

Pharmaceutical Waste: Why Is It An Issue Now?

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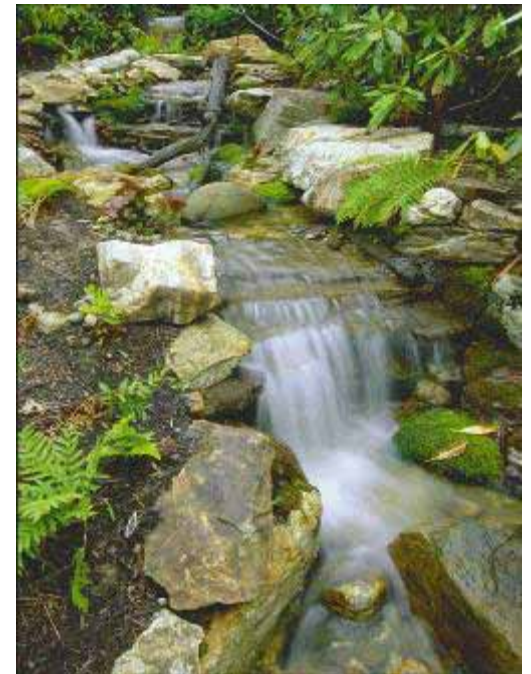
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Key Issues to Cover Today

- Concerns about Pharmaceuticals in the Environment
 - ✓ US Geological Survey Study
 - ✓ Health Impacts
- Current EPA RCRA Requirements
 - ✓ P and U Listed, Other RCRA Haz. Waste Characteristics and Non-Hazardous Waste
- Waste Planning, JCAHO and Resources

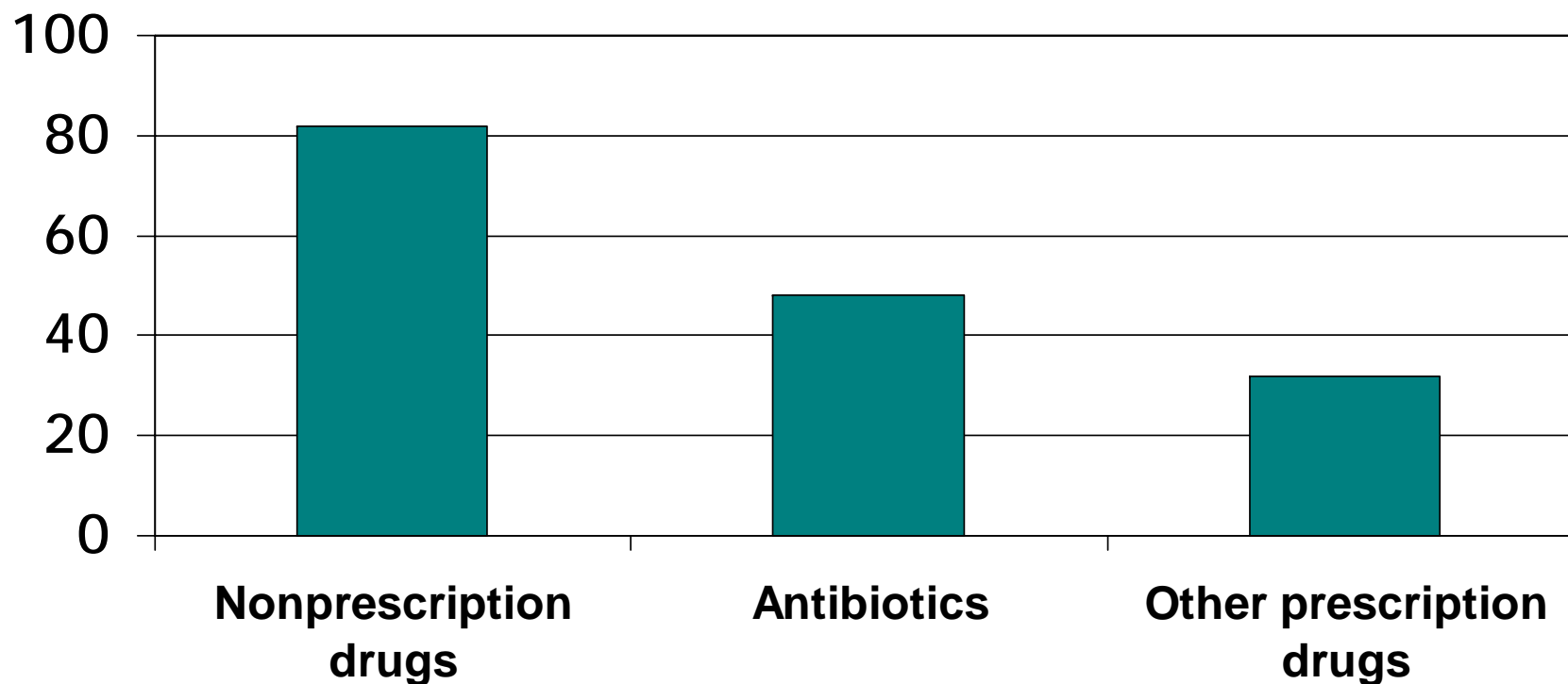
Looming Issue: Drugs in Waters

- USGS Study finding pharmaceuticals in streams...
- ...though not present at therapeutic doses
- Potential adverse impacts:
 - ✓ Water quality degradation
 - ✓ Endocrine disruption (physical, mental, sexual development)
 - ✓ Antibiotic resistance
 - ✓ Public perception



- First nationwide reconnaissance of occurrence of pharmaceuticals, hormones, other organic wastewater contaminants (OWCs)
- 139 streams in 30 states, analyzed for 95 different OWCs
 - ✓ Many OWCs: 82 of the 95 OWCs detected in at least one stream sample
 - ✓ Widespread: One or more OWCs found in 80% of stream samples
- 13% of streams had more than 20 OWCs

USGS Stream Survey¹: Frequency of Detection by Drug Class



¹ Streams susceptible to contamination were sampled (139)



Below the Dose/Response Curve: Endocrine Disruptors

- Endocrine Disruptors:
 - ✓ Disrupt hormone regulation in the body
 - ✓ Interfere with the normal function of the endocrine system (glands including thyroid, adrenals, ovaries, testicles)
 - ✓ Mimic hormones
 - ✓ Affect reproduction, development, and behavior
 - ✓ Multi-generational effects.



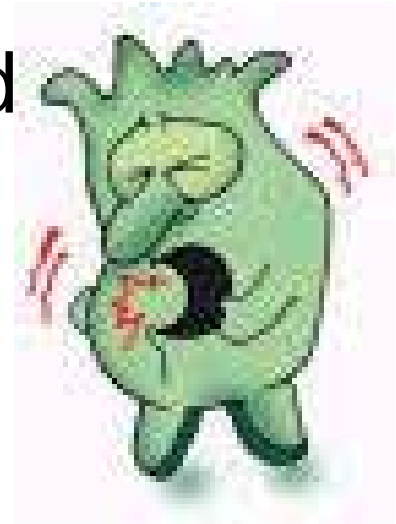
Below the Dose/Response Curve: Endocrine Disruptors

- Do not follow the normal dose/response curve.
- Active at much lower doses, especially in the fetus and newborn.
- Estradiols, progesterone, testosterone.
- Questions: Evidence of human effects at low concentrations?



Antibiotic Resistance

- Ampicillin-resistant bacteria found in every U.S. river tested in a 1999 study
 - ✓ 4 - 59% of population resistant
 - ✓ All Ohio River samples, contained E. coli with some degree of resistance to penicillin, tetracycline, and vancomycin in a 2000 study
 - ✓ Samples containing the highest levels of antibiotics also contained bacteria with greatest resistance



Pathways to Sewers



Human
Waste



Dumping in Sinks
and Toilets



Showering and
Handwashing



Hospitals for a Healthy Environment

- Enhanced focus on hazardous waste and pharmaceutical waste
 - ✓ <http://www.h2e-online.org/tools/chem-hwm.htm>
 - ✓ <http://www.h2e-online.org/tools/chem-pharm.htm>
- EPA grant to H2E to develop best management practices for managing pharmaceutical waste at facilities
- EPA grant to H2E to develop environmental compliance and improvement guide to improve performance on joint commission (JCAHO) surveys
- www.h2e-online.org



Working Together
to Create
Healthy
Communities!

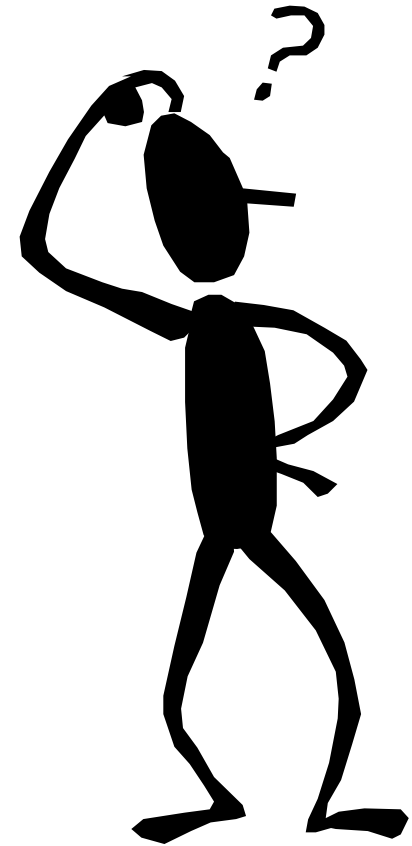


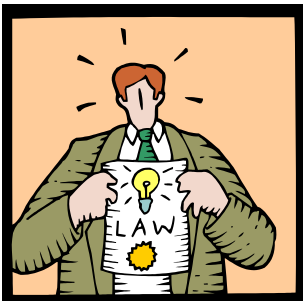
- Healthcare Environmental Resource Center
- Funded by EPA Office of Enforcement and Compliance Assistance and H2E
- Launched in April, 2005
- Environmental Compliance and Improvement Guide
 - ✓ "To improve compliance with JCAHO Environment of Care Standards"
 - ✓ www.hercenter.org/regsandstandards/jcahointro.html
- Hazardous waste determination
 - ✓ www.hercenter.org/hazmat/hazdeterm.html



Overview of Pharmaceutical Disposal for Hospitals

- Radioactives
 - ✓ special handling
- RCRA hazardous waste
 - ✓ must be hauled off as hazardous waste
- Solid waste
 - ✓ some flexibility





RCRA: The Defining Regulation

- Resource Conservation & Recovery Act
 - ✓ Enacted in 1976, enforced by the EPA
 - ✓ Federal regulation of the disposal of solid wastes
 - ✓ Encourages the minimization of waste generation
- Defines “hazardous waste”
- “Cradle to Grave” tracking of hazardous waste
- Households are exempt





RCRA Risk Management & Liability

- Civil and criminal liability
 - ✓ Civil: State/USEPA enforcement
 - ✓ Criminal: FBI, Attorney General, Grand Jury
- Corporate fines: \$32,500 per violation/day
- Personal liability: fines and/or imprisonment
- No statute of limitations
- Managers up through CEO



Recommended Disposal Strategy

RCRA Hazardous

 FLAMMABLE TOXIC SOLID LIQUID CORROSIVE REACTIVITY OTHER _____', 'D.O.T. PROPER SHIPPING NAME AND UN OR NA NO. WITH PREFIX _____', 'HANDLE WITH CARE!', 'CONTAINS HAZARDOUS OR TOXIC WASTES', and 'CP-3' in the bottom right corner."/>

RCRA Hazardous
Waste

IV bags with
salts/nutrients



Sewer

Everything Else



Medical Waste



Minimizing Pharm Waste

- Minimize inventory to extent feasible
- Rotate inventory - use oldest stock first
- Centralized disposal of physician's samples
- Avoid unnecessary prescriptions, especially antibiotics-Note pharmacy has very little control
- Use pharmacy reverse distribution



Minimize Hazardous RX Waste Generation?

- Inherent limitations on substitution of a less hazardous drug since the hazardous nature of the chemical often provides the therapeutic effect
- Tighter inventory control to reduce outdate generation, both original manufacturers' containers and repacks
- Single dose vials vs. multiple dose vials
- Patient specific oral syringes vs. 10 cc. repacks (e.g. choral hydrate for pediatric use)
- Reformulation of heavy metal concentration, especially mercury and m-cresol as preservatives



What Pharms Can Be Sewered?

- Up to individual POTWs
- Generally okay to sewer solutions in IV bags containing only:
 - ✓ saline solution
 - ✓ lactate (i.e., Ringer's)
 - ✓ nutrients such as glucose (i.e., D5W)
 - ✓ vitamins
 - ✓ potassium
 - ✓ other salts and electrolytes



Which Discarded Drugs Become Hazardous Waste?

- P-listed chemicals - acute hazardous waste
 - ✓ Sole active ingredient (Sect. 261.33(e))
- U-listed chemicals - toxic hazardous waste
 - ✓ Sole active ingredient (Sect. 261.33(f))
- Characteristic of hazardous waste
 - ✓ Ignitability
 - ✓ Toxicity
 - ✓ Corrosivity
 - ✓ Reactivity
- Please note that *the following lists are not intended to be complete*. The full lists of all P- and U-listed wastes appear in the Code of Federal Regulations, 40 CFR 261.33.



When is an Outdated Drug a Waste?

- At the time and place the decision is made to discard it
- Two EPA guidance letters to the industry:
 - ✓ Merck & Co., 1981
 - ✓ BFI Pharmaceutical, 1991
- Enables shipping of potentially creditable outdates to a reverse distributor as product
- PROHIBITS the shipping of waste-like items, such as unused IVs, partial vials



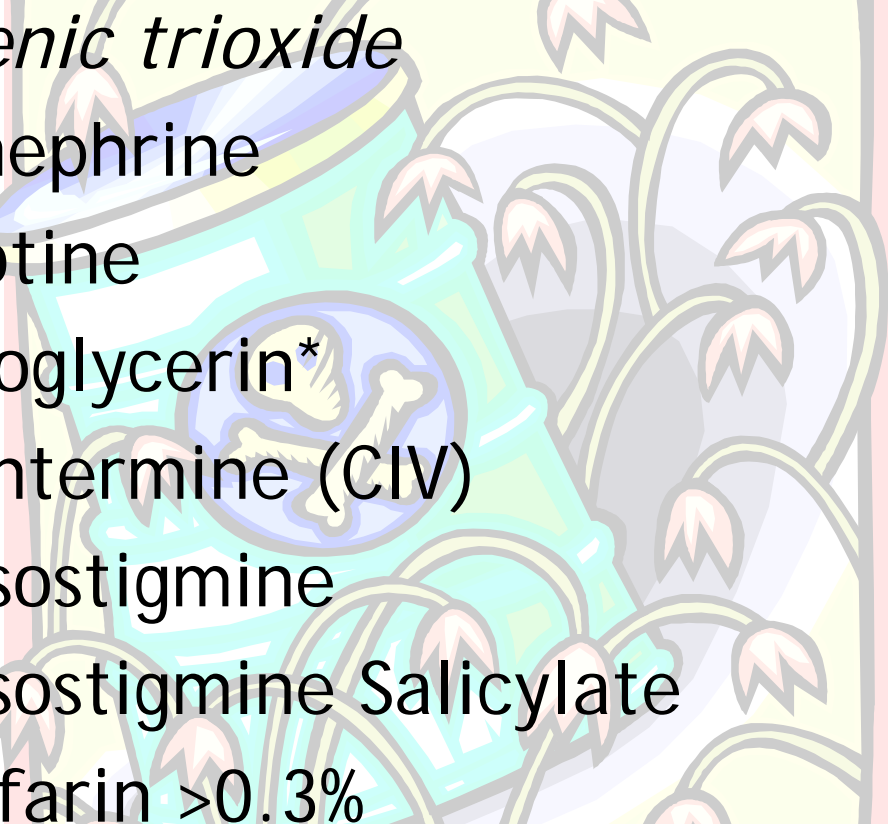
Federal Waste Generation Status

- Large Quantity Generator (LQG): generates more than 1000 kg/month of hazardous waste or >1 kg/month "P" listed waste.
- Small Quantity Generator (SQG): Generates <1000 kg/month but >100 kg/month of hazardous waste & < or = 1 kg/month "P" listed waste.
- Conditionally Exempt Small Quantity Generator (CESQG): Generates < or = 100 kg haz waste/month, < or = 1kg P listed waste/month

Bottom Line? Know your status.



P-Listed Pharmaceutical Waste

- 
- *Arsenic trioxide* P012
 - Epinephrine P042
 - Nicotine P075
 - Nitroglycerin* P081
 - Phentermine (CIV) P046
 - Physostigmine P204
 - Physostigmine Salicylate P188
 - Warfarin >0.3% P001

*Nitroglycerin in finished dosage forms excluded federally and in many states for reactivity; must evaluate for ignitability

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P-Listed Pharmaceutical Waste



Common U-Listed Pharmaceuticals:

- Chloral Hydrate (CIV) U034
- Chlorambucil (chemo) U035
- Chloroform U044
- Cyclophosphamide (chemo) U058
- Daunomycin (chemo) U059
- Dichlorodifluoromethane U075
- Diethylstilbestrol(chemo) U089
- Formaldehyde U122
- Hexachlorophene U132
- Lindane U129
- Melphalan (chemo) U150
- Mercury U151
- Mitomycin C (chemo) U010
- Paraldehyde (CIV) U182
- Phenacetin U187
- Phenol U188
- Reserpine U200
- Resorcinol U201
- Saccharin U202
- Selenium sulfide U205
- Streptozotocin (chemo) U206
- Trichloromonofluoromethane U121
- Uracil mustard (chemo) U237
- Warfarin <0.3% U248



U-Listed Pharmaceutical Waste



Chemotherapy Waste

- Eight chemotherapy agents are U-listed; one is P-listed
- Medical waste hauler protocols for “Chemo Waste”
 - ✓ Empty vials, syringes, IV’s
 - ✓ Treated as infectious medical waste preferably through regulated medical waste incineration
- If not empty, should be placed into Hazardous Waste container
- “Empty” for U-listed waste means all contents removed that can be removed through normal means and no more than 3% by weight remains
 - ✓ 3 ml allowance in common practice is a misunderstanding of the definition of “RCRA empty”



Chemotherapy Residue: Infectious and Hazardous

- If chemo IV bag has been hung, is not completely used and can be separated from patient exposed sharp without exposing the employee, remove and dispose as RCRA hazardous waste
- If chemo residue cannot be removed safely, check with your state regulatory agency for their requirements for disposal
- If waste is mixed hazardous and infectious be sure to contract with a hazardous waste vendor that can also accept infectious waste
- No consensus yet on this issue among hazardous waste regulators



Selected chemotherapy agents by brand name

- A number of the chemicals used to treat cancer patients during chemotherapy are on either the U or P lists. These agents are often referred to by their brand names rather than the chemical designations appearing on the lists. For your convenience, we have listed *some* common brand names below, together with their chemical names and RCRA waste codes.
- Since new products may be introduced at any time, this list may not include all brand names composed of RCRA listed chemicals.



Selected chemotherapy agents by brand name

Brand name	Chemical name	Code
Alkeran	Melphalan	U150
Cerubidine	Daunomycin	U059
CTX	Cyclophosphamide	U058
Cytotoxan	Cyclophosphamide	U058
Daunorubicin	Daunomycin	U059
DaunoXome	Daunomycin	U059
Leukeran	Chlorambucil	U035
Liposomal Daunorubicin	Daunomycin	U059
L-PAM	Melphalan	U150
Mitomycin	Mitomycin C	U010
Mutamycin	Mitomycin C	U010
Neosar	Cyclophosphamide	U058
Procytox	Cyclophosphamide	U058
Rubidomycin	Daunomycin	U059
Streptozocin	Streptozotocin	U206
Trisenox	Arsenic Trioxide	P012
Zanosar	Streptozotocin	U206



Chemotherapy Agents: Many Are Not Regulated by RCRA

- Over 100 chemotherapy agents not regulated by EPA
- Examples:
 - ✓ Alkylating agents: Cisplatin, Thiotepea
 - ✓ Antimetabolites: Fluorouracil, Methotrexate
 - ✓ Hormonal (antiandrogen): Lupron® (leuprolide)
 - ✓ Hormonal (antiestrogen): Tamoxifen
 - ✓ Mitotic Inhibitor: Taxol® (paclitaxol)



Trace Chemotherapeutic Waste

“items which are RCRA empty, but which have held, or potentially exposed to any chemotherapy”

- ✓ Avoid autoclaving or microwaving
- ✓ Requires incineration at an RMW incinerator; may be infectious such as used needles
- ✓ IV tubes primed with saline by the pharmacy and flushed with saline before being removed from patient can be managed as trace chemotherapeutic waste,
 - reducing the volume of hazardous waste generated
 - reducing contamination of PPE
 - lessening employee exposure



Traditional Chemo Waste Containers

New Hazardous Waste Containers



Empty vials, syringes, IVs, tubing, gowns, gloves, etc.

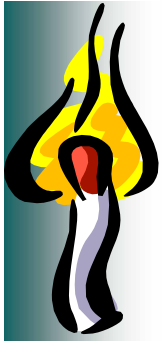
Bulk chemo in vials, unused IV's, P, U. toxic D

Hospitec



Kendall





Characteristic of Ignitability

- Aqueous Solution containing 24% alcohol or more by volume & flash point $< 140^{\circ}$ F.
- Hazardous Waste Number: D001
- Rubbing Alcohol
- Topical Preparation
- Injections





Characteristic of Corrosivity

- An aqueous solution having a pH $<$ or $=$ 2 or $>$ or $=$ to 12.5
- Examples: Primarily compounding chemicals
 - ✓ Glacial Acetic Acid
 - ✓ Sodium Hydroxide
- Hazardous waste number: D002



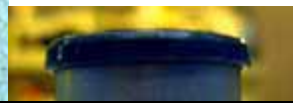


Characteristic of Toxicity

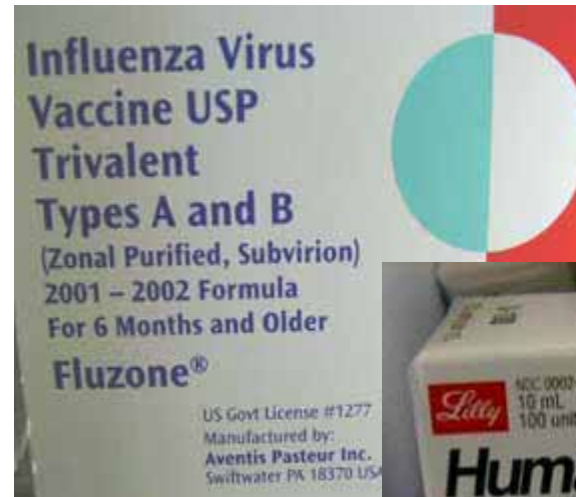
- Approximately 40 chemicals which meet specific leaching concentrations
- Examples of potential toxic pharmaceuticals:
 - ✓ Arsenic
 - ✓ Barium
 - ✓ Cadmium
 - ✓ Chloroform
 - ✓ Chromium
 - ✓ Lindane
 - ✓ m-Cresol
 - ✓ Mercury (thimerosal)
 - ✓ Selenium
 - ✓ Silver



Pharmaceuticals Exhibiting the Characteristic of Toxicity



Heavy Metals: Selenium, Chromium and Silver

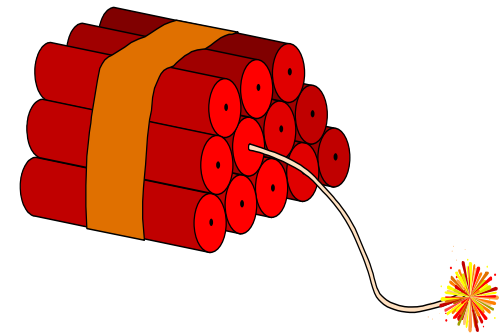


Preservatives: thimerosal & m-cresol



Characteristic of Reactivity

- Meet eight separate criteria identifying certain explosive and water reactive wastes
- Nitroglycerin formulations are exempted federally as of August 14, 2001 under FR: May 16, 2001. Many states have adopted exemption. Must still be evaluated for ignitability.
- Hazardous Waste Number: D003




How Can a RCRA Hazardous Waste Be Identified?



- Web-based databases enabling search by product for waste management recommendations
- Search by NDC, product or generic name, active ingredient
 - ✓ Recommendations citing federal regulations and recommended waste streams
 - ✓ State regulation alerts if more stringent than federal
 - ✓ Risk Management alerts based on professional knowledge (e.g. chemotherapy agents not regulated at the state or federal level)



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How Does the Search Logic Work?
What Is "PharmE Hazardous™ Waste" ?
Product Questions? Contact Us
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Individual Product Search Batch Product Search PharmEcology Admin

Search By NDC Number NEW SEARCH

NDC number:
 (For example: 12340-45610 or 1234-456-10 or 1234-456)

Search by Product Name

Product name: Strength (optional):

Search by Generic Name or Active Ingredient

Generic name: Manufacturer (optional): Strength (optional):

*Hints SEARCH >>

1. Enter a full or partial NDC number, with or without hyphens
2. Enter a full or partial product or generic name
3. Enter the beginning of the strength, ignoring the concentration or additional ingredients

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 Analysis for: WISCONSIN

Federal Hazardous Waste
 PharmE Hazardous™ Waste
 Non-Hazardous Waste

What Products are in the Database?
 How Does the Search Logic Work?
 What Is "PharmE Hazardous™ Waste"?
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Individual Product Search Additional Information

Federal Hazardous Waste

Product:	00008-0263-01 EPINEPHRINE INJ 1MG/ML	1.00 ML Rx
Generic:	Epinephrine HCl	DEA: Non-Controlled
Manufacturer:	WYETH	

Recommended Waste Classification

**Regulated as federal hazardous waste:
 P042-Epinephrine**

Recommended Waste Stream

**Handle as hazardous waste:
 Toxic**

Highlights

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Where Should a RCRA Hazardous Waste Be Stored?

- Hazardous Waste Storage Accumulation Site:
 - ✓ Same locked area as mercury, xylene, formaldehyde, lab chemicals
 - ✓ Maximum storage time: 90 or 180 days based on generator status



RCRA Hazardous Wastes Must Be Properly Labeled!



How Should a RCRA Hazardous Waste Be Disposed?

- Either contract with a hazardous waste broker or develop internal expertise for:
 - ✓ Lab packing
 - ✓ Manifest preparation
 - ✓ Land ban preparation
- Contract with a federally permitted RCRA hazardous waste incineration facility (TSDF: Treatment, Storage & Disposal Facility)



What About Non-Hazardous Drugs?

- Segregate into a non-red, non-yellow container, such as beige or white with blue top (California Pharmaceutical Waste)
- Label "Non-hazardous Pharmaceutical Waste - Incinerate Only"
- Dispose at a regulated medical waste or municipal incinerator that is permitted to accept non-hazardous pharmaceutical waste



Benefits of a Comprehensive Hazardous Waste Disposal Plan

- JCAHO Environment of Care Performance Improvement Initiative
 - ✓ New 2004 Standards - see both Medication Management and Environment of Care
- Reduces EPA liability and risk exposure to a minimum
- Protects employees and patients
- Demonstrates responsible care in dealing with hazardous substances, hazardous wastes



What About Household Pharms?

- Non-controlled substances
 - ✓ May be able to take to a household hazardous waste roundup - not currently available in AZ, but check with your county soon
 - ✓ or treat as below
- Controlled substances
 - ✓ Render unpalatable - pepper, turmeric, strong spices
 - ✓ Remove labeling, duct tape shut
 - ✓ Mix with undesirable trash and put in regular trash right before pickup
- **NO DRUGS DOWN THE DRAIN**



Reverse Distribution

- For pharmaceuticals - an alternative that is not available for most other hazardous substances
- Expired pharms can be returned to the manufacturer for credit by pharmacies, not by consumers
- Not to be used as a “waste management system.”
- Exclusion applies only to bona fide returns for credit, and not to broken containers, spilled contents, compounding leftovers, unused IVs, etc.



Take Home Messages

- USGS Study found pharmaceuticals at detectable levels in many U.S. surface waters!
- First manage for P2, then dispose of properly.
- Pharmacists not always conversant in waste regulations (and may need support).
- EPA Resource Conservation & Recovery Act regulations carry significant liability, comparable to Drug Enforcement Administration

Resources

- <http://epa.gov/nerlesd1/chemistry/pharma/>
- www.pharmacology.com
- Pharmaceutical Waste: www.h2e-online.org/tools/chem-pharm.htm
- www.hercenter.org/hazmat/pharma.html
- RCRA On-Line: www.epa.gov/rcraonline
- NIOSH Hazardous Drug Alert:
www.cdc.gov/niosh/docs/2004-165/



Resources

- Pharmaceutical Waste Survey, King County, Washington State, April 29, 2003, <http://www.govlink.org/hazwaste/publications/index.cfm#187>
- Your Risks in Handling Outdated and Unusable Drugs: A Guide to JCAHO and Regulatory Standards. Capital Returns, Inc., 1998 Call 1-800-950-5479
- Guidelines for Reverse Distributors: Minimum Federal Regulatory Standards, www.returnsindustry.com
- Improper Discard of Toxic Drugs Hurts Environment, Leads to Fines, AJHP, Vol 58, #17 September 1, 2001 pp 1576-1578.

