"Pharmaceuticals as Emerging Contaminants:
A Rationale for Reduction in New York State's Waters"

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Authors' Note - This technical document provides background and support for an effort to reduce the flushing of unused pharmaceuticals, and more broadly outlines the concerns about both pharmaceuticals and personal care products in our waters. It also includes discussion of additional measures to address this issue in the future.

Background - Pharmaceuticals in our Waters

Pharmaceuticals have almost certainly been in the state's - and nation's - waters since people began manufacturing and taking medicines. Along with personal care products, pharmaceuticals are just part of the universe of "emerging contaminants" that are attracting media and government attention.

As analytical methods improve, the environmental occurrence of a broadening range of pharmaceuticals and personal care products (PPCPs) has been acknowledged. Although much is yet to be understood about long-term, low-level exposure, a growing body of evidence suggests there are a variety of potential environmental and health effects. While pharmaceuticals are only one group of emerging contaminants, the potential risks they pose to human and aquatic life necessitates early action. As a precautionary measure, programs to divert pharmaceuticals from our wastewater stream are an essential part of the solution. In the longer term, improved methods of treating wastewaters will also be needed.

Of the approximately 30 million chemical compounds that have been identified to date, nearly half are commercially available. More and more are being added each year, yet only a fraction are monitored or regulated. New York, a leader among states in water protection programs, has established ambient water quality standards for several hundred chemicals. New York State Department of Health (NYSDOH) drinking water standards do have a 50 ppb limit for unspecified organic contaminants. PPCPs, however, are rarely tested for at the low levels that may be present in water and wastewater.

Pharmaceuticals are designed to have a biologic consequence. They are intended to cause some effect in the living organism. They may also be resistant to some forms of degradation, in order to retain their biological activity through manufacture, shipping, storage, and retail distribution. Significant portions of some drugs pass through the body unchanged, or are metabolized to a different biologically active substance. These substances may be excreted unchanged, conjugated, or metabolized, and enter municipal waste water (i.e., sewage) treatment plants (WWTPs) which are not specifically designed to treat them. The removal efficiency of a WWTP will vary based on its treatment processes and the characteristics of the chemical in question.

Numerous studies have clearly demonstrated the occurrence of PPCPs in streams receiving WWTP effluents. These come from the myriad of individual consumers of medicines (via drugs that pass through the body as well as flushing of unused or expired products) and from specific sources such as hospitals, nursing homes, and pharmaceutical manufacturing facilities.

PPCPs may also be detected in leachate from landfills that have received PPCPs for disposal and/or biosolids from a wastewater treatment plant. While modern landfills are designed to collect the leachate generated, the leachate is typically taken to a wastewater treatment plant where release of PPCPs could potentially occur.

The land application of biosolids is another potential pathway for PPCPs to enter the environment. Furthermore, the land application of animal manure may also contribute to PPCPs entering the environment from veterinary drugs used to treat farm animals and cleaning agents used at a farm. Septic tank effluent may also contain PPCPs which could be discharged to the environment through leachfields.

Synopsis of U.S. Environmental Protection Agency's Efforts

The U.S. EPA's strategy is to 1) strengthen scientific knowledge through several projects where data are being collected on occurrences of pharmaceuticals in various media (water, fish tissue, biosolids); 2) improve public understanding and risk communication; 3) build partnerships through stewardship; and 4) utilize its regulatory tools when warranted. The EPA considers collaboration with the states and stakeholders to be a key component during this process. A series of meetings was recently held with states, environmental groups and water organizations to discuss how to effectively work together. The White House Committee on the Environment and Natural Resources organized a federal interagency workgroup, co-chaired by EPA, FDA and USGS, on Pharmaceuticals in the Environment to develop a federal research strategy.

Potential Concerns for Human Health and Aquatic Life

Although the human health effects of the *intended uses* of pharmaceuticals are well known, the effects on humans and aquatic life from these chemicals at low levels in water are not well characterized. While the U.S. Environmental Protection Agency has stated that "to date, scientists have found no evidence of adverse human health effects from PPCPs in the environment," it is clear additional research is necessary.

Human Health

A number of health concerns (*e.g.,* microbial antibiotic resistance, endocrine disruption, psychotropic action) have been raised about the presence of pharmaceuticals in water bodies used as drinking water sources. The majority of environmental research has focused on testing sewage treatment plant influent and effluent, receiving waterways downstream of agricultural and/or industrial facilities, and water sources for drinking water.

Tests have looked at different classes of pharmaceuticals, and at different representative compounds from various pharmaceutical classes. Not all compounds or pharmaceutical classes have been tested for, and the presence of some compounds at a single test point can vary with time and season. When detected, concentrations of pharmaceuticals in water are generally reported to be low (i.e., in the nanogram to low microgram per liter range; part per trillion or part per billion respectively).

Concerns about pharmaceuticals as contaminants include, but are not limited to, the following:

- the presence of antibiotics based on finding increased levels of antibiotic resistance in bacteria living in waters where large amounts of antibiotics or antibiotic wastes are discharged from hospitals, pharmaceutical manufacturing facilities and fish farms. Some evidence suggests antibiotic resistant bacteria are also more prevalent downstream of urban sewage treatment plant discharges.

- the presence of endocrine-disrupting pharmaceuticals due to the detection of low concentrations of synthetic steroids (e.g., estrogens) downstream of a sewage treatment plant that are suspected to be a cause of feminization in male fish. Detecting potential human health impacts associated with the presence of low levels of endocrine-disrupting pharmaceuticals in drinking water may be difficult. Even at potentially vulnerable developmental stages, low levels of estrogenic compounds in drinking water may not alter naturally occurring internal levels associated with routine physiological fluctuations, and which vary with sex, age and reproductive status.

- the presence of psychotropic drugs, such as anticonvulsants and antidepressants, due to discovery in low concentrations in receiving waters from sewage treatment plants. A specific concern has been raised for the anticonvulsant *carbamazepine* which is excreted unchanged, is resistant to environmental degradation, and was detected (< 1 microgram per liter) in one study of finished drinking water (Stackleberg et al. 2004).

In general, for all categories of pharmaceuticals, the concentrations detected in drinking water sources (ppb or ppt) are well below levels associated with human health effects, and there is very limited information on levels of specific pharmaceuticals in finished drinking water. Additionally, pharmaceuticals are not likely to be bioaccumulated by humans from drinking water, so exposure to low levels over longer periods of time is not anticipated to produce health effects.

We found only one scientific study that measured pharmaceuticals in finished drinking water from a single water treatment plant in the United States (Stackleberg et al. 2004). In that study, only four pharmaceuticals were detected (*caffeine, carbamazepine, cotinine and dihydronefedipine*) out of forty-seven that were measured. The scarcity of data regarding the prevalence of specific pharmaceuticals in finished drinking water makes assessment of the potential for human health effects uncertain.

Aquatic Life

The risk to aquatic life from PPCPs in water is perhaps of greater immediate concern. Fish, other aquatic animals, and invertebrates are exposed continuously to contaminants in water throughout their life including sensitive, developmental life stages. Some PPCPs with certain chemical characteristics (i.e., low water solubility, lipophilic, and resistant to biodegradation) might be bioaccumulated from very low concentrations in water to concentrations in fish tissue capable of stimulating a biological response. PPCPs that are capable of mimicking hormones, known as endocrine-disruptors, are particularly problematic because hormone systems function at very low concentrations. Many different hormone systems could potentially be impacted by PPCPs, but harmful impacts to fish reproduction have already been attributed to wastewater-derived contaminants (including PPCPs, pesticides, and industrial chemicals) that mimic the hormone estrogen.

In England, both caged and wild fish exposed to effluent discharges from sewage treatment plants showed responses attributable to estrogen exposure for several kilometers downstream. In some United Kingdom rivers, widespread "feminization" has been demonstrated in the roach (a fish, *Rutilus rutilus*) with a clearly established correlation to exposure from sewage treatment effluent. A second study found feminization of a second species of wild fish, the gudgeon (*Gobio gobio*), in those same rivers. Indicators of feminization included: induction of vitellogenin (a female-specific yolk protein precursor), intersexual gonads (containing both male and female tissue), and/or aberrant (female-like) reproductive ducts in male fish (Rodgers-Gray, et al. 2000).

In Florida, effluents from paper mills discharging kraft mill effluent have been suspected of causing just the opposite effect, that is, the "masculinization" of female mosquitofish (*Gambusia affinis*) (Bortone and Davis 1994). Impacts of this type clearly have the potential to be manifested by reduced reproductive success exposed populations of fish species.

In the city of Boulder, Colorado, white suckers (*Catostomus commersoni*) were collected from immediately upstream and downstream of the WWTP outfall in the fall of 2003 and the spring of 2004. Gonadal intersex (having both male and female sex organs), altered sex ratios, reduced gonad size, disrupted ovarian and testicular histopathology, and vitellogenin induction consistent with exposure to estrogenic wastewater contaminants were identified in white suckers downstream from the WWTP outfall, but not in those located at the upstream site. In addition, while the sex ratio was female-biased at the effluent site the frequency of males (17–21%) was half that of the upstream site (36–46%). Intersex white suckers comprised 18–22% of the population at the effluent site but no intersex fish were found at the upstream site. Chemical analyses determined that the WWTP effluent contained a complex mixture of endocrine-active chemicals, including 17β-estradiol (E2) 17α-ethynylestradiol, alkylphenols, and bisphenol A.

Specific Studies on Levels of Pharmaceuticals in Waters

The presence of pharmaceuticals in our waters is an *emerging issue* meaning that it has come to light relatively recently as analytical detection methods have improved and researchers have begun looking for these compounds. In 2002, the U.S. Geological Survey (USGS) published a seminal paper (Kolpin et al.), and along with the Environmental Protection Agency (EPA) are currently conducting major studies. The EPA has begun monitoring about 40 pharmaceuticals in an effort to target those that are present in discharges most often and pose the highest risk.

Closer to home, the NYSDOH in conjunction with the New York City Department of Environmental Protection (DEP) has conducted research in the NYC Watershed. The NYSDOH work indicated that although some target pharmaceuticals were consistently detected in WWTP effluent, they were not consistently detected in the reservoir system. When they were detected, the target pharmaceuticals were far below any levels that have been demonstrated to be associated with human health effects.

Additionally, within New York State, the USGS has conducted a study to investigate the environmental occurrence of 12 selected pharmaceuticals, which represent some of the most commonly prescribed medications, in wastewater and streams. This study tentatively identified the occurrence of additional pharmaceuticals that may be present in wastewater discharges. The USGS study also assessed the potential for pharmaceutical manufacturing facilities to affect concentrations in WWTP effluents and to evaluate the removal of these compounds during treatment at the WWTP. This study, which compared influent and effluent concentrations of these pharmaceuticals, indicated that the concentrations of drugs at WWTPs receiving waste from pharmaceutical manufacturing facilities are much higher than those reported in the literature for other non-industrial WWTP effluents. Furthermore, the USGS study indicated that effluent concentrations at New York's WWTPs receiving domestic sewage are similar to effluent concentrations in the national network database.

The USGS study also identified pharmaceuticals in streams receiving wastewater. As expected, the levels identified were a function of effluent concentration and proportion of discharge to streamflow. The USGS work did not include an assessment of the fate of these compounds in the aquatic environment. The presence of these compounds suggests that the potential effects on aquatic organisms warrant further investigation.

Regulation of Discharge

New York State regulates WWTPs through State Pollutant Discharge Elimination System (SPDES) permits that limit the quantity of a specific pollutant that may be discharged. These limits are typically based on preventing a water quality standard (which is derived to protect the best uses of a particular waterbody), from being exceeded in the receiving water.

Pharmaceuticals and related contaminants present a complicated situation for permitting

because most do not have standards and are not monitored. Development of standards may not be practical at this time due to a lack of resources and, in some cases, necessary tools to derive standards for individual chemicals. An interim model similar to the NYSDOH's unspecified organic contaminant limit for drinking water (50 ppb) could be used. Particularly for aquatic life, existing procedures are not fully adequate to capture the subtle effects of PPCPs. The EPA is working on revisions that New York will be able to use in the future.

Within the NYC Watershed, a study by USGS evaluated the removal of these compounds during treatment at the WWTP through the various components at the facility. In many instances, the WWTP did not affect the levels in the discharge. It is important to note that WWTPs in the NYC Watershed employ a significant level of treatment, including microfiltration after tertiary treatment, and yet, some compounds were still detected.

Steps to Minimize Risks - General Considerations

1. Avoid the disposal of pharmaceuticals into waste water systems

   While the precise risk of pharmaceuticals in our water ways has not yet been defined, there is sufficient evidence to support a precautionary approach. Such an approach dictates that we work to exclude pharmaceuticals from the wastewater system to the extent possible. As such, the NYS DEC recommends that households and individuals immediately cease the practice of disposing of unused medications by flushing or otherwise discharging them into the wastewater system. Recommendations for disposal are included on the DEC website.

   The Department is working with the Department of Health and other state agencies to develop alternative disposal methods for pharmaceutical waste generated at hospitals, nursing homes, and other institutions to reduce or eliminate the practice of flushing at these facilities.

2. Research on Health and Ecological Effects

   Further studies on health and ecological effects of PPCPs are needed to determine what levels in the water, including both drinking water sources and downstream of WWTPs, may cause risk to human health and/or aquatic life.

3. Better Understanding of Fate & Transport

   A significant component of future research will require enhanced monitoring of the environment. In addition to continued monitoring of those compounds currently identified in WWTP discharges, monitoring for the wide variety of hormones, including estrogen and androgens, is needed so that correlations can be established between the two sets of organic data.

   To date, monitoring has focused on identifying compounds in WWTP discharges and quantifying the levels in the receiving stream and downstream reservoirs. An

appraisal is needed of the spatial extent to which fish in waters of New York State might be affected by PPCPs, natural and synthetic hormones from WWTPs. Additional information on fate and transport of PPCPs could better characterize the potential threat that these hormones may pose to local fish communities and to public drinking water supplies.

4. Regulating Discharges

The risks that pharmaceuticals and personal care products in our waters pose are not fully characterized, and very difficult to address. Additional monitoring of waste water treatment effluent, and better understanding of the capacities of different types of treatment systems to reduce the concentrations of these substances in WWTP discharge, are needed. Results from an ongoing EPA study that involves sampling of influent, effluent, and sludge for more than 150 pharmaceuticals, pesticides, and steroids/hormones, expected to be completed in 2009, should be a major step forward in this area.

Another potential approach to regulate discharges might be to utilize whole effluent toxicity (WET) testing requirements within SPDES permits. The intent of toxicity testing, which is employed when ambient water quality standards do not exist, is to ensure that no chemicals are discharged to surface waters in amounts that are toxic to aquatic life. It is important to note that toxicity testing does not address bioaccumulation or evaluate effects of chronic low-level exposure. It also does not assure the protection of water as a drinking water supply.

A further option would be to include additional industrial pretreatment requirements within SPDES permits for waste water treatment facilities that have pharmaceutical manufacturing facilities tributary to the treatment plant. This method would require the reduction of pharmaceuticals at the source rather than necessitating additional treatment at the WWTP.

As noted above, significant portions of some pharmaceuticals can pass through the body unchanged, or changed to a different biologically active substance, and then enter a WWTP that is not designed to remove them. Current studies indicate that the removal efficiency of a WWTP will vary based on its treatment process and the characteristics of the compound in question. Further research is needed to determine which kinds of treatment are most effective at removing pharmaceuticals and then develop strategies to implement and improve upon those processes.

5. Pollution Prevention

Many drugs remain biologically active as they are naturally excreted through the human body. Drug companies could be encouraged to develop “greener” drugs that would: (a) generate less waste when they are manufactured; and, (b) lose their potency after passing through the body. The collective efforts of many states and the Federal government would likely be required to achieve these significant changes.

6. Precautionary Approach to Regulate Manufacturers

   Too often, information on the effects of a potential contaminant, as well as action to address it, has not come until after it has been widely used and discharged. Although significant testing is already required for new pharmaceuticals, these requirements could be expanded to better identify the long-term effects from low-level exposure on both humans and aquatic life.

Specific Actions Undertaken by NYSDEC

- NYSDEC established an interdisciplinary work group on pharmaceuticals which includes experts from the Divisions of Water, Solid and Hazardous Materials, Legal, Public Affairs, and Policy programs, and the Department of Health.

- NYSDEC and the NYSDOH co-sponsored a successful Roundtable Discussion (*Managing Unused Pharmaceuticals in New York State - May 15, 2008*) which included panel discussions on pharmaceutical waste issues related to both households and institutions. [A record of proceedings from the roundtable will be made available at DEC's webpage: www.dec.ny.gov]

- DEC is participating in the New England Interstate Water Pollution Control Commission (NEIWPCC) work group on PPCPs which will help foster interstate communication, track and disseminate scientific information, develop regional policy positions, and comment on EPA regulatory developments.

- DEC Commissioner Grannis sent a letter to EPA's Assistant Administrator for Water, Benjamin Grumbles, regarding the need for action at the federal level. (A copy of this letter is available at www.dec.ny.gov)

- NYS DEC is also a member of the Product Stewardship Institute (www.productstewardship.us). Through that organization, DEC intends to participate in a stakeholder dialogue with the aim of developing a product stewardship system for managing unused pharmaceuticals.

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