

STATEMENT OF
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BEFORE THE
COMMITTEE ON NATURAL RESOURCES
SUBCOMMITTEE ON INSULAR AFFAIRS, OCEANS AND WILDLIFE

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Madam Chairwoman and Members of the Subcommittee, thank you for the opportunity to provide the views of the Department of the Interior on the spread of endocrine-disrupting chemicals (EDCs) in the environment, the associated effects of EDCs on fish and wildlife species, and possible solutions for reducing EDCs in the environment.

Background

Endocrine disruption is disturbance of the proper function of the endocrine or hormone system in vertebrates (including mammals, birds, amphibians, and fish) and selected invertebrates (mollusks). Hormones are chemical messengers within the body that regulate biological processes throughout all life stages from conception to old age, including the development of the brain and nervous system, the growth and function of the reproductive system, metabolism, and stress response.

Endocrine disruption can produce adverse effects on developmental, reproductive, neurological, and immune systems, affecting individuals, their offspring, or a population. Endocrine disruption can be caused by exposure to synthetic or naturally occurring chemicals often referred to as EDCs. EDCs comprise a wide range of environmental contaminants, including biogenic hormones (hormones formed in people or animals and excreted), synthetic hormones (used pharmaceutically as ovulation inhibitors, hormonal supplements, or growth promoters), and a wide range of pesticides and other household and industrial chemicals that mimic, block or otherwise interfere with normal hormone function.

A variety of chemicals have been found to disrupt the endocrine systems of aquatic and terrestrial organisms in laboratory studies. Many of these chemicals have been found in the environment, and, in some environmental settings, many EDCs occur together in complex mixtures.

Exposure to extremely low (parts per trillion) concentrations of EDCs can lead to endocrine disruption resulting in adverse aquatic health effects on fish and wildlife. EDCs can have additive or interactive effects (Brian et al., 2005, 2007); for example, a number of chemicals can mimic the effects of estrogen, the female reproductive hormone. As a result of these adverse aquatic health effects, it is essential to understand the total exposure of an organism to the range of chemicals present in its environment to estimate the potential risk from endocrine disruption.

Furthermore, the effects of endocrine disruption may not become evident until much later in life or in a subsequent generation. Even small disturbances in endocrine function can have profound and lasting health effects, especially if they occur during highly sensitive prenatal periods (McLachlan, 1980, 1985; Colburn and Clement, 1992; Cooper and Kavlock, 1997; Newbold 1999).

Endocrine-Disrupting Chemicals in the Environment

EDCs have been measured in the environment for many decades. The known toxicological effects of some, including the industrial chemicals PCBs and dioxins, and the pesticides DDT and chlordane, have resulted in cessation or restriction of their use. Some of these chemicals have been found to persist in the environment and are still observed in the environment today.

Many EDCs are now used or are integral parts of products that are used daily in our homes or places of work. They include human and veterinary pharmaceuticals, detergents, fragrances, fire retardants, disinfectants, plastics, resins, pesticides, and insect repellants. Therefore, they are in our wastes and can enter the environment in a manner related to the way we handle and dispose of our wastewaters and solid wastes. Other EDCs are used in gardens, parks, and agricultural fields and spread within the environment through runoff and infiltration. As a result, EDCs are commonly found together in mixtures in various environmental settings. These environmental settings include streams receiving significant quantities of wastewater treatment plant effluent (Glassmeyer et al., 2005), groundwaters affected by a high density of domestic septic systems (Conn et al., 2006), and runoff from densely cultivated areas (Kolpin et al., 2002).

Animal wastes also can have elevated levels of EDCs. Animals produce and excrete significant quantities of hormones and excrete hormonally active pharmaceuticals that they are given for growth promotion, estrus modulation, or other prophylactic or therapeutic purposes. Wastes from animal feeding operations (AFOs), where large numbers of animals are maintained in a small area, can concentrate the release of EDCs to the environment (Durhan et al., 2006). Animal feeding operations across the United States generate more than 450 million tons of manure per year (U.S. Census of Agriculture, USDA-NASS, 1997).

Widespread application of manure and biosolids to lands as fertilizer provide a widespread source of EDCs to the environment. Lands where reclaimed wastewater, biosolids, or manure are applied for irrigation and/or fertilizer also can be susceptible to EDCs (Kinney et al., 2006a, 2006b, 2008). Over 3 million dry tons of biosolids are applied to fields as fertilizer each year in the United States (USEPA).

In 2002, the U.S. Geological Survey (USGS) published a national reconnaissance that found one or more of 95 different organic wastewater contaminants in 80 percent of surveyed streams (Kolpin et al., 2002). The streams were selected because they were considered to be susceptible to these human and animal waste-related chemicals. The streams sampled drained areas of high urban/suburban development or high density of animal agriculture. Sufficient evidence existed in the scientific literature to identify 34 of these 95 chemicals as potential EDCs, including biogenic

and synthetic hormones, pharmaceuticals, and personal care products. The USGS, often in collaboration with partners, including EPA, NOAA, CDC, FWS and others, has conducted numerous studies on EDCs and other emerging contaminants in the environment and has developed methods to measure EDCs in environmental samples, as well as methods to collect environmental samples that more effectively quantify exposure of aquatic organisms.

Effects of Endocrine-Disrupting Chemicals on Fish and Wildlife

The fact that we detect EDCs in the environment alone does not indicate that they are an environmental health concern. Although detection is an important component of environmental assessment, controlled studies of the toxicological effects of the levels and mixtures of EDCs that we find in environmental settings are essential.

EDCs are stressors with the potential to impact the reproductive potential or behavioral responses of animals and to increase the susceptibility of populations to significant deterioration. These effects can include

- masculinization of female and feminization of male fish, reptiles, birds, and mammals;
- abnormal thyroid function in birds;
- decreased hatching success in fish, birds, and turtles;
- altered immune function in birds, mammals, and fish;
- altered behavior such as overt aggression and reduced predator avoidance in fish; and
- reproductive incompetence (e.g., infertility) in birds, fish, shellfish, and mammals.

Some of these responses are reversible if exposure is eliminated, but other anatomical, physiological and genetic alterations are permanent.

There is compelling evidence that endocrine systems of certain fish and wildlife have been affected by exposure to EDCs in the environment. The exposure to EDCs and indicators of endocrine disruption (such as intersex, the presence of female characteristics in males or male characteristics in females) has been documented together in the same places in fish species across the Nation and in many countries across the world, including the United Kingdom, Denmark, South Africa, Germany and more. A national USGS study of sex hormones and intersex biomarkers in common carp in the mid-1990s indicated the potential for widespread endocrine disruption in fish and the need for more detailed cause-and-effect studies (Goodbred et al., 1996). Fish are highly susceptible to endocrine disruption because they can live in waters with sustained levels of EDCs. Conclusive demonstration of the cause and effect relation between exposure to EDCs and endocrine disruption in the environment has remained elusive until recently

Recent studies have demonstrated conclusively that EDC levels in the environment have the potential to severely impact a fish population. Kidd et al. (2007) demonstrated that the addition of ethinylestradiol (one of the active ingredients in birth control pills) at observed environmental concentrations to an experimental lake in Canada caused feminization and near extinction of fathead minnows in the lake. USGS studies in Boulder Creek, Colorado, demonstrated significantly different indicators of endocrine disruption in fish populations upstream and downstream of a low head dam, which separates upstream waters minimally affected by

development from downstream waters enriched in wastewater effluent (Vajda et al., 2008). Other streams being investigated by the USGS and the U.S. Fish and Wildlife Service (FWS) include Lake Mead, Nevada (Rosen et al., 2006), the Upper Mississippi River, Minnesota (Lee et al., 2008a & b), the Missouri River (Papoulias et al., 2006), Lake Erie, and the Potomac River.

Investigations of fish health in the Potomac River were initiated in 2004 in response to recurring fish kills and high incidence of fish lesions. Since then, the USGS and the FWS have identified high levels of intersex in bass and have recently identified evidence that endocrine disruption may contribute to impaired immune response and increased susceptibility to other stressors (Blazer et al., 2007, Ripley et al., 2008, Robertson et al., 2009, Iwanowicz et al., 2009; Alvarez et al., 2009). We are continuing to explore whether a linkage exists between EDCs and these fish kills and lesions.

Studies into the effects of EDCs on wildlife examined a wide range of species in many environments and locations, including river otters in Oregon; alligators and panthers in Florida; barn swallows in the lower Mississippi River, Louisiana; reptiles in Arizona; polar bears and eiders in Alaska; sturgeon along the middle Mississippi River in Illinois, Missouri, and Iowa; mussels and paddlefish in Ohio; common loons in Maine; terns and cormorants in New York; cormorants in Michigan; and amphibians in Texas. All of these investigations involved wildlife and habitat sampling to determine how animals were being exposed to EDCs and provided suggested management actions to alleviate the documented impacts from these toxic compounds.

In 1991, the FWS began investigating the potential reproductive effects of EDCs on wildlife with studies on the endangered Florida panther and polar bears and their prey. To date, the FWS has funded and participated in 23 studies that specifically looked at the effects of EDCs on wildlife across the country. Many of these studies have been directly associated with endangered species recovery actions or threats to the recovery of listed species. These studies typically included management recommendations for the removal of threats from contaminants or other corrective actions to alleviate the impacts of EDCs on wildlife. The USGS and FWS are continuing to work closely together to understand and address these issues.

Exposure to certain EDCs results in a variety of adverse reproductive effects in wildlife. Alterations in the differentiation, growth and function of wildlife reproductive organs can result from perinatal and neonatal exposure to EDCs. Examples of effects include smaller than normal sexual organs in male alligators, ambiguous gonads in amphibians and altered sex behavior in birds (Fry, 1995; Guillette, LJ, et al., 1995, 1996; Vos et al., 2000; Hayes et al., 2002; Milnes et al., 2005; Grove and Henny, 2008).

Results from the preliminary river otter study correlated concentrations of known EDCs with observed underdevelopment of juvenile male reproductive organs. In an expanded study, Grove (2006) found significant inverse relationships between EDC concentrations in the liver and size and mass of reproductive organs. Some of these changes appear to be carried into adulthood as a permanent effect. If the EDC-related reduction in testes size found in juvenile male river otters is permanent, then fertility could potentially be reduced as well. Regional differences existed in river otter contaminant body burdens, with otters from heavily populated and industrialized

regions, as well as from areas of intensive agriculture, having significantly higher liver concentrations of many contaminants.

While focusing on the environmental effects of EDCs, we understand that information that we provide on the occurrence of EDCs in drinking water has great value to those evaluating the human health significance of EDCs in the environment. Past USGS studies have assessed the occurrence of EDCs and other emerging contaminants in the sources of drinking water (Focazio et al., 2008) and in treated drinking water (Stackelberg et al., 2004 and 2007), and the USGS is currently working with the U.S. Environmental Protection Agency (EPA) to provide additional information on these chemicals in drinking water. Similarly, effects studies conducted on animals may also contribute to an understanding of the potential impacts on human health.

Solutions for Reducing Endocrine-Disrupting Chemicals in the Environment

Research and monitoring by the USGS and others have demonstrated that

- The manner in which we handle and dispose of our wastes can concentrate these chemicals in some environmental settings to levels that may be an ecological health concern, and
- Many of these trace organic chemicals associated with human and animal wastes have been entering the environment for as long as we have used them.

Growing public awareness has prompted significant public interest regarding potential adverse health effects and actions they can take to mitigate release of these chemicals to the environment. As a result, pharmaceutical take-back programs are emerging across the country to reduce the amount of unused drugs that are flushed down toilets to our streams. Furthermore, industries are inquiring about the treatment technologies and best management practices that are most effective at removing trace organic chemicals from surface and ground waters and solid and liquid wastes (Phillips et al., 2008; Kinney et al., 2006b). Information that we can provide on the comparative performance of alternative treatment technologies enables industries to invest resources wisely on a voluntary basis.

The FWS has taken a proactive approach for addressing potential contaminants of concern on its National Wildlife Refuges and Fish Hatchery facilities. The FWS has also joined with corporate partners to engage the public in reducing the amount of EDCs in the environment and helping everyone to become a better steward of our environment.

The FWS, along with corporate partners the American Pharmacists Association and the Pharmaceutical Research and Manufacturers of America, have taken a proactive role in reducing EDCs in the environment. In March 2008, a memorandum of understanding was signed to help protect the Nation's fish and wildlife resources from the improper disposal of unwanted medication, some of which are EDCs. FWS developed and implemented the "SMAR_xT DisposalTM" campaign to educate people on the environmental threat posed by flushing medicines down the toilet or pouring them down the drain and provided them a safer alternative

involving disposal of medications in the trash. The SMAR_xT Disposal™” campaign recommendations [see Appendix] , together with similar efforts by the White House Office of National Drug Control Policy,, EPA, FDA, and other agencies, provide the standard practice recommendation of the Federal government.

The EPA’s Endocrine Disruptor Screening Program (EDSP) is currently proceeding in three areas: (1) performing scientific and technical testing needed to validate the endocrine disruptor screens and tests; (2) setting priorities for selecting chemicals for initial screening and testing; and (3) developing the policies and procedures the Agency will use to require testing. USGS researchers are collaborating with EPA to evaluate the effectiveness of a new multigenerational assay protocol in generating data applicable to the EPA’s risk assessment modeling and to evaluate the sensitivity of the endpoints currently used for detection of EDC exposure and effect.

In April 2009, the EPA released its final list of 67 initial pesticide active and inert ingredients to be screened under the EDSP. Once fully implemented, EDSP will provide a systematic means of testing of potential EDCs found in the environment.

The USGS is working on providing technical assistance for the National Wildlife Refuge System on total maximum daily loads (TMDLs) of chemical contaminants, such as those responsible for endocrine disruption in effluent water. This technical assistance will use geospatial information and a risk assessment approach that will enable Refuges to manage water quality and reduce impacts of potential EDCs. FWS facilities have a regular maintenance schedule and annual facility assessment programs to ensure contaminants are properly disposed of and the facilities remain in an adequate state of repair. In addition, FWS has developed a contaminant assessment database for its National Wildlife Refuges to identify and address threats posed from contamination on refuges and is completing a similar database for its National Fish Hatchery System. The USGS and FWS will continue to work closely together to provide the scientific understanding and management needed to address this serious threat to our waters and wildlife.

Conclusion

The Department of the Interior, primarily through the USGS and the FWS, is continuing to conduct research and monitoring on endocrine-disrupting chemicals in the environment and other chemicals of emerging environmental concern. Research priorities include

- Identifying susceptible environmental settings by quantifying the chemical loads of various sources including wastewater treatment plants, Animal Feeding Operations, landfills, and other industrial and commercial facilities,
- Assessing ecological effects, including the extent of endocrine disruption in fish and wildlife species resulting from the mixtures and levels of contaminants found in environmental settings,
- Quantifying the occurrence of emerging contaminants in waters that are used for drinking water, and
- Providing information on the comparative performance of varying water and waste treatment processes to remove emerging contaminants.

The Department conducts this research with a number of partner Federal agencies, including the EPA, Centers for Disease Control and Prevention, and National Oceanic and Atmospheric Administration. The USGS, with EPA and FDA, co-chairs the Federal Interagency Working Group on Pharmaceuticals in the Environment, of which the FWS is a member. This working group is under the auspices of the National Science and Technology Council. This working group has further increased coordination of Federal research.

We welcome the opportunity to provide any further information or assistance to the Subcommittee as you investigate this important issue. Thank you, Madam Chairwoman, for the opportunity to present this testimony, and I will be pleased to answer questions you and other Members might have.

For more information

Alvarez et al., 2009, Reproductive health of bass in the Potomac, USA, drainage: Part 2. Seasonal occurrence of persistent and emerging organic contaminants: *Environmental Toxicology and Chemistry*, v. 28, no. 5, p. 1084–1095.

Ankley, GT, *et al.*, 2009, Endocrine disrupting chemicals in fish: Developing exposure indicators and predictive models of effects based on mechanism of action: *Aquatic Toxicology* v. 92, p. 168–178.

Beldomenico, PM, *et al.*, 2007, *In ovum* exposure to pesticides increases the egg weight loss and decreases hatchlings weight of *Caiman latirostris* (Crocodylia: Alligatoridae): *Ecotoxicology and Environmental Safety*, v. 68, issue 2, p. 246-251.

Blazer VS, *et al.*, 2007, Intersex (testicular oocytes) in smallmouth bass from the Potomac River and selected nearby drainages: *Journal of Aquatic Animal Health*, v. 19, no. 4, p. 242-253, doi:10:1577/H07-031.1.

Brian JV, *et al.*, 2005, Accurate prediction of the response of freshwater fish to a mixture of estrogenic chemicals: *Environmental Health Perspectives*, v. 113, p. 721-728.

Brian JV, *et al.*, 2007, Evidence of estrogenic mixture effects on the reproductive performance of fish: *Environmental Science and Technology*, v. 41, no. 1, p. 337-344.

Brown, KH, Schultz, IR, and Nagler, JJ, 2009, Lack of a heritable reproductive defect in the offspring of male rainbow trout exposed to the environmental estrogen 17 α -ethynylestradiol: *Aquatic Toxicology*, v. 91, p. 71–74.

Cai, Xiao-Quan, *et al.*, 2009, Humoral immune response suppresses reproductive physiology in male Brandt's voles (*Lasiopodomys brandtii*): *Zoology*, v. 112, p. 69–75.

Colborn, T, and Clement, C, 1992, *Advances in Modern Environmental Toxicology, Vol. 21*; Mehlman, M. A., Ed.; Princeton Scientific Publishing Company Inc: Princeton, NJ.

- Conn, KE, *et al.*, 2006, Occurrence and fate of organic contaminants during onsite wastewater treatment: *Environmental Science and Technology*, 40, no. 23, p. 7358-7366.
- Cooper, R. L.; Kavlock, R. J., 1997, *Journal of Endocrinology*. v. 152, p. 159-166.
- Davis, LK, *et al.*, 2009, Effects of o,p'-DDE, heptachlor, and 17 β -estradiol on vitellogenin gene expression and the growth hormone/insulin-like growth factor-I axis in the tilapia, *Oreochromis mossambicus*: *Comparative Biochemistry and Physiology*, part C 149, p. 507–514.
- Dorts, Jennifer, *et al.*, 2009, The genomic transcriptional response of female fathead minnows (*Pimephales promelas*) to an acute exposure to the androgen, 17 β -trenbolone: *Aquatic Toxicology*, v. 91, p. 44–53.
- Durhan, EJ, *et al.*, 2006. Identification of metabolites of trenbolone acetate in androgenic runoff from a beef feedlot: *Environmental Health Perspectives*, v. 114, Suppl.1: p. 65-68.
- Focazio, MJ, *et al.*, 2008, A national reconnaissance for pharmaceuticals and other organic wastewater contaminants in the United States: II) Untreated drinking water sources: *Science of the Total Environment*, v.402, p. 201-216.
- Fry, DM, 1995, Reproductive effects in birds exposed to pesticides and industrial chemicals: *Environmental Health Perspectives*, v. 103 (Supplement 7), p. 165-171.
- Glassmeyer, ST, *et al.*, 2005, Transport of chemical and microbial compounds from known wastewater discharges: Potential for use as indicators of human fecal contamination. *Environmental Science and Technology*, v. 39, no.14, p. 5157-5169.
- Goodbred, SL., *et al.*, 1996, Reconnaissance of 17 β -estradiol, 11-ketotestosterone, vitellogenin, and gonad histopathology in common carp of United States streams: Potential for contaminant-induced endocrine disruption: U.S. Geological Survey Open-File Report 96-627, 47 p.
- Grove, RA., 2006, Environmental contaminants in male river otters collected from Oregon and Washington, 1994-99, with reproductive organ hypoplasia observed in otter males: Corvallis, Oregon State University, Ph.D. dissertation, 335 p.
- Grove, RA, and Henny, CJ, 2008, Environmental contaminants in male river otters from Oregon and Washington, USA, 1994-1999: *Environmental Monitoring and Assessment*, v. 145, p. 49-73.
- Guillette, LJ, *et al.*, 1996, Reduction in penis size and plasma testosterone concentrations in juvenile alligators living in a contaminated environment: *General and Comparative Endocrinology*, v. 101, p. 32-42.
- Guillette, LJ, *et al.*, 1995, Gonadal steroidogenesis in vitro from juvenile alligators obtained from contaminated or control lakes: *Environmental Health Perspectives*, v. 103 (Supplement 4), p. 31-36.

Iwanowicz et al., 2009, Reproductive health of bass in the Potomac, USA, drainage: Part 1. Exploring the effects of proximity to wastewater treatment plant discharge: *Environmental Toxicology and Chemistry*, v. 28, no. 5, p. 1072–1083.

Jin, Yuanxiang, *et al.*, 2009, Photoperiod and temperature influence endocrine disruptive chemical-mediated effects in male adult zebrafish: *Aquatic Toxicology*, v. 92, p. 38-43.

Kidd, KA, *et al.*, 2007, Collapse of a fish population after exposure to a synthetic estrogen. *Proceedings of the National Academy of Sciences*, v. 104, p. 8897-8901.
<http://www.pnas.org/content/104/21/8897.full>

Kinney, CA, *et al.*, 2006a, Presence and distribution of wastewater-derived pharmaceuticals in soil irrigated with reclaimed water. *Environmental Toxicology and Chemistry*, v. 25, p. 317-326.
<http://pubs.acs.org/cgi-bin/abstract.cgi/esthag/2008/42/i06/abs/es702304c.html>

Kinney, CA, *et al.*, 2006b, Survey of organic wastewater contaminants in biosolids destined for land application. *Environmental Science and Technology*, v. 40, p. 7207-7215.
<http://www.setacjournals.org/perlserv/?request=get-abstract&doi=10.1897%2F05-187R.1>

Kinney, CA, *et al.*, 2008, Bioaccumulation of pharmaceuticals and other anthropogenic waste indicators in earthworms from agricultural soil amended with biosolid or swine manure. *Environmental Science and Technology*, v. 42, no. 6, p. 1863–1870.
<http://pubs.acs.org/cgi-bin/abstract.cgi/esthag/2006/40/i23/abs/es0603406.html>

Kolpin, DW, *et al.*, 2002, Pharmaceuticals, hormones, and other organic wastewater contaminants in US streams, 1999-2000: A national reconnaissance. *Environmental Science and Technology*, v. 36, p. 1202-1211. http://pubs.acs.org/hotartcl/est/es011055j_rev.html

Lee, KE, *et al.*, 2008, Alkylphenols, other endocrine-active chemicals, and fish responses in three streams in Minnesota—Study design and data, February-September 2007: U.S. Geological Survey Data Series 405, 44 p (plus appendixes).

Lee, KE, *et al.*, 2008, Occurrence of endocrine active compounds and biological responses in the Mississippi River—Study design and data, June through August 2006: U.S. Geological Survey Data Series 368, 27 p (plus appendix).

McGee, MR, *et al.*, 2009, Predator avoidance performance of larval fathead minnows (*Pimephales promelas*) following short-term exposure to estrogen mixtures: *Aquatic Toxicology*, v. 91, p. 355-361.

McLachlan, J A, 1980 *Estrgens in the environment*; Elsevier: New York.

McLachlan, J A, 1985 *Estrogens in the environment II*, Elsevier: New York.

Milnes, MR, and Guillette, LJ, Jr., 2008, Alligator tales: New lessons about environmental contaminants from a sentinel species: *BioScience*, December 2008, v. 58, no. 11, p. 1027-1036.

- Newbold, R. R. 1999. Diethylstilbestrol (DES) and environmental estrogens influence the developing female reproductive system. In R. K. Naz (ed.), *Endocrine disruptors*, pp. 39–55. CRC Press, Boca Raton, FL.
- Oehlmann, J, and Schulte-Oehlmann, U, 2003, Endocrine disruption in invertebrates: *Pure and Applied Chemistry*, v. 75, no. 11-12, p. 2207–2218.
- Papoulias, DM, Chapman, D, and Tillitt, DE, 2006, Reproductive condition and occurrence of intersex in bighead carp and silver carp in the Missouri River: *Hydrobiologia*, v. 571, p. 355-360.
- Phillips, PJ, *et al.*, 2008, A multi-disciplinary approach to the removal of emerging contaminants in municipal wastewater treatment plants in New York State, 2003-2004: *Clearwaters*, v. 38, no. 3, p. 48-59.
- Richter, CA, *et al.*, 2007, *In vivo* effects of bisphenol A in laboratory rodent studies: *Reproductive Toxicology*, v. 24, no. 2, p. 199-224, doi10.1016/j.reprotox.2007.06.004.
- Ripley, Jennifer, *et al.*, 2008, Utilization of protein expression profiles as indicators of environmental impairment of smallmouth bass (*Micropterus dolomieu*) from the Shenandoah River, Virginia, USA: *Environmental Toxicology and Chemistry*, v. 27, no. 8, p. 1756-1767, doi:10.1897/07-588.1.
- Robertson, LS, Iwanowicz, LR, and Marranca, JM, 2009, Identification of centrarchid hepcidins and evidence that 17 β -estradiol disrupts constitutive expression of hepcidin-1 and inducible expression of hepcidin-2 in largemouth bass (*Micropterus salmoides*): *Fish and Shellfish Immunology*, v. 26, no. 6, p. 898-907.
- Rosen, MR, *et al.*, 2006, Investigations of the effects of synthetic chemicals on the endocrine system of common carp in Lake Mead, Nevada and Arizona: U.S. Geological Survey Fact Sheet 2006-3131, 4 p.
- Stackelberg, PE, *et al.*, 2007, Efficiency of conventional drinking-water-treatment processes in removal of pharmaceuticals and other organic compounds: *Science of the Total Environment*, v. 377, no. 2-3, p. 255-272.
- Stackelberg, PE, *et al.*, 2004, Persistence of pharmaceutical compounds and other organic wastewater contaminants in a conventional drinking-water-treatment plant: *Science of the Total Environment*, v. 329, no. 1-3, p. 99-113.
- USEPA, Land application of biosolids containing EDCs, http://www.epa.gov/nrmrl/EDC/projects/edc_biosolids.htm, Accessed June 8, 2009.
- Vajda, AM, *et al.*, 2008, Reproductive disruption in fish downstream of an estrogenic wastewater effluent: *Environmental Science and Technology*, v. 42, no. 9, p. 3,407-3,414, doi:10.1021/es0720661.

Vos, JG, et al., 2000, Health effects of endocrine-disrupting chemicals on wildlife, with special reference to the European situation: *Critical Reviews in Toxicology*, v. 30, p. 71-133.

Wrobel, Michal, Mlynarczuk, Jaroslaw, and Kotwica, Jan, 2009, The adverse effect of dichlorodiphenyltrichloroethane (DDT) and its metabolite (DDE) on the secretion of prostaglandins and oxytocin in bovine cultured ovarian and endometrial cells: *Reproductive Toxicology*, v. 27, p. 72–78.

Zhao, Jian-Liang, 2009, Determination of phenolic endocrine disrupting chemicals and acidic pharmaceuticals in surface water of the Pearl Rivers in South China by gas chromatography–negative chemical ionization–mass spectrometry: *Science of the Total Environment*, v. 407, p. 962–974.

Appendix

Using the simple SMARTSMAR_xT Disposal™ steps, people can easily understand and implement the campaign. The SMART SMAR_xT Disposal™ steps include the following:

- 1) Check for and use if available approved state and local unwanted medication collection programs.
- 2) Do not flush* unused medications or pour them down a sink or drain.
- 3) To dispose of unused medication in household trash and ensure that children and pets are not exposed to these chemicals:
 - a) Put medication into a sealable plastic bag.
 - b) Add water to dissolve it.
 - c) Add to the bag kitty litter, sawdust, coffee grounds or any other material that mixes with the medication and makes it less appealing for pets and children.
 - d) Seal the bag and put it in the trash.
 - e) Remove and destroy all identifying personal information, such as prescription labels, from medication containers and dispose of them in the trash.

* By law, certain specifically regulated and labeled medications have to be flushed down the drain.

The supporters of our the campaign are numerous and span national and international audiences. Some of the supporters include the following: AARP, American Nurses Association, DARE America, Johnson & Johnson, National Ground Water Association, Rite Aid Pharmacy, Safeway Food and Drug, Shawnee Preservation Society Veterans Against Drugs Program, and Virginia Department of Environmental Quality.