



U.S. Food and Drug Administration



Pharmaceuticals in Water Regulatory Landscape FDA Perspective

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Research Triangle Environmental Health Collaborative
2008 Summit: Pharmaceuticals in Water
November 10-11, 2008

FDA Works to Ensure that...



- Americans have access to safe and effective drug products.
- Foods and food additives, are safe, wholesome, and properly labeled.
- Blood used for transfusions, blood products, vaccines, are safe and in adequate supply.
- Medical devices and transplanted tissues are safe and effective.
- Animal drugs and medicated feeds are safe and effective, and foods from treated animals are safe for human consumption.
- Radiation-emitting electronic products are safe.
- Cosmetics are safe and properly labeled.



New Drug Applications

- Pre-clinical studies
 - *In vitro* and *in vivo* studies including: mutagenicity, carcinogenicity, acute, chronic toxicology, reproductive and developmental toxicology, immunotoxicology
- Human clinical trials
 - Phase 1, Phase 2, Phase 3, Phase 4 commitments
 - Toxicity / most common adverse effects
 - Pharmacokinetics and pharmacodynamics
 - absorption, distribution, metabolism, and excretion (ADME)
 - Safety and efficacious
- Post-marketing studies and adverse-event monitoring
- Environmental Assessments (EAs)
- Benefits must outweigh risks for a specific population and specific use (risk:benefit relationship)



National Environmental Policy Act (NEPA)

- National Environmental Policy Act of 1969
 - Requires all Federal agencies to assess the environmental impact of their 'actions' and to ensure that the interested and affected public is informed of the environmental analyses.
- FDA requires drug sponsors to submit an EA that adequately addresses potential environmental impacts of the Agency's action.
- Some actions can be categorically excluded from the requirement to submit an EA.
- Environmental analysis considered in decision-making for NDA.
- *Guidance for Industry: Environmental Assessment of Human Drug and Biologics Applications* (Issued 7/1998) provides detailed information on a variety of topics related to preparing and filing EAs.



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Environmental Assessments

A concise document that provides sufficient information for the Agency to determine whether an Environmental Impact Statement (EIS) or a Finding of No Significant Impact (FONSI) should be prepared.

- Focus:
 - Environmental fate and ecotoxicology based on drug use patterns, consumer use, and disposal,
 - Harvesting of wild animals and plants for drug substances,
 - Containment of 'transgenic' organisms during investigations and post-approval
- Mitigating FONSI (labeling/manufacturing changes)
- Publicly available document after application approval



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Environmental Impact Statement

A detailed statement on (i) the environmental impact of the proposed action, (ii) any adverse environmental effects which cannot be avoided, (iii) alternatives to the proposed action, (iv) options to mitigate impacts.

- Proposal to Amend the Food Additive Regulations to Permit the Safe Use of Selenium as A Nutrient in the Feed of Chickens, Turkeys and Swine
- Proposal to Limit the Use of Subtherapeutic Levels of Tetracyclines (Oxytetracycline and Chlortetracycline) and Penicillin in Animal Feeds
- Pacific Yew/Taxol Final Environmental Impact Statement (USDA/BLM/FDA)
- Prohibition of the Nonessential Use of Chlorofluorocarbons as Propellants in Self- Pressurized (Aerosolized) Containers in Products Subject to the FFD&C Act



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CDER Retrospective Review of Ecotoxicity Data

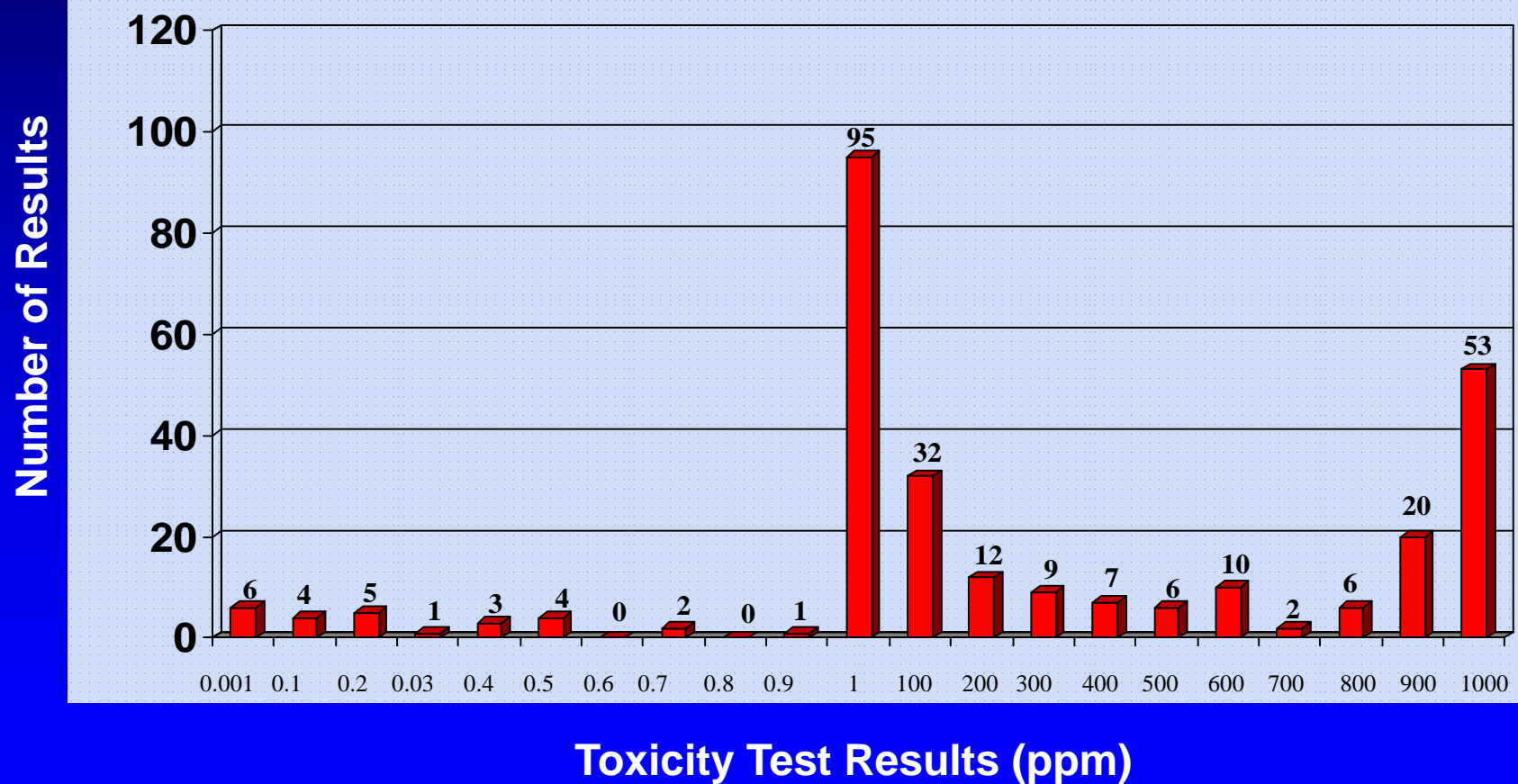
- In support of revised regulations
- Analysis of 76 + APIs / 276 + test results
- Acute and chronic toxicity studies:
 - Fish toxicity, aquatic invertebrate immobilization studies, algal growth inhibition, plant early growth, earthworm toxicity, microbial inhibition/toxicity
 - NOEC, LOEC , MIC ($LD_{50}/1000 = NOEC$)
 - OECD/EPA/FDA Guidelines



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CDER Retrospective Review of Ecotoxicity Data



CDER Environmental Impact Regulations

- Code of Federal Regulations: 21 CFR 25
 - CDER routinely requires applicants to submit EAs for NDAs with predicted WWTP effluent introductory concentrations (EIC) of ≥ 1 ppb.
 - Estimate based on high-end projected sales and worse-case, end-of-pipe effluent discharges.
 - NEPA “**extraordinary circumstances**” provision:
 - Used by Agency to require EAs for NDAs with EIC < 1 ppb when available information indicates potential environmental impacts.
 - EAs may be required for drug applications where the drug or biologic product is derived from non-cultivated ESA- or CITES - listed plants or animals.



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Drug Disposal Guidelines



SMART DISPOSAL

A Prescription for a Healthy Planet

October 17, 2008 [En Español con palabras de traducción automática.](#) [Email a Friend About SMART Disposal](#)

Home
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About the Partnership
Become a Supporter
Common Questions

Responsible Medication Disposal Safeguards Lives and Protects the Environment.

A few small steps can make an important difference in safeguarding lives and protecting the environment.


Welcome to a site for anyone who is concerned about the environment, human safety, wildlife and aquatic resource conservation. As Americans, most of us enjoy an unparalleled quality of life. We have diverse hobbies, numerous economic opportunities, tremendous cultural and outdoor resources and the best health care in the world. In fact, many of us combine our hobbies with our passion for the natural environment. And protecting these resources is an important part of our overall enjoyment.

A concern we must all address is the disposal of medications and their effect on human life, wildlife, lakes, rivers and streams throughout our country. This issue is relevant to everyone's personal health safety and the protection of our environment.

The SMART DISPOSAL™ campaign is designed to raise awareness about the potential environmental impact from improperly disposed of medications and to provide proactive guidance through proper disposal alternatives.



SMART DISPOSAL
Demonstration



Proper Disposal of Prescription Drugs

Office of National Drug Control Policy February 2007

Federal Guidelines:

- Take unused, unneeded, or expired prescription drugs out of their original containers and throw them in the trash.
- Mixing prescription drugs with an undesirable substance, such as used coffee grounds or kitty litter, and putting them in impermeable, non-descript containers, such as empty cans or sealable bags, will further ensure the drugs are not diverted.
- Flush prescription drugs down the toilet *only* if the label or accompanying patient information specifically instructs disposal (see below).

The FDA advises that the following drugs be flushed down the toilet instead of thrown in the trash:

- Actiq** (fentanyl citrate)
- Daytrana Transdermal Patch** (methylphenidate)
- Duragesic Transdermal System** (fentanyl)
- OxyContin Tablets** (oxycodone)
- Avinza Capsules** (morphine sulfate)



How to Dispose of Unused Medicines

Is your medicine cabinet filled with expired drugs or medications you no longer use? How should you dispose of them?

Most drugs can be thrown in the household trash, but consumers should take certain precautions before tossing them out, according to the Food and Drug Administration (FDA). A few drugs should be flushed down the toilet. And a growing number of community-based "take-back" programs offer another safe disposal alternative.

Guidelines for Drug Disposal

FDA worked with the White House Office of National Drug Control Policy (ONDCP) to develop the first consumer guidance for proper disposal of prescription drugs. Issued by ONDCP in February 2007, the federal guidelines are summarized here:

- Follow any specific disposal instructions on the drug label or patient information that accompanies the



Controlled Substances

- Product labeling advises flushing certain drug products to make them completely unavailable upon disposal
- These drugs contain controlled substances and have documented potential for misuse, abuse, and accidental overdose
- Drug disposal instructions typically developed as part of a more comprehensive **risk management strategy**
- DEA restrictions on take-back programs
 - **Actiq** (fentanyl citrate)
 - **Daytrana Transdermal Patch** (methylphenidate)
 - **Duragesic Transdermal System** (fentanyl)
 - **OxyContin Tablets** (oxycodone)
 - **Avinza Capsules** (morphine sulfate)
 - **Meperidine HCl Tablets**
 - **Percocet** (oxycodone and acetaminophen)
 - **Xyrem** (sodium oxybate)
 - **Fentora** (fentanyl buccal tablet)

Disposal

Dispose of any unopened *FENTORA* tablets remaining from a prescription as soon as they are no longer needed.

To dispose of unused *FENTORA*, remove *FENTORA* tablets from blister packages and flush down the toilet. Do not flush the *FENTORA* blister packages or cartons down the toilet.

If you need help with disposal of *FENTORA*, call Cephalon Medical Services at 1-800-896-5855.



Drug Take-Back Programs



Store REYATAZ Capsules at room temperature, 59° to 86° F (15° to 30° C). Do not store this medicine in a damp place such as a bathroom medicine cabinet or near the kitchen sink.

Keep your medicine in a tightly closed container.

Keep all medicines out of the reach of children and pets at all times.

Do not keep medicine that is out of date or that you no longer need.

Dispose of unused medicines through *community take-back disposal programs* when available or place REYATAZ in an unrecognizable, closed container in the household trash.



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Federal Interagency Workgroup on Pharmaceuticals in the Environment

- Executive Office of the President / National Science and Technology Council / Committee on Environment and Natural Resources
- EPA/FDA/USGS (Co-leads), CDC, NIEHS, NOAA, USDA, FWS
- Development of Federal interagency research strategy
 - Improve the ability to assess human and ecological risks due to pharmaceutical residues in environmental media
- Goals
 - Develop interagency database of ongoing research and regulatory activities
 - Define data needs and prioritize research areas
 - Recommend areas for collaboration among Federal agencies



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National Academy of Sciences

- Board on Environmental Studies and Toxicology workshop:
 - Characterizing the Potential Human Toxicity from Low Doses of Pharmaceuticals in Drinking Water: Are New Risk Assessment Methods or Approaches Required
 - December 11-12, 2008
 - National Academy of Sciences
2101 Constitution Avenue, NW, Washington, DC



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Summary

- FDA continues to work with NEPA, its federal partners - EPA, USGS, CDC - and the regulated industry on potential ecological and human health effects of pharmaceutical residues in the environment.
- NDA pharmaceutical data can help support risk assessment development for pharmaceutical residues in water.
- FDA worked with stakeholders to develop the safe disposal methods described in the Federal Drug Disposal Guidelines.



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Thank You