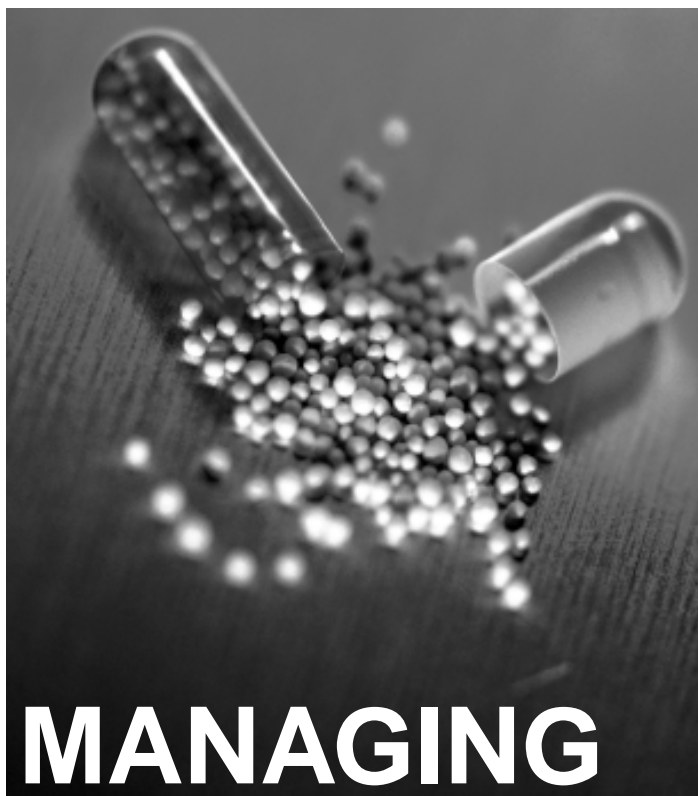


by Charlotte A. Smith, RPh, MS



MANAGING PHARMACEUTICAL WASTE — What Pharmacists Should Know

While not everyone considers the development of knowledge and systems to properly manage pharmaceutical waste to be an inherently glamorous field of study, we can all relate to how important it is have our household waste managed. A strike by city environmental services personnel or a backed up sewer system suddenly becomes a major priority for our health and wellbeing.

The disposal of waste pharmaceuticals has been a much more subtle, but no less important, issue. For many years, pharmacists have been primarily concerned with ensuring that wasted drugs were rendered unrecoverable through sewerage or incinerating. The focus was on insuring that children did not gain access or that illegal diversion did not occur.

Not too much has changed, except that hospital incinerators are a thing of the past and more waste pharmaceuticals are now being disposed of in biohazardous¹ sharps containers, in lieu of a dedicated pharmaceutical waste stream. Sewering remains a common choice.

So why should we be concerned about this historically rather simple process? Unfortunately, since pharmacists do not routinely receive instruction in environmental regulations,

we have been largely unaware of a large body of law: the federal Resource Conservation and Recovery Act, enforced by the Environmental Protection Agency and authorized states, which regulates the disposal of solid waste in the United States.

EPA and hazardous chemical waste

In addition to defining “solid waste,” which includes liquids and gases, RCRA (pronounced rec-rah) also defines hazardous waste — those chemicals or formulations deemed to be so detrimental to the environment that they must be segregated for special waste management and cannot be sewerage or landfilled. A number of drug entities and pharmaceutical formulations meet the definition of hazardous waste, including such common drugs as epinephrine, nitroglycerin, warfarin, nicotine, and seven common chemotherapy agents.

Endocrine disruptors

As if violating the law weren't enough to get our attention, being a generally law-abiding group of professionals, there are other compelling reasons to take a hard look at the final resting place of any drug waste we generate. Growing evidence indicates that “endocrine disruptors,” — those chemicals that mimic natural hormones, trigger an identical response, or block natural hormones — are having a dramatic negative impact on critical developmental stages in the fetus and newborn. The book *Our Stolen Future*² documents the research of pharmacist, Theo Colburn, who identified this phenomenon

among wildlife populations. In addition to the obvious impacts of the estradiols, testosterone and progesterone related drugs, pesticides such as lindane (an estrogen mimic) can cause significant damage if they enter the environment inappropriately. Lindane was recently banned for all use, both human and pesticide, in California and Canada.

With human male sperm counts dropping 50%³ on average world-wide since 1939, an increase in infertility, genital deformities, hormonally triggered cancers such as breast cancer and prostate cancer, and an upswing in neurological disorders in children, we have an even greater responsibility as health care professionals to ensure that our activities as pharmacists “do no harm” through inadvertent secondary exposure.

Pharmaceuticals in surface waters

In March of 2002, the United States Geological Society released the results of the first nationwide reconnaissance of the occurrence of pharmaceuticals, hormones and other organic wastewater contaminants (OWCs) in surface waters.⁴ USGS surveyed 139 streams across the country, including three in Wisconsin, looking for 95 different OWCs. One or more contaminants was found in 80% of the samples, and

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included common pharmaceuticals. Water treatment plants to date are designed to filter out sediment, bacteria and viruses. They have not in the past been designed to identify and remove organic molecules.

How do we generate pharmaceutical waste?

In the past, much of the pharmaceutical waste occurring at a pharmacy was due to expired pharmaceuticals. The development of reverse distribution companies has enabled pharmacies to ship all outdated drugs as products back through these firms for the purpose of returning them to the manufacturer for credit. Any outdated items that do not meet the manufacturers' return policy become waste at the reverse distributor which becomes the waste generator, since this is where the decision to discard the item is made. This practice has been supported by the EPA through two guidance letters to the industry.^{5,6} The letters make it clear, however, that while EPA will consider an outdated drug to remain a product until the decision is made to discard it, reverse distribution cannot be used solely as a waste management tool. Obviously wastelike materials, such as partial vials, compounded IVs, and broken or spilled materials, must be considered waste at the pharmacy and managed in compliance with RCRA.

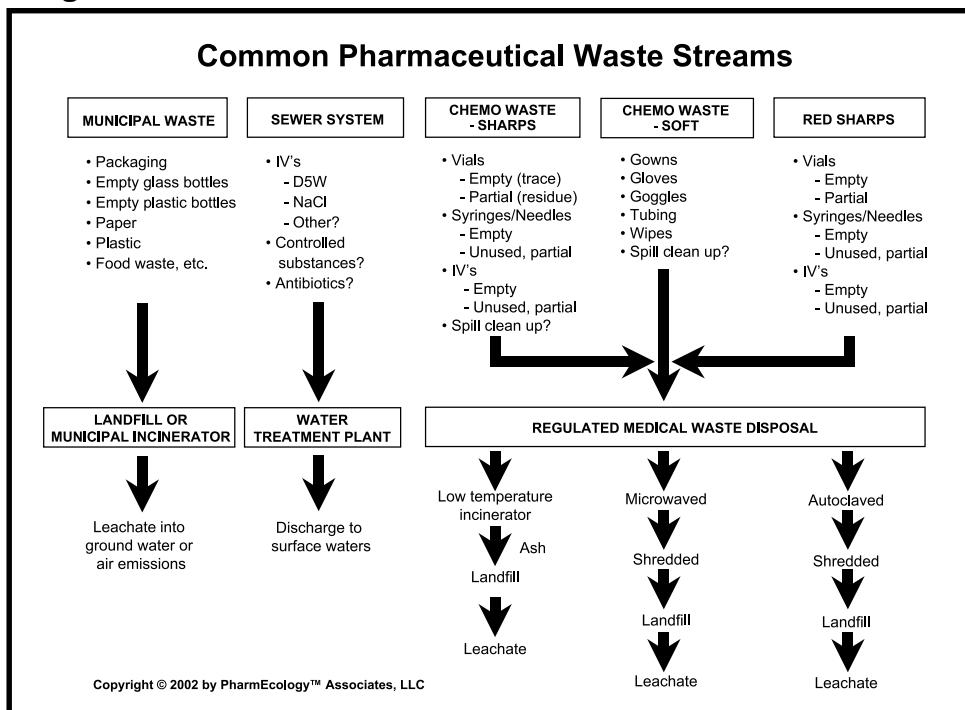
Other sources of pharmaceutical waste include undispensed compounded products, discontinued indated items, unused unit dosed items, unused IVs, and patients' personal medications.

The Resource Conservation and Recovery Act

Enacted in 1976 as a response to national environmental disasters, the purpose of RCRA is to encourage waste minimization, define hazardous waste, and provide for a system of "cradle to grave" tracking of hazardous waste. Since the word "hazardous" is used in multiple contexts within health care, it is important to recognize that we are not talking about biohazardous, infectious waste, OSHA hazardous materials as featured in employee *Right to Know* programs, or DOT hazardous substances. EPA has an entirely different set of criteria for defining hazardous chemical waste as it impacts human health and the environment when discarded.

In case the compelling evidence surrounding species viability is not sufficient to encourage compliance, EPA has provided for more prosaic motivators, such as personal and corporate liability. Corporate fines may be levied at a rate of \$27,500 per violation per day and responsibility extends from

Diagram 1



the manager level up through the CEO of the organization. Personal liability carries no statute of limitations and, in criminal cases of knowing, willful violation, can involve prison sentences.

Waste generation status

If an organization generates hazardous waste, it falls into one of three categories, based on the amount generated per month:

1. Conditionally Exempt Small Quantity⁷
2. Small Quantity
3. Large Quantity

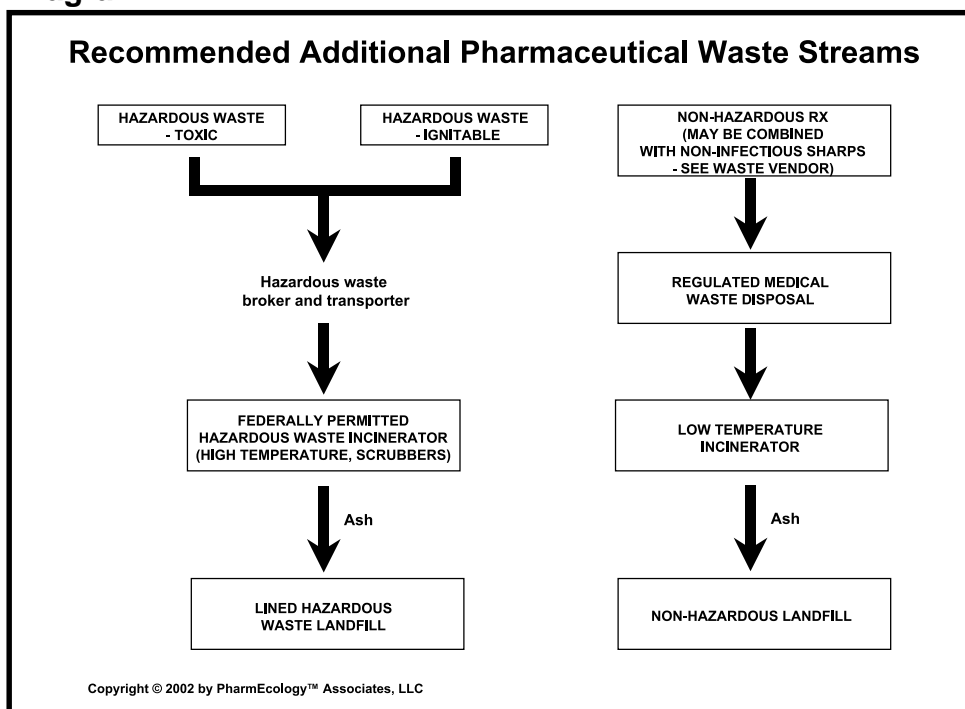
Small and large quantity generators⁸ must notify EPA of their generation activities and receive an EPA identification number which remains with the physical site regardless of change in ownership or operation. The caveat which boosts pharmacy waste generation into large quantity status is the generation of more than 1 Kg. (2.2 lbs) of P-listed waste in a calendar month. Which leads to the question, which drugs become hazardous waste when discarded?

Defining hazardous pharmaceutical waste

Applying RCRA to waste pharmaceuticals, we find the following definitions:

- The P list⁹
- The U list¹⁰
- The four characteristics of hazardous waste
 - ignitability¹¹
 - toxicity¹²
 - corrosivity¹³
 - reactivity.¹⁴

Diagram 2



P-listed chemicals are considered “acutely hazardous” by EPA — the worst of the worst. If a chemical on the P list is the sole active ingredient of a discarded product, it causes the entire product, including the solvent and container, to be contaminated and must be treated as a hazardous waste. Pharmaceuticals on the P list include:

- arsenic trioxide (P012)
- epinephrine (P042)
- nicotine (P075)
- nitroglycerin (P081)
- physostigmine (P204)
- physostigmine salicylate (P188)
- warfarin over 0.3% (common dosage forms) (P001)

U-listed chemicals include a broader range of pharmaceuticals and again must be the sole active ingredient to come under regulation. From the scientific perspective of a pharmacist, the sole active ingredient criterion is suspect. For example, the topical anesthetics Fluori-Methane® and Aerofreeze® both contain two U-listed chemicals, dichlorodifluoromethane and trichloromonofluoromethane. Technically, these items would not be regulated as hazardous waste when discarded since neither U-listed ingredient is the sole active ingredient. Common sense and professional knowledge, however, should lead us to manage these as hazardous wastes.

This same lack of rationality plagues the regulation in the case of chemotherapeutic agents. The P and U lists have not been updated substantially since 1976, when only the seven chemotherapy agents in use at the time were U-listed:

- chlorambucil (U035)
- cyclophosphamide (U058)
- daunomycin (U059)
- melphalan (U150)
- mitomycin C (U010)
- streptozotocin (U206)
- uracil mustard (U237)

Our professional knowledge of the toxicity of chemotherapeutic agents should encourage us to manage all bulk and residue chemotherapy agents as chemical hazardous waste. See Table 1 for a complete list of pharmaceuticals that are P- and U-listed.

Chemotherapy waste vs. hazardous waste

Before we proceed to the description of the four characteristics of hazardous waste, it is very important to distinguish between what the industry terms “chemowaste” and RCRA

hazardous waste. Currently, medical waste disposal firms offer a waste stream for chemotherapy waste. They accept empty¹⁵ vials, syringes, and IVs, plus other paraphernalia, such as tubing, gowns and gloves that contain trace amounts of chemotherapy agents. Unbeknownst to most pharmacists, this waste stream is managed as biohazardous, infectious waste. At best, it is incinerated in a medical waste incinerator. At worst, it is microwaved or autoclaved, then shredded and landfilled. None of these processes ensures the destruction of the organic molecules and their proper final disposition. Bulk and residue chemotherapy agents should be segregated into containers labeled RCRA Toxic Hazardous Waste along with other P- and U-listed waste and D-listed wastes we’ll address below.

Characteristics of hazardous waste

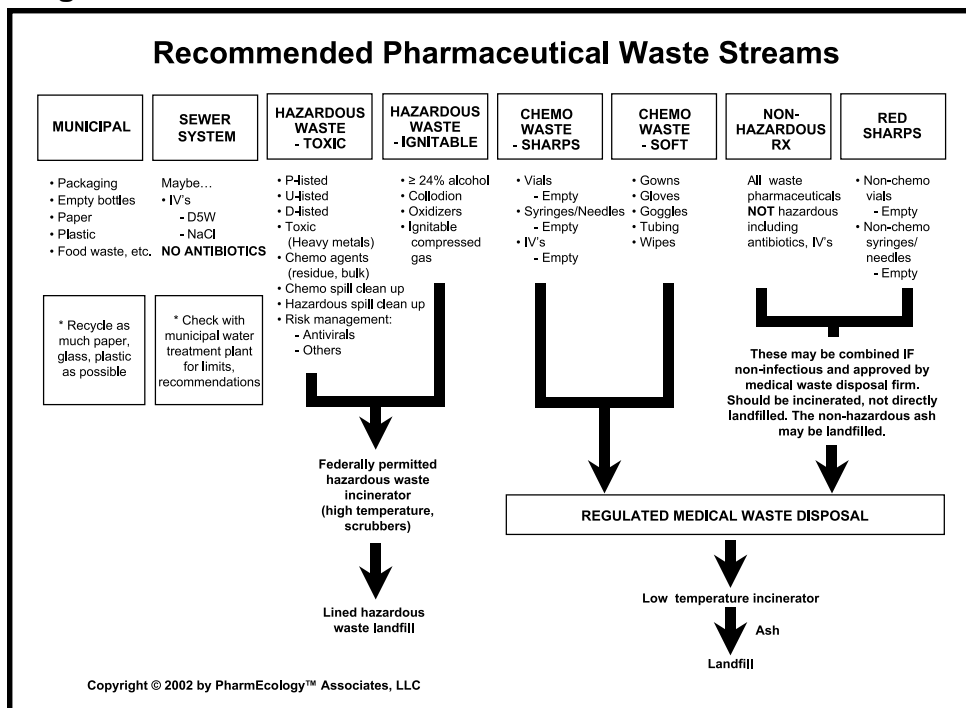
The EPA defines four characteristics of hazardous waste:

- ignitability (D001)
- toxicity (D number specific to the chemical)
- corrosivity (D002)
- reactivity (D003)

Ignitability has a great impact on pharmaceuticals since any aqueous formulation containing 24% or more alcohol is ignitable under this definition. In addition, a nonaqueous solution such as flexible collodion meets the flashpoint definition of less than 140° F. Oxidizers such as silver nitrate and potassium permanganate and aerosols with flammable propellants also qualify.

Toxicity is by far the most difficult characteristic to identify. The good news is that, of about 40 chemicals listed by

Diagram 3



How should hazardous waste be managed?

If we consider common pharmaceutical waste streams, we can usually identify five basic types: municipal waste, sewer system, chemo-waste sharps, chemo-waste soft, and red sharps. Non-infectious sharps may also be segregated. Note in Diagram 1, Common Pharmaceutical Waste Streams, that it is not unusual for controlled substances and antibiotics to be sewered, along with other IV fluids such as D5W and NaCl.

To properly manage RCRA hazardous waste, we need to establish at least two other waste streams: toxic hazardous waste and ignitable hazardous waste (Diagram 2, Recommended Additional Pharmaceutical Waste Streams). Based on the medical waste vendor being used, the pharmacy may also need to segregate and identify nonhazardous pharmaceutical waste.

EPA, only ten of them apply to pharmaceuticals and only in concentration levels above a certain regulatory limit (See Table 2 Toxicity Characteristic Regulatory Limits). The bad news is that the waste generator is responsible for determining if their waste meets that criteria and the exit levels are different for each chemical. For example, mercury, which is D009, has an exit level of less than .2mg/Liter causing any preparation containing a mercury preservative to come under regulation as a hazardous waste. Vaccines and topical eye and ear preparations often contain mercury and must therefore be discarded as hazardous waste.

Corrosivity is much easier to manage, since it involves very acidic (pH < or + to 2) or very basic (pH > or = to 12.5) chemicals. Normally these would only be found in the compounding area. The simplest way to manage these chemicals is to review the compounding area annually and contract with a hazardous waste broker to properly package and manage any discarded items.

The final characteristic, that of reactivity, is interesting in that the only relevant chemical is nitroglycerin. It is also P-listed, making it significant. Fortunately, the EPA recently exempted dosage forms of nitroglycerin from federal regulation.^{16,17} Because the Wisconsin Department of Natural Resources has mirroring regulations at the state level, an exemption must also be granted by the WDNR before waste nitroglycerin dosage forms can be removed from hazardous waste management by Wisconsin pharmacies and health care facilities. Even then, if the waste is being transported to a state which has not exempted it, nitroglycerin may need to remain a hazardous waste.

Medical waste vendors are NOT permitted to accept RCRA hazardous waste and are becoming much more cautious when accepting any waste pharmaceuticals to prevent violations in their acceptance procedures.

A new schema of pharmaceutical waste management would therefore include these three additions, with P-, U- and D-listed wastes, bulk and residue chemotherapy and chemo spill clean-up materials being placed into the toxic hazardous waste containers. (See Diagram 3, Recommended Pharmaceutical Waste Streams.) Those items meeting the criteria for ignitable hazardous waste would be segregated into the Ignitable Hazardous Waste containers. These containers would be properly labeled, stored, manifested, transported and disposed of by a hazardous waste broker and a federally permitted RCRA incineration firm. The management of these wastes at the pharmacy or health care facility can be accomplished either by internal expertise, if available, or through commercial hazardous waste brokers.

Nonhazardous waste pharmaceuticals may be segregated and could potentially continue to be disposed of by the current medical waste disposal firm, based on their permits.

How do we make this happen?

The profession of pharmacy is looking at a new system for identifying and managing this newly recognized waste stream. Therefore, new tools and resources must be developed to assist pharmacies in making this transition in a cost-effective manner. To address the need for hazardous waste containment

Table 1. P- and U-Listed Pharmaceuticals

<u>Name</u>	<u>Hazardous Waste Number</u>	<u>Name</u>	<u>Hazardous Waste Number</u>
Arsenic trioxide	P012	Hexachlorophene	U132
Epinephrine	P042	Lindane	U129
Nicotine	P075	Melphalan (chemo)	U150
Nitroglycerin ¹	P081	Mercury	U151
Physostigmine	P204	Mitomycin C (chemo)	U010
Physostigmine salicylate	P188	Paraldehyde (CIV)	U182
Warfarin >0.3%	P001	Phenacetin	U187
Chloral Hydrate (CIV) ²	U034	Phenol	U188
Chlorambucil (chemo)	U035	Reserpine	U200
Chloroform	U044	Resorcinol	U201
Cyclophosphamide (chemo)	U058	Saccharin	U202
Daunomycin (chemo)	U059	Selenium sulfide	U205
Dichlorodifluoromethane	U075	Streptozotocin (chemo)	U206
Diethylstilbestrol	U089	Trichloromonofluoromethane	U121
Formaldehyde	U122	Uracil mustard (chemo)	U237
		Warfarin <0.3%	U248

NOTE: This is not a comprehensive list of P and U listed chemicals. For a complete list, refer to Section 4, 40 CFR Section 261.33 Discarded commercial chemical products, off-specification species, container residues and spill residues. Available at http://www.access.gpo.gov/nara/cfr/cfrhtml_00/Title_40/40cfr261_00.html Accessed September, 2002.

1 Nitroglycerin in finished dosage forms has been exempted federally based on a Federal Register Notice dated May 16, 2001 (Volume 66, Number 95)(Page 27266-27297). Since every state except Iowa and Alaska have mirroring regulations, check with the Wisconsin Department of Natural Resources to determine the status of waste nitroglycerin dosage forms in Wisconsin.

2 Chloral hydrate and paraldehyde are controlled substances regulated by the Drug Enforcement Administration in schedule IV as an indication of moderate abuse potential. Since controlled substances must be destroyed through a witnessed destruction process, their status as a RCRA hazardous waste makes disposal very difficult.

Table 2. D List of Chemicals*

<u>Name</u>	<u>Hazardous Waste No.</u>	<u>Regulatory Level (mg/L)</u>
Arsenic	D004	5.0
Barium	D005	100.0
Cadmium	D006	1.0
Chloroform	D022	6.0
Chromium	D007	5.0
M-Cresol	D024	200.0
Lindane	D013	0.4
Mercury	D009	0.2
Selenium	D010	1.0
Silver	D011	5.0

* D List of Chemicals Present in Pharmaceuticals that Cause a Waste to Exhibit the Toxicity Characteristic When Present at or above the Maximum Concentration or Regulatory Level. Note: For a complete listing of all 40 chemicals and their regulatory limits, see Section 4, 40 CFR 261.24 Toxicity Characteristic. Available at: http://www.access.gpo.gov/nara/cfr/cfrhtml_00/Title_40/40cfr261_00.html Accessed August, 2002.

three criteria of hazardous waste: P-listed, U-listed or characteristic waste. These items must be segregated into the appropriate waste stream and managed as hazardous waste, utilizing either internal expertise or a hazardous waste broker. ■



Charlotte A. Smith is President of PharmEcology® Associates, LLC in Brookfield, WI. For more information, contact Ms. Smith at 262-814-2635 or csmith@pharmecology.org.

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continued . . .

geared to the pharmacy and health care environment, the SharpsSafety Division of the Kendall® Healthcare Company is currently working with PharmEcology® Associates, LLC to develop EPA and DOT compliant collection containers and appropriate labels. To address the need for a simple method of identifying which waste pharmaceuticals are hazardous waste under RCRA, PharmEcology® Associates, LLC is currently developing a subscription web-based search engine that will enable subscribers to enter the National Drug Code, brand or generic name of any drug product on the market and determine if it is a hazardous waste.

Summary

Regulatory pressure and environmental concerns are causing pharmacists to take a new look at how waste pharmaceuticals are being managed by their organizations. The EPA’s Resource Conservation and Recovery Act defines hazardous chemical waste, which applies to a number of common pharmaceuticals when they are discarded. Each organization needs to evaluate which of the pharmaceuticals it discards meet the

Managing Pharmaceutical Waste *continued . . .*

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Title_40/40cfr261_00.html](http://www.access.gpo.gov/nara/cfr/cfrhtml_00/Title_40/40cfr261_00.html) Accessed September, 2002.

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ERATORS OF HAZARDOUS WASTE Available at: [http://
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9. 40 CFR § 261.33 Discarded commercial chemical products, off-
specification species, container residues, and spill residues thereof.
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regulations, which state that first, all contents that can be removed
by normal means, including aspirating, have been removed. Then,
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