharmaceuticals were special order for the patients, and resulted in numerous expired drugs and the inventory not being rotated frequently enough. Therefore, the pharmacist recommended placing the medications only where they are needed and rotating the stock on a more regular basis.

Therapeutic Substitution

In order to reduce the amount of drugs at the hospital, the pharmacist recommended using therapeutic substitution lists. For example, there are five medications in a class of drugs called proton pump inhibitors, or PPI. Instead of having all five medications on the formulary, FMH chose to carry just two of them. This would ensure that the hospital was not carrying multiple medications in the same category and make it easier to rotate stock. If a patient comes into the hospital on a PPI not on the formulary, they will be automatically switched to an equivalent dose of a PPI that is on the formulary.

Multiple dosage types were also noted. The number of dosage forms have been reduced to those used most often and multiples of those to achieve the strengths for esoteric doses. The pharmacy now also searches out and purchases only from those vendors that have the least packaging.

Pollution Prevention Impacts

Due to FMH's inventory reduction project, the facility is ordering and stocking fewer drugs, reducing packaging waste and shipping costs. This project reduced FMH's monthly overhead from $210,000 in January 2006 to $87,000 in October 2007 and dramatically reduced the amount of waste from expiring medications and excess stock.