Pharmaceutical Dispensing and Wasting In Health Care Facilities, Amounts, Costs and Evaluation of Potential Ecologic Effects

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Abstract

Drug waste from hospitals contributes to environmental contamination. Patient excreta, bathing or discarding of excess drugs are some sources of drug waste. We report on the wasting of 84 drugs of 14 therapeutic classes in two hospitals in Albany, NY. We consider drug metabolism, excretion, disposal and ecotoxicity in strategies for reducing drug waste, costs and potential environmental damage.

Medication (12,345) and waste collection (199) records for: drugs dispensed, returned and wasted were examined. Of 2,700 drugs available, 84 drugs from 14 classes, weighing 56 kg were dispensed to patients, and 2.3 kg were wasted. Twelve drugs accounted for 80 percent of the drug waste and cost \$111,000. Of the top wasted and dispensed drugs, all but ibuprofen are persistent and none were bioaccumulative. Ibuprofen, ipratropium, ondansetron and oxymetazoline are "very highly toxic" or "highly toxic". Environmental Risk Ratio (PEC/PNEC) for the 20 top drugs were "Insignificant" or "Cannot Be Excluded".

Acetazolamide is the most toxic to fish. Dexamethasone has the greatest chronic toxicity to Ceriodaphnia. Ibuprofen is predicted to be very highly toxic (acute and chronic) to zebra mussel, crab and fish. Neostigmine is the most acutely toxic (LC50 < 1 mg/L) to Daphnia. Ondansetron is the most acutely toxic to green algae. All but 2 of the drugs were 5 to 100% excreted. Fourteen were metabolized. Active metabolites were formed from 2 drugs. Nicardipine, ondansetron and prednisone formed drug conjugates which were excreted. Incineration was the manufacturer's recommended disposal method.

We recommend excess drugs be returned to the hospital pharmacy for disposal by incineration. Drug use and disposal should be monitored by an expert committee according to recognized guidelines of pharmaceutical management. Knowledge of the adverse impacts from the release of highly toxic drugs into the environment must influence drug selection and disposal.

Key words: Waste; Ecotoxicity; Wastewater;

Abbreviations

AMCH = Academic Medical Center Hospital; ASTER = Assessment Tools for the Evaluation of Risk. United States Environmental Protection Agency https://archive.epa.gov/med/med_archive_03/web/html/aster.html Last accessed 6/4/17; B = Bioaccumulation is the general term describing a process by which chemicals are taken up by an organism either directly from exposure to a contaminated medium or by consumption of food containing the chemical; EC50 = Effective Concentration producing an adverse effect in 50% of a test species; EbC50 or ErC50 = EC50 in terms of reduction of growth rate; EyC50 = EC50 in terms of change in biomass yield; Ecosar = Ecologic Structure Activity Relationships is a computerized predictive system that estimates aquatic toxicity. The program estimates a chemical's acute (short-term) toxicity and chronic (long-term or delayed) toxicity to aquatic organisms such as fish, invertebrates, and plants by using computerized Structure Activity Relationships (SARs). <https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecostar-predictive-model>. Last accessed 6/4/17; EPA = United States Environmental Protection Agency; FDA = United States Food and Drug Administration; IC50 = Half maximal inhibitory concentration is a measure of the effectiveness of a substance in inhibiting a specific biological or biochemical function; LC50 = Lethal Concentration producing 50% mortality in test species; MIC = Minimum Inhibitory Concentration is the lowest concentration of an antimicrobial that will inhibit the visible growth of a microorganism after overnight incubation; MSDS = Material Safety Data Sheet. Since 2009, known as SDS or Safety Data Sheet; Neutral Organics QSAR = Subset of chemicals within Ecosar Suite; OECD = Organization for Economic Cooperation and Development; P = Persistence is the length of time a substance resides in

the environment; PBT = Persistence, Bioaccumulation, Toxicity index; PEC = Predicted Environmental Concentration; PNEC = Predicted No Effect Concentration, highest concentration of a substance that does not have a harmful effect in the environment; PNN = Probabilistic Neural Network modeling; QSAR = Quantitative Structure Activity Relationship; REACH = Registration, Evaluation and Authorization of Chemicals legislation of the European Union; SAR = Structure Activity Relationship; SCC = Surgical Care Center; STP = Sewage Treatment Plant; T or iT = Toxicity or Inherent Toxicity is the hazard a substance presents to the environment or human health;

Highlights

1. This extends our reports on drug waste practices at two hospitals in Albany, NY.
2. 84 drugs from 14 therapeutic classes weighing 56 kg were dispensed to patients.
3. Twelve drugs accounted for 80 percent of the drug waste (2.3 kg) and cost an estimated \$111,000.
4. Of the drugs, all but ibuprofen are persistent and none are bioaccumulative.
5. Four drugs are toxic (EC50 or LC50<1.0 mg/L) to invertebrates, two (acetazolamide, ibuprofen) to fish and two to green algae (ondansetron) or duckweed (ibuprofen).
6. Drug waste should be returned to the pharmacy or reverse distributors for incineration.

Introduction

Pharmaceutical and personal care product (PPCP) waste is an emerging environmental concern. Low levels of antibiotics, anti-inflammatory, endocrine disruptors, psychotropics and mood altering drugs and X-ray contrast media have been detected in surface waters, soils, wastewaters and in drinking water sources of major cities, both within the USA and worldwide [1-4]. Recent reviews have described the occurrence and possible effects of drug residues in tissues of aquatic organisms and wildlife [5-7]. Pharmaceuticals are introduced into the aquatic environment from a variety of sources, such as: hospitals [2, 8-12]; wastewater treatment plants [13-16]; drug manufacturers [17-19]; livestock farms [20-22]; and veterinary facilities [23, 24].

Hospitals and patient care facilities are major dispensers of pharmaceuticals [12, 25] with a number of studies and reviews evaluating hospital drug dispensing patterns and estimations of sewage outflow concentrations [12]. These have led to conflicting conclusions as to the magnitude of this pollution discharge relative to other non-hospital based activities. Disposal of drugs by hospitals and healthcare facilities into the environment by flushing is a concern [26, 27] and this practice needs to be reconsidered or discontinued [20, 28-29]. For the general public and other unregistered end users of prescription medications, the U.S. Food and Drug Administration (FDA) has provided guidelines for disposal of excess medications. These guidelines do not apply to hospitals, pharmacies and other facilities registered with the U.S. Drug Enforcement Administration (DEA) or State regulatory authorities (for a review of the legal complexities refer to Yeh [31]). The US Environmental Protection Agency (EPA) has

proposed a change to hazardous waste regulations which ban the flushing of hazardous waste pharmaceuticals and discourages the flushing of non-regulated drugs.

In addition to direct disposal of excess pharmaceuticals (e.g., discarding or wasting), up to 100% of some drugs are directly excreted by patients [32]. Others may undergo significant metabolism to inactive compounds or to other active drugs prior to excretion [33-35]. Some drugs undergo conjugation in the body to enhance water solubility [36-38]. These conjugates may be recirculated either within the body (enterohepatic recirculation) or outside the body where the conjugates are cleaved by bacteria to reconstitute the active drug [34, 39]. Bathing and laundry effluents have also been proposed as pathways for the introduction of pharmaceuticals into the environment [40-42].

Investigations to assess whether drugs in drinking water adversely impact human health are continuing [43-45]. Direct relationships between the low levels of pharmaceuticals identified in drinking water and adverse impacts to human health are not being observed at this time [46, 47]. However, numerous laboratory studies [48-56] and literature reviews [57-59] have demonstrated the negative impacts of drugs to aquatic organisms.

Sewage treatment plants (STPs) are not designed to remove most pharmaceuticals [60-62] and biodegradability tests have shown that many drugs are not totally removed during sewage treatment [63]. As a result, many pharmaceuticals remain in raw sewage or are only partially removed [61, 64-65]. Pharmaceuticals released from STPs flow into receiving waters, such as streams and rivers [20, 61, 66]. Studies conducted on water quality in various countries have detected a number of antibiotics (Ab) in the low µg/L or parts per billion ranges. For example in Korea, over 95% of the Ab in the influent to a livestock wastewater treatment plant was present in the effluent [67]. Laboratory analysis of water samples collected at the influent and effluent of STPs confirms that they are a primary source of pharmaceuticals, which originate from disposal or excretion [15, 68-70].

In prior publications [71-73] the patterns of wasting and potential environmental effects of propofol and other surgical drugs (e.g., lidocaine, succinylcholine, bupivacaine, ephedrine, epinephrine, atracurium, proparacaine and atropine) were reported from a surgical care center in Albany, NY. Of interest was how a small change in availability (e.g., removal of 50 and 100 mL vials of propofol from automated dispensing machines in the operating rooms) reduced propofol wastage from 29.2 to 2.8 mL for each waste receptacle per day [71]. In a second communication [72], wasting of 15 controlled substance from two hospitals in Albany, New York was evaluated over a two year period. Three controlled substances (midazolam, acetaminophen-codeine and fentanyl) contributed nearly 90% by weight of the total controlled drug waste. The third publication [73] reported the patterns of antibiotic/antimicrobial drug wasting. The present study reports on the patterns of wasting and dispensing of an additional 85 pharmaceuticals in 12 pharmacologic classes given to patients at two acute care hospitals in Albany, NY. The study considered drug metabolism, excretion, disposal and toxicity to aquatic organisms (ecotoxicity). Potential strategies for drug waste minimization and possible impacts on healthcare costs are discussed.

Materials and Methods

As part of a pharmaceutical waste reduction pilot program, a total of 12,345 drug records for dispensing and waste collection were reviewed from two hospitals in Albany, NY. There were 4,889 automated drug dispensing machine (PYXIS®) records which were collected and tabulated at the Albany Medical Center Hospital (AMCH; 630-bed, acute care) and 7,257 PYXIS® records from the South Clinical Campus (SCC; 20 bed surgical care center). Additionally, the contents of 199 pharmaceutical waste collection containers placed at SCC were sorted by hand and their contents tabulated.

Data were recorded by location, medication form, weight and number of units dispensed, returned, “bedside wasted” or discarded (e.g., a 1g dose of phenylephrine was recorded as 1g regardless of the total weight of the drug formulation.). No human subject or patient identifier information was accessed; all data were recorded as summary aggregates. The funding agency (US EPA) did not participate in the design, conduct, or analysis of the study. All numeric data were entered and archived on a Windows® based personal computer and analyzed by standard software packages (Microsoft Access®, Excel®).

N.b., Bedside wasted at health care facilities refers to the discharge of excess drug withdrawn for patient administration, but only partially given to a patient. The leftover medication is then discarded by a healthcare professional who documents the wasting in the medication record.

Persistence, bioaccumulation, toxicity (PBT), environmental risk ratio (<http://www.janusinfo.se>), and ecotoxicity (<http://www.msdsonline.com>) were summarized for each drug wasted or discarded and displayed in Table 1 and Supplemental Table 1.

Table 1 (and Supplemental Table 1) provides a summary of ecotoxicity information for the pharmaceuticals of interest. Inhibitory and lethal concentration data were considered to be the same for our review (e.g., EC50 = IC50 = LC50). These values (EC50, IC50, and LC50) were selected as they represent the most reproducible point on the dose-response curve.

In addition to the laboratory derived toxicity information presented in the MSDS/SDS (Material Safety Data Sheet/Safety Data Sheet) and outside literature, mathematically modeled values are provided in Table 1 (and Supplemental Table 1): Aster (http://www.epa.gov/med/prods_pubs/aster.htm), ECOSAR (Ecological Structure Activity Relationships – <http://www.epa.gov/oppt/newchems/tools/21ecosar.htm>), Neutral Organics QSAR (Quantitative Structure Activity Relationship), Oasis Forecast M, PNN, and Topkat. Data from the WikiPharma database (<http://www.wikipharma.org>) is also summarized in Tables 1 and Supplementary Table 1 where appropriate.

Pharmacokinetic data (metabolism, conjugation and excretion) are summarized in Table 2 (and Supplemental Table 2) from official government drug monographs and labels (Drugs@FDA; <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>) and the Hazardous Substances Data Bank, United States National Library of Medicine TOXNET Toxicology Data Network (<http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>).

For those drugs for which no data (designated as ND) were found

for PBT, environmental risk ratio, ecotoxicity or pharmacokinetics, a computerized search of the available primary literature was conducted (<http://www.ncbi.nlm.nih.gov/pubmed>) and referenced in footnotes to Tables 1 and 2 (and Supplemental Tables 1 and 2).

Results

Formulary Overview

As part of our evaluation of drug dispensing and disposal, the formulary for the academic medical center hospital and surgical care center was evaluated by a commercial contractor. As depicted in the pie chart (Figure 1), of 2,700 drug formulations (represented by unique National Drug Codes – NDCs), most (90%) are not regulated but include such major therapeutic drug classes as: endocrine disruptors, steroids, antibiotics, mood altering drugs, heart and blood pressure medications, antiinflammatory drugs, and cholesterol lowering drugs as well as innocuous salts, buffers, nutritional and emollients. The remaining drug formulations possess one or more hazardous or regulated

Figure 1: Formulary Pie Chart Based on 2,700 Drug Formulations (NDC's)

characteristics. Controlled substances are the more numerous at 4.8% of the drugs; followed closely by those whose wastes are regulated by the US EPA (so called “RCRA” – Resource Conservation and Recovery Act or hazardous chemicals; e.g., flammable, corrosive, reactive, mercury containing, etc.) at 4.4%; cytotoxic and antimetabolite drugs (used in treating cancer patients) regulated by the US Occupational Safety and Health Administration (US OSHA) or the National Institutes of Occupational Safety and Health (NIOSH) comprise 3.2%; vaccines and biologicals (biohazardous, infectious or recombinant DNA) at 2.7%; and aerosols (inhalers, pressurized dispensers) regulated by the US Department of Transportation (US DOT) at but 0.3% of the hospital’s formulary. Please note that the total exceeds 100% as a number of drug formulations have multiple hazard characteristics, e.g. a RCRA hazardous waste and a controlled substance – (paraldehyde, chloral hydrate), a RCRA hazardous waste and a cytotoxic (cyclophosphamide, actinomycin), a RCRA hazardous waste and biohazardous infectious drug (vaccines with preservatives), etc. The current communication focuses upon unregulated drugs and those few pharmaceuticals which meet the criteria for regulation under current state and federal hazardous waste laws (“RCRA”). As noted in figure 1, these comprise nearly 90% of the “On Formulary” NDC’s (Not Currently Regulated) and about 4.4% of the “On Formulary” NDC’s (RCRA regulated).

Table 1: Summary of the Most Frequently Wasted, Discarded or Dispensed Pharmaceuticals and Potential Ecotoxic Effects from an Academic Medical Center and a Surgical Care Center over a Two							
Pharmaceutical – DrugClas				Ecotoxicity ^b			
Generic Name CAS ^c # Trade ^d name [®]	Class ^a	PBT ^e Score	Risk ^f	Invertebrates	Fish	Other	Disposal ^g
Acetazolamide 59-66-5 Diamox [®]	Ophtho	ND	ND	MSDS; Literature: ND ^h Predicted: <i>Daphnia</i> ⁱ or mysid shrimp EC ₅₀ ^j or LC ₅₀ ^k >1000 mg/L (Ecosar v0.99g); <i>Daphnia</i> chronic EC ₅₀ >100 mg/L (Ecosar v0.99g)	MSDS: ND Literature: <i>Cyprinodon</i> ^l LC ₈₃ 10E-3M 120h [114] Predicted: Fish LC ₅₀ >1000 mg/L (Ecosar v0.99g); fish LC ₅₀ >1000 mg/L(Aster); fish LC ₅₀ 59mg/L (PNN); fish LC ₅₀ >100 mg/L (Neutral Organics QSAR)	MSDS; Literature: ND Predicted: Algae EC ₅₀ or LC ₅₀ >1000 mg/L (Ecosar v0.99g); algae chronic EC ₅₀ >100 mg/L (Ecosar v0.99g)	ND
Albuterol 51022-70-9 Proventil [®]	Pulmonary	4 (3,0,1)	Cannot be excluded	MSDS: <i>Daphnia</i> LC ₅₀ >100 mg/L 48h.; LC ₅₀ 243 mg/L 48h Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	ND
Albuterol and Ipratropium 66985-17-9 and 51022-70-9 Combivent [®]	Pulmonary	Albuterol 4(3,0,1); Ipratropium 6 (3,0,3)	Albuterol: cannot be excluded. Ipratropium: Insignificant	Albuterol MSDS: <i>Daphnia</i> LC ₅₀ >100 mg/L 48h.; LC ₅₀ 243 mg/L 48h Literature; Predicted: ND Ipratropium MSDS: <i>Daphnia</i> EC ₅₀ >100 mg/L 48h. Literature; Predicted: ND	MSDS; Predicted; Literature: ND	MSDS; Predicted; Literature: ND	ND
Dexamethasone 50-02-2 Decadron	ED	ND (ND,0,ND)	Cannot be excluded	MSDS: <i>Daphnia</i> EC ₅₀ 48 mg/L 24h. Literature, Predicted: ND WikiPharma: <i>Brachionus</i> ^m LC ₅₀ 48 mg/L 24h; <i>Ceriodaphnia</i> ⁿ EC ₅₀ 0.05ppm (or mg/L) 7d; <i>Daphnia</i> 48 mg/L 24h; <i>Thamnocephalus</i> ^o LC ₅₀ 60 mg/L 24h.	MSDS; Literature; Predicted: ND	MSDS: <i>Pseudokirchneriella</i> ^p EC ₅₀ >100 mg/L 72h. Bioaccumulation unlikely; Harmful to aquatic organisms. Literature; Predicted: ND	Do not release material and cleaning waters into the environment. Incineration in accordance with laws.
Diatrizoatemeglumine 131-49-7 Gastrografin [®]	Radiology	ND	ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	ND
Gadodiamide 131410-48-5 Omniscan [®]	Radiology	3 (3,0,0)	Insignificant	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	ND
Glycopyrrolate 596-51-0 Rubinol [®]	Ophtho	ND	ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	ND

Ibuprofen 15687-27-1 Advil®	NSAID	2 (0,0,2)	Insignificant	MSDS: ND Literature: <i>Daphnia</i> EC ₅₀ 132.6 mg/L 48h [104] EC ₅₀ 31 mg/L 48h [105]; EC ₅₀ 108 mg/L 48h [51]; EC ₅₀ 7.87 mg/L 21d [103] Predicted: <i>Daphnia</i> or mysid shrimp EC ₅₀ or LC ₅₀ 2.6 mg/L (Ecosar v0.99g); <i>Daphnia</i> chronic EC ₅₀ 4.3 mg/L (Ecosar v0.99g). WikiPharma: <i>Carcinus</i> EC ₅₀ 0.0007 mg/L 28d; <i>Daphnia</i> EC ₅₀ 9.1 mg/L 48h; >100 mg/L 48h; LC ₅₀ >100 mg/L 48h; <i>Dreissena</i> ^v EC ₅₀ 0.4 mg/L; <i>Hydra</i> ^w EC ₅₀ 1.7mg/L 96h ; 3.9 mg/L 96h; IC ₅₀ 3.9 mg/L 96h; LC ₅₀ 22 mg/L 96h; <i>Planorbis</i> ^s LC ₅₀ 17 mg/L 48h.	MSDS: ND Literature: <i>Oryzias</i> ^a LC ₅₀ 89 mg/L 96h [105]. Predicted: <i>Cyprinodon</i> LC ₅₀ 49 mg/L (Topkat v6.1); fish LC ₅₀ 2.6 mg/L; 32 mg/L (Ecosar v0.99g); 4.2 mg/L (Oasis Forecast M v1.10); 5.3 mg/L (Aster); 8.2 mg/L (PNN); 0.0318 mg/L (Neutral Organics QSAR in Ecosar v0.99g). WikiPharma: <i>Lepomis</i> ^u LC ₅₀ >100 mg/L 96h.	MSDS: ND Literature: <i>Pseudokirchneriella</i> EC ₅₀ 360 mg/L 96h [105]; <i>Desmodesmus</i> ^r EC ₅₀ 315 mg/L 3d; <i>Lemna</i> ^s EC ₅₀ 22 mg/L 7d (Cleuvers 2003) Predicted: Algae EC ₅₀ or LC ₅₀ 2.6 mg/L (Ecosar v0.99g); algae chronic EC ₅₀ 4.3 mg/L (Ecosar v0.99g). WikiPharma: <i>Desmodesmus</i> EC ₅₀ >100 mg/L 3d; <i>Lemna</i> EC ₅₀ 1.0; 4.0; 19 and 22 mg/L7d; <i>Pseudokirchneriella</i> EC ₅₀ 2.3 mg/L 96h <i>Skeletonema</i> ^t EC ₅₀ 40 mg/L 5d; <i>Vibrio</i> ^y EC ₅₀ 11, 12 and 19 mg/L 15min; <i>Xenopus</i> ^z EC ₅₀ 40 mg/L 96h; LC ₅₀ 57 mg/L 96h.	ND
Insulin 160337-95-1 Lantus®	ED RCRA	ND	ND	MSDS: <i>Daphnia</i> EC ₅₀ >100 mg/L 48h Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS: Algae EC ₅₀ 19 mg/L96h; 33 mg/L 72h; activated sludge EC ₅₀ >1000 mg/L96h Literature; Predicted: ND	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.
Iopamidol 60166-93-0 Isovue®	Radiology	ND	ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	Must not be disposed of together with household garbage. Do not allow product to reach sewage system.
Ketorolac 74103-07-4 Toradol®	NSAID	4 (3,0,1)	Insignificant	MSDS: <i>Daphnia</i> LC ₅₀ >1000 mg/L 48h Literature; Predicted: ND	MSDS: <i>Lepomis</i> LC ₅₀ >1000 mg/L 96h; <i>Oncorhynchus</i> ^{aa} LC ₅₀ >1000 mg/L 24h; (fingerling) LC ₅₀ >1000 mg/L 24 h Literature; Predicted: ND	MSDS: <i>Chlorella</i> ^{bb} EC ₅₀ >1000 mg/L. Literature; Predicted: ND	ND
Mepivacaine 1722-62-9 Polocaine®	LA	4 (3,0,1)	Cannot Be Excluded	MSDS; Literature: ND Predicted: <i>Daphnia</i> or mysid shrimp EC ₅₀ or LC ₅₀ 5.3 mg/L (Ecosar v0.99g).	MSDS; Literature: ND Predicted: Fish LC ₅₀ 72 mg/L (Ecosar v0.99g); >100 mg/L (Oasis Forecast M v1.10); 75 mg/L (Aster); 23 mg/L (PNN); 1.99 mg/L (Neutral Organics QSAR); EC ₅₀ or LC ₅₀ 5.3 mg/L (Ecosar v0.99g).	MSDS; Literature: ND Predicted: Algae EC ₅₀ or LC ₅₀ 5.3 mg/L (Ecosar v0.99g)	ND

Metoprolol 83-43-2 Lopressor®,	CVS	4 (3,0,1)	Insignificant	MSDS: <i>Daphnia</i> EC ₅₀ >100 mg/L 48 h Literature: <i>Daphnia</i> LC ₅₀ 76.2 mg/L 48h [115]; EC ₅₀ 200 mg/L 48h [116]; EC ₅₀ >100 mg/L 48h [51]; LC ₅₀ 63.9 mg/L 48h; EC ₅₀ 2.6 mg/L 24 and 48h [117]; <i>Hyalella</i> ^{cc} LC ₅₀ >100 mg/L 48h; 8.8 mg/L 48h [53]; <i>Ceriodaphnia</i> EC ₅₀ 45.3 mg/L 48h [118]. Predicted: ND. WikiPharma: <i>Daphnia</i> EC ₅₀ >100 mg/L 48h; <i>Daphnia</i> LC ₅₀ 64 mg/L; 76 mg/L 48h; <i>Ceriodaphnia</i> LC ₅₀ 8.8 mg/L 48h; <i>Hyalella</i> LC ₅₀ >100mg/L 48h; <i>Thamnocephalus</i> EC ₅₀ >100 mg/L 1h; LC ₅₀ 78 mg/L 24h.	MSDS: <i>Onchorhynchus</i> LC ₅₀ >100 mg/L 96h Literature: <i>Oryzias</i> LC ₅₀ ≥100 mg/L 48h (Huggett et al. 2002) Predicted: ND. WikiPharma: <i>Danio</i> ^{dd} LC ₅₀ >100 mg/L 72h; EC ₅₀ 31 mg/L 72h; <i>Oryzias</i> LC ₅₀ >100 mg/L 48h.	MSDS: Green algae ErC ₅₀ 58.3 mg/L 72h Literature: <i>Desmodesmus</i> EC ₅₀ 7.3 mg/L 3d; <i>Lemna</i> EC ₅₀ >320 mg/L 7d [51] ; <i>Vibrio</i> EC ₅₀ 14.5 mg/L [117]. Predicted:ND. WikiPharma: <i>Desmodesmus</i> EC ₅₀ 40 mg/L 24h; 7.9 mg/L 48h; 7.3 mg/L 3d; <i>Lemna</i> EC ₅₀ >100 mg/L 7d; <i>Vibrio</i> EC ₅₀ >100 mg/L 30min.	ND
Neostigmine 59-99-4 Prostigmin®	Ophtho	ND	Cannot Be Excluded	MSDS: <i>Daphnia</i> EC ₅₀ <1 mg/L 24 h Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS: Not easily biodegradable. Harmful for water organisms. Literature; Predicted: ND	ND
Nicardipine 54527-84-3 / 55985-32-5 Cardene IV®	CVS	ND	ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.
Nitroglycerine 55-63-0 Nitrostat®	CVS	ND	ND	MSDS: <i>Daphnia</i> EC ₅₀ 46 mg/L 48h. Literature: ND Predicted: <i>Daphnia</i> EC ₅₀ 1.56 E-05 mg/L (Topkat v6.1); <i>Daphnia</i> or mysid shrimp EC ₅₀ or LC ₅₀ >100 mg/L (Ecosar v0.99g); <i>Daphnia</i> chronic EC ₅₀ 21 mg/L (Ecosar v0.99g)	MSDS: Freshwater fish: LC ₅₀ 1.4 mg/L 96h Literature: ND Predicted: Fish LC ₅₀ >100 mg/L (Ecosar v0.99g); fish LC ₅₀ >100 mg/L (Oasis Forecast M v1.10); fish LC ₅₀ >1000 mg/L (Aster); fish LC ₅₀ >1000 mg/L (PNN); fish LC ₅₀ 4.86 mg/L (Neutral Organics QSAR); fish, <i>Daphnia</i> , algae or mysid shrimp EC ₅₀ or LC ₅₀ >100 mg/L (Ecosar v0.99g).	MSDS: ND Literature: ND Predicted: Algae EC ₅₀ or LC ₅₀ >100 mg/L (Ecosar v0.99g); algae chronic EC ₅₀ 21 mg/L (Ecosar v0.99g)	ND
Ondansetron 99614-02-5 ZOFRAN®	GI	6 (3,0,3)	Insignificant	MSDS: <i>Daphnia</i> EC ₅₀ 28 mg/L 48h Literature; Predicted: ND.	MSDS: Adult <i>Oncorhyncus</i> EC ₅₀ 6.5 mg/L 96h. Literature; Predicted: ND	MSDS: Activated sludge respiration IC ₅₀ : >1000 mg/L 3h: <i>Pseudokirchneriella</i> IC ₅₀ ^{ee} : 0.87 mg/L 72h. Literature; Predicted: ND	ND
Oxymetazoline 2315-02-8 Afrin®	NS	5 (3,0,2)	Cannot Be Excluded	MSDS: <i>Daphnia</i> EC ₅₀ 21 mg/L 48h Literature; Predicted: ND	MSDS: Fish LC ₅₀ >100 mg/L 96h Literature; Predicted: ND	MSDS: Algae IC ₅₀ 24 mg/L 72h. Harmful to aquatic organisms and may cause long term adverse effects in the aquatic environment. Literature; Predicted: ND	ND

Phenylephrine 61-76-7 Neo-Synephrine®	CVS	ND	ND	MSDS; Literature: ND Predicted: Toxicity to <i>Daphnia</i> or mysid shrimp (EC ₅₀ or LC ₅₀) 58 mg/L (Ecosar v0.99g).	MSDS; Literature: ND Predicted: fish LC ₅₀ >100 mg/L (Ecosar v0.99g); Aster; PNN; Neutral Organics QSAR); fish EC ₅₀ or LC ₅₀ 58 mg/L (Ecosar v0.99g).	MSDS; Literature: ND Predicted: Algae EC ₅₀ or LC ₅₀ 58 mg/L (Ecosar v0.99g)	
Prednisone 53-03-2 Deltasone®	ED	ND	Cannot be excluded	MSDS; Literature, Predicted: ND WikiPharma: <i>Ceriodaphnia</i> IC ₅₀ >2.0 mg/L 7 d; <i>Brachionus</i> LC ₅₀ 55 mg/L 24h.	MSDS; Literature; Predicted: ND	MSDS: Algae IC ₅₀ : 31 mg/L 72h. Harmful to aquatic organisms Literature, Predicted: ND WikiPharma: <i>Pseudokirchneriella</i> IC ₅₀ 31 mg/L 72h.	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.

A total of 12,345 drug records for dispensing and waste collection were reviewed; 4,889 records from the 630 bed Albany Medical Center Hospital and 7,257 records from the 20 bed South Clinical Campus of Albany Medical Center. The contents of 199 pharmaceutical waste collection containers placed at SCC were sorted by hand and the results tabulated by location, medication form and weight of units discarded. Weights are for active ingredient, e.g. a 1 g dose of acetazolamide was recorded as 1 g regardless of the total weight of the drug formulation. N.b. MSDS = Material Safety Data Sheet (Safety Data Sheet –Global Harmonization).WikiPharma =WikiPharma database (<http://www/WikiPharma.org>) is a compilation of publicly available ecotoxicity data for human pharmaceuticals available in Sweden.

a. Class – pharmaceutical is used to treat disease (e.g., Optho = eye; Pulmonary – lung function; Psy = mood altering; CVS = cardiovascular; CNS = central nervous system; ED = endocrine; Mus = musculo-skeletal; NS – nervous system, GI – gastrointestinal; Renal – kidney; Radiology – imaging, LA = local anesthetic).

b. Ecotoxicity: from material safety data sheets (MSDSs).

c. CAS# - Chemical Abstracts Services unique chemical identification number.

d. A trade name is included for illustrative purposes.

e. PBT : persistence, bioaccumulation, and toxicity (0 – 3 range for each, with zero being the most benign).

f. *Risk*: defined as - cannot be excluded, insignificant, low, moderate, and high

g. Disposal – from MSDSs - n.b., does not apply to consumers or end users – refer to US FDA guidelines and office of national drug control policy (ONDCP, 2007).

h. ND = no data available or not determined.

i. *Daphnia*: crustacean, water flea.

j. *EC50*: concentration of a material which is expected to cause an adverse biological effect on 50% of the test organisms – acute toxicity.

k. *LC50*: lethal concentration that kills 50% of the test organisms – acute toxicity.

l. *Cyprinodon*: minnow, fish.

m. *Brachionus*: rotifer, invertebrate plankton.

n. *Ceriodaphnia*: waterflea, invertebrate.

o. *Thamnocephalus*: shrimp.

p. *Pseudokirchneriella* (AKA: *Synechococcus*):unicellular cyanobacteria.

q. *Oryzias*: ricefish.

r. *Desmodesmus*: green algae.

s. *Lemna*: duckweed.

t. *Skeletonema*: diatom.

u. *Carcinus*: crab.

v. *Dreissena*: freshwater mussel.

w. *Hydra*: freshwater invertebrate.

x. *Planorbus*: Freshwater snail.

y. *Vibrio*: gram negative bacteria.

z. *Xenopus*: clawed frog.

aa. *Oncorhynchus*: rainbow trout, fish

bb. *Chlorella*: green algae.

cc. *Hyalella*: amphipod invertebrate.

dd. *Danio*: zebrafish, fish.

ee. *IC50*: concentration of a material in water which is expected to cause an inhibitory effect on 50% of the test organisms – acute toxicity.

Supplementary Table 1: Summary of Wasted, Discarded or Dispensed Pharmaceuticals and Potential Ecotoxic Effects from an Academic Medical Center and a Surgical Care Center over a Two-Year Period in Albany NY [115,116,119-128]							
Pharmaceutical – Drug Class ^a				Ecotoxicity ^b			
Generic Name CAS ^c # Trade name [®]	Class	PB Score ^d	Risk ^e	Invertebrates	Fish	Other	Disposal ^f
Acetylcholine 60-31-1 Miochol [®]	Ophtho	ND ^g	ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	Do not dispose in ground water or sewage systems.
Adenosine 58-61-7 Adenocard IV [®]	CVS	ND	ND	MSDS; Literature: ND Predicted: <i>Daphnia</i> ^h or mysid shrimp EC ₅₀ ⁱ or LC ₅₀ ^j 300 mg/L (Ecosar v0.99g).	MSDS; Literature: ND Predicted: Fish LC ₅₀ 10718 mg/l (Ecosar v0.99g);78 mg/l (PNN); 2.98E+003 mg/L(Neutral Organics QSAR); EC ₅₀ or LC ₅₀ 300 mg/L (Ecosar v0.99g)	MSDS; Literature: ND Predicted: Algae EC ₅₀ or LC ₅₀ 300 mg/L (Ecosar v0.99g)	ND
Alprazolam 28981-97-7 Xanax [®]	Psy	ND	Cannot be excluded	MSDS; Literature: ND Predicted: <i>Daphnia</i> or mysid shrimp EC ₅₀ or LC ₅₀ 0.5 mg/L (Ecosar v0.99g)	MSDS; Literature: ND Predicted: Fish EC ₅₀ or LC ₅₀ fish 0.5 mg/L (Ecosar v0.99g); fish LC ₅₀ 5.4 mg/L (Ecosar v0.99g) LC ₅₀ 3.3 mg/L (Oasis Forecast M v1.10); 50 mg/L (PNN); 4.00E-002 mg/L (Neutral Organics QSAR).	MSDS; Literature: ND Predicted: Algae EC ₅₀ or LC ₅₀ 0.5 mg/L (Ecosar v0.99g).	ND
Alteplase 105857-23-6 Activase [®]	CVS	ND	ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	Chemical waste incinerator
Aminophylline 317-34-0 Truphylline [®]	CVS	ND	ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	Dissolve or mix the material with a combustible solvent and burn in a chemical
Amiodarone 1951-25-3 Cordarone [®]	CVS	7 (3,3,1)	Cannot Be Excluded	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	ND
Aripiprazole 129722-12-9 Abilify [®]	Psy	6 (3,0,3)	Insignificant	MSDS; Literature; Predicted: ND	MSDS: <i>Oncorhynchus</i> ^k LC ₅₀ >0.12 mg/L 96h. Literature; Predicted: ND	MSDS: Activated Sludge EC ₅₀ >1,000 mg/L 3h. Expected to bioaccumulate Literature; Predicted: ND	ND
Benztropine 132-17-2 Cogentin	CNS	ND	ND	MSDS; Literature: ND Predicted: <i>Daphnia</i> or mysid shrimp EC ₅₀ or LC ₅₀ 0.29 mg/L (Ecosar v0.99g)	MSDS; Literature: ND Predicted: <i>Cyprinodon</i> ^l LC ₅₀ 0.05 mg/L (Topkat v6.1); fish LC ₅₀ 2.9 mg/L (Ecosar v0.99g); fish LC ₅₀ 8.1 mg/L (Aster); fish LC ₅₀ 14.7 mg/L (PNN); fish LC ₅₀ 1.64E-002 mg/L (Neutral Organics QSAR)	MSDS; Literature: ND Predicted: Algae EC ₅₀ or LC ₅₀ 0.3 mg/L (Ecosar v0.99g)	Incineration is the preferred method of disposal

Betamethasone 378-44-9 Celestone ®	ED	9 (3,3,3)	Cannot Be Excluded	MSDS; Literature: ND Predicted: <i>Daphnia</i> or mysid shrimp EC ₅₀ or LC ₅₀ 924 mg/L (Ecosar v0.99g)	MSDS; Literature: ND Predicted: Fish LC ₅₀ 388 mg/L (Ecosar v0.99g); 10,576 mg/L (Oasis Forecast M v1.10); 1.3 mg/L (PNN); 5.33E+000 mg/L (Neutral Organics QSAR); EC ₅₀ or LC ₅₀ 924 mg/L (Ecosar v0.99g)	MSDS; Literature: ND Predicted: Algae EC ₅₀ or LC ₅₀ 924 mg/L (Ecosar v0.99g)	Incineration is the preferred method of disposal
Betaxolol 63659-18-7 Kerlone®	CVS	ND (ND,0,ND)	Cannot Be Excluded	MSDS: ND Literature: <i>Daphnia</i> EC ₅₀ >300mg/L 48 h Predicted: ND. WikiPharma: <i>Daphnia</i> EC ₅₀ >300mg/L 48h.	MSDS; Literature; Predicted: ND	MSDS; Do not allow product to enter drinking water supplies, wastewater or soil. Literature; Predicted: ND	Burn in an incinerator equipped with afterburner and scrubber.
Brimonidine 59803-98-4 Alphagan®	Ophtho	ND	Cannot be excluded	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.
Bupropion 31677-93-7 BudeprionXL®	Psy	6(3,0,3)	Insignificant	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS: Products of biodegradation are possibly hazardous. Short-term degradation products are not likely. Long-term degradation products may arise. The products of degradation are more toxic than the parent drug.	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.
Citalopram 59729-32-7 Celexa®	Psy	6(3,0,3)	Cannot Be Excluded	MSDS: ND Literature: <i>Daphnia</i> EC ₅₀ 20 mg/L 48h; <i>Ceriodaphnia</i> ™LC ₅₀ 3.9 mg/L 48h Predicted: ND. WikiPharma: <i>Ceriodaphnia</i> EC ₅₀ 20 mg/L 48h; LC ₅₀ 3.9 mg/L 48h.	MSDS; Literature; Predicted: ND	MSDS: ND Literature: <i>Pseudokirchneriella</i> ° EC ₅₀ 1.6 mg/L 48h [119] Predicted: ND. WikiPharma: <i>Pseudokirchneriella</i> EC ₅₀ 1.6mg/L 48h.	ND
Clonazepam 1622-61-3 Klonopin®	Psy	4 (3,0,1)	Insignificant	MSDS: <i>Daphnia</i> EC ₅₀ 30 mg/L 48h. Literature: ND Predicted: <i>Daphnia</i> , algae or mysid shrimp EC ₅₀ or LC ₅₀ 3.1 mg/L (Ecosar v0.99g)	MSDS: <i>Oncorhynchus</i> LC ₅₀ 1000 mg/L 96h. Literature: ND Predicted: Fish EC ₅₀ or LC ₅₀ 3.1 mg/L (Ecosar v0.99g); <i>Cyprinodon</i> LC ₅₀ 0.9 mg/L (Topkat v6.1); fish LC ₅₀ 40 mg/L (Ecosar v0.99g); 76 mg/L (Oasis Forecast M v1.10); 107 mg/L (Aster); 122 mg/L (PNN); 7.43E-001 mg/L (Neutral Organics QSAR)	MSDS: <i>Scenedesmus</i> ° EC ₅₀ >100 mg/L; <i>Desmodesmus</i> ° ErC ₅₀ °>240 mg/L 72h; not inherently biodegradable 0 %, 21 d. Literature: ND Predicted: Algae or mysid shrimp EC ₅₀ or LC ₅₀ 3.1 mg/L (Ecosar v0.99g)	ND

Clozapine 5786-21-0 Clozaril®,	Psy	9 (3,3,3)	Low	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.
Cyclopentolate 512-15-2 Cyclogyl®)	Ophtho	ND (ND,0,ND)	Cannot be excluded	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	ND
Dantrolene 14663-23-1 Dantrium IV®	Mus	ND	ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	Do not dispose of the material in any sanitary sewer or storm sewer system, which includes sinks, toilets, and floor drains.
Digoxin 20830-75-5 Digitek®	CVS	ND	Cannot be excluded	MSDS: <i>Daphnia</i> LC ₅₀ 192 mg/L 24h; EC ₅₀ 24 mg/L 24h. Literature: ND Predicted: <i>Daphnia</i> or mysid shrimp EC ₅₀ or LC ₅₀ 21,239 mg/L (Ecosar v0.99g). WikiPharma: <i>Artemia</i> ^r LC ₅₀ 9996 mg/L 24h; <i>Brachionus</i> ^s LC ₅₀ 9996 mg/L 24h; <i>Daphnia</i> EC ₅₀ 9996 mg/L 24h; EC ₅₀ 24 mg/L 24h; <i>Streptocephalus</i> ^t LC ₅₀ 9996mg/L 24h; <i>Hydra</i> ^u EC ₅₀ 0.1 mg/L 7d; chronic <i>Hydra</i> EC ₅₀ 0.01mg/L 17d.	MSDS; Literature: ND Predicted: Fish LC ₅₀ 1.49E+002 mg/L (Neutral Organics QSAR); Fish EC ₅₀ or LC ₅₀ 21,239 mg/L (Ecosar v0.99g).	MSDS; Literature: ND Predicted: algae EC ₅₀ or LC ₅₀ 21,239 mg/L (Ecosar v0.99g). WikiPharma: <i>Photobacterium</i> ^v EC ₅₀ 9996mg/L 5min; <i>Spirostomum</i> ^w LC ₅₀ 35 mg/L 24h; EC ₅₀ 8.8 mg/L 24h; <i>Tetrahymena</i> ^x EC ₅₀ 26 mg/L 24h.	ND
Diltiazem 33286-22-5 Cardizem®	CVS	4(3,0,1)	Cannot be excluded	MSDS; Literature: ND Predicted: <i>Daphnia</i> , or mysid shrimp EC ₅₀ or LC ₅₀ 2.9 mg/L (Ecosar v0.99g). WikiPharma: <i>Thamnocephalus</i> ^v LC ₅₀ 73 mg/L 24h; EC ₅₀ 10 mg/L 1h; <i>Daphnia</i> EC ₅₀ 8.2 mg/L 96h; 28 mg/L 48h.	MSDS; Literature: ND Predicted: <i>Cyprinodon</i> LC ₅₀ 0.002 mg/L (Topkat v6.1); Fish LC ₅₀ 23 mg/L (Ecosar v0.99g); LC ₅₀ 5.8 mg/L (Aster); LC ₅₀ 11 mg/L (PNN); LC ₅₀ 1.85E+001 mg/L (Neutral Organics QSAR). WikiPharma: <i>Oryzias</i> ^z LC ₅₀ 15 mg/L 96h; LC ₅₀ 26 mg/L 48h.	MSDS; Literature: ND Predicted: algae EC ₅₀ or LC ₅₀ 2.9 mg/L (Ecosar v0.99g). WikiPharma: <i>Vibrio</i> ^{aa} EC ₅₀ 264 mg/L 15min; EC ₅₀ 407 mg/L 5min; EC ₅₀ 152 mg/L 24h.	ND
Diphenhydramine 58-73-1 Benadryl ®	Pulmonary	ND	ND	MSDS; Predicted: ND Literature: <i>Daphnia</i> LC ₅₀ 0.37 mg/L 48h [121]; <i>Ceriodaphnia</i> IC ₅₀ 2.0 mg/L 6-8d [122]. WikiPharma: <i>Ceriodaphnia</i> LC ₅₀ 3.9 mg/L 48h; EC ₅₀ 1.0 mg/L 7d.	MSDS; Predicted: ND Literature: <i>Pimephales</i> ^{bb} LC ₅₀ @ pH 6.5 59.3 mg/L 48h; LC ₅₀ @ pH 8.5 2.1 mg/L 48h[121]; <i>Danio</i> ^{cc} LC ₅₀ ^{dd} 16.6 mg/L 5d[122]	MSDS; Predicted: ND Literature: <i>Pseudokirchneriella</i> IC ₅₀ 1.2 mg/L 72h[122]	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.
Divalproex 76584-70-8 Depakote®)	CNS	ND	ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	Incinerate in an approved facility.

Dobutamine 49745-95-1	CVS	ND	ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.
Dopamine 62-31-7	CVS	ND	Cannot be excluded	MSDS: <i>Daphnia</i> EC ₅₀ 25 mg/L 48h. Literature: Predicted: ND	MSDS: <i>Leuciscus</i> ^{ee} LC ₅₀ 2200 - 4600 mg/L 96h Literature: Predicted: ND	MSDS:Algae EC ₅₀ <1 mg/L 72h; not readily biodegradable; bioaccumulation is unlikely; very toxic to aquatic life with long lasting effects Literature: Predicted: ND	ND
Dorzolamide and Timolol 130693-82-2 & 26921-17-5 Cosopt®	Optho	Dorzolamide: 3(3,0,0) Timol ND(ND,0,ND)	Dorzolamide: Cannot be excluded Timolol: Cannot be excluded	Dorzolamide: MSDS; Literature: ND Predicted: <i>Daphnia</i> or mysid shrimp EC ₅₀ or LC ₅₀ 9 mg/L (Ecosar v0.99g) Timolol: MSDS: <i>Daphnia</i> LC ₅₀ 161 mg/L 48 h Literature; Predicted: ND	Dorzolamide:MSDS; Literature: ND Predicted: Fish LC ₅₀ 126 mg/L (Ecosar v0.99g); 2334 mg/L (Oasis Forecast M v1.10); 548 mg/L (Aster); 32 mg/L (PNN); 4.03E+000 mg/L (Neutral Organics QSAR); EC ₅₀ or LC ₅₀ 9 mg/L (Ecosar v0.99g). Timolol: MSDS: <i>Pimephales</i> LC ₅₀ 411 mg/L 96 h Literature; Predicted: ND	Dorzolamide: MSDS; Literature: ND Predicted: Algae EC ₅₀ or LC ₅₀ 9 mg/L (Ecosar v0.99g). Timolol: MSDS; Does not have significant aquatic toxicity. Based on ASRIT results, concentrations must be >1000 mg/L to inhibit an unacclimated sludge system in a sewage treatment plant. Literature; Predicted: ND. WikiPharma: <i>Eisenia</i> ^{ff} LC ₅₀ >2000 mg/L 14d.	Dorzolamide: ND. Timolol: Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.
Droperidol 548-73-2 Inapsine®	CNS	ND	Cannot Be Excluded	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	Product may be burned in an incinerator equipped with afterburner and scrubber.
Enalapril 75847-73-3 Vasotec®	CVS	3 (3,0,0)	Cannot Be Excluded	MSDS; Literature, Predicted: ND. WikiPharma: <i>Thamnocephalus</i> LC ₅₀ 184 mg/L 24h.	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	ND
Eptifibatide 148031-34-9 / 188627-80-7 Integrilin®	CVS	ND (ND,0,ND)	Cannot Be Excluded	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	Do not allow product to enter drinking water supplies, waste water or soil. Dissolve or mix material with a suitable combustible solvent and incinerate in a chemical incinerator equipped with an After burner and scrubber.
Escitalopram 219861-08-2 Lexapro®	Psy	6 (3,0,3)	Cannot Be Excluded	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	ND

Esmolol 81161-17-3 Brevibloc®	NS	ND	Cannot Be Excluded	MSDS; Literature: ND Predicted: <i>Daphnia</i> or mysid shrimp EC ₅₀ or LC ₅₀ 6.0 mg/L (Ecosar v0.99g).	MSDS; Literature: ND Predicted: <i>Cyprinodon</i> LC ₅₀ 70 mg/L (Topkat v6.1); fish LC ₅₀ 45 mg/L (Ecosar v0.99g); 84 mg/L (Aster); 6.5 mg/L (PNN); 7.30E+001 mg/L (Neutral Organics QSAR); EC ₅₀ or LC ₅₀ 6.0 mg/L (Ecosar v0.99g).	MSDS; Literature: ND Predicted: Algae EC ₅₀ or LC ₅₀ 6.0 mg/L (Ecosar v0.99g).	ND
Esomeprazole 119141-88-7 Nexium®	GI	2 (0,0,2)	Insignificant	MSDS: <i>Daphnia</i> EC ₅₀ >100 mg/L 48h. Literature; Predicted: ND	MSDS: <i>Danio</i> LC ₅₀ 42 mg/L 96h. Literature; Predicted: ND	MSDS: Harmful to aquatic organisms. Green algae EbC ₅₀ ^{gg} 19 mg/L 72h; not biodegradable; low potential for bioaccumulation. Literature; Predicted: ND	ND
Fluoxetine 54910-89-3 Prozac®	Psy	6 (3,0,3)	Low	MSDS: <i>Daphnia</i> EC ₅₀ 0.9 mg/L 48h. Literature: <i>Daphnia</i> LC ₅₀ 0.8 mg/L 48h [123]; EC ₅₀ 6.4 mg/L 48h; LC ₅₀ 0.5 mg/L 48h[120]; <i>Ceriodaphnia</i> LC ₅₀ 0.2 mg/L 48h[123]; <i>Chironomus</i> ^{hh} chronic LC ₅₀ 15 mg/kg 10d; <i>Hyalella</i> ⁱⁱ LC ₅₀ >43 mg/kg 10d [123] Predicted:ND WikiPharma: <i>Artema</i> EC ₅₀ 14 mg/L 48h; <i>Brachionus</i> LC ₅₀ 0.3 mg/L 24h; 0.97 mg/L 15min; <i>Ceriodaphnia</i> LC ₅₀ 0.5 mg/L 48h; 0.2 mg/L 48h; <i>Daphnia</i> EC ₅₀ 6.4 mg/l 48h; 5.9 mg/L 48h; LC ₅₀ 0.8 mg/L 48h; <i>Hyalella</i> LC ₅₀ >43mg/L 10d; <i>Hydra</i> EC ₅₀ 7.9 and 8.7 mg/L 96h; <i>Plationus</i> ^{jj} LC ₅₀ 0.06 and 0.2 mg/L 48h; <i>Thamnocephalus</i> LC ₅₀ 0.9 mg/L 24h; 1.2 mg/L 15min.	MSDS: <i>Oncorhynchus</i> LC ₅₀ 1.6 mg/L 96h. Literature: <i>Oryzias</i> LC ₅₀ 5.5 mg/l at pH 7 96h; LC ₅₀ 1.3 mg/L at pH 8 96h; LC ₅₀ 0.2 mg/L at pH 9 96h[124]; <i>Pimephales</i> LC ₅₀ 0.7 mg/L 48h[123]; LC ₅₀ 0.212 mg/L for R-fluoxetine 48h; LC ₅₀ 0.198 mg/L for rac-fluoxetine 48h; and LC ₅₀ 0.216 mg/L for S-fluoxetine 48h [125] Predicted: ND WikiPharma: <i>Cyprinodon</i> LC ₅₀ >2,000 mg/L 96h; <i>Gambusia</i> ^{kk} LC ₅₀ 546 ppb 7d; <i>Pimphales</i> LC ₅₀ 0.2 mg/L 24h; 0.7 mg/L 24h. Predicted: ND.	MSDS: Very toxic to aquatic life. <i>Pseudokirchneriella</i> EC ₅₀ 0.02 mg/L 96h [123]; IC ₅₀ 0.4 mg/L 96h; EC ₅₀ 0.03 mg/L 48h [119]; <i>Scenedesmus</i> LC ₅₀ 0.09 mg/L 96h; IC ₅₀ 0.2 mg/L 96h; <i>Chlorella</i> ^{ll} IC ₅₀ 4.3 mg/L 96h [161] Predicted: algae EC ₅₀ 0.8 mg/L Ecosar (v0.99g). Wikipharma: <i>Chironomus</i> LC ₅₀ 15 mg/L 10d; <i>Crassostrea</i> ^{mm} EC ₅₀ 189 mg/L 24h; 192 mg/L 30h; <i>Davaliella</i> ⁿⁿ IC ₅₀ 0.2 mg/L 96h; <i>Haliotis</i> ^{oo} EC ₅₀ 2.4 and 16 mg/L 48h; <i>Lemna</i> ^{pp} EC ₅₀ >1 mg/L 7d; <i>Pseudokirchneriella</i> EC ₅₀ 0.2 mg/L 72h; 0.02, 0.03 and 0.04 mg/L 120h; IC ₅₀ 0.045 mg/L 96h; <i>Scenedesmus</i> IC ₅₀ 0.09 and 0.2 mg/L 96h; <i>Skeletonema</i> ^{qq} EC ₅₀ 0.04 mg/L 72h; <i>Xenopus</i> ^{rr} (egg) EC ₅₀ 4.9 mg/L 96h; LC ₅₀ 7.5 mg/L 96h.	ND
Flurbiprofen 5104-49-4 Ocufen®	Ophtho	ND	ND	MSDS; Literature: ND Predicted: <i>Daphnia</i> EC ₅₀ 0.6 mg/L (Topkat v6.1); <i>Daphnia</i> chronic EC ₅₀ 5.0 mg/L; <i>Daphnia</i> or mysid shrimp EC ₅₀ or LC ₅₀ 2.9 mg/L (Ecosar v0.99g).	MSDS; Literature: ND Predicted: <i>Cyprinodon</i> LC ₅₀ 0.5 mg/L (Topkat v6.1); fish LC ₅₀ 36 mg/L; fish EC ₅₀ or LC ₅₀ 2.9 mg/L (Ecosar v0.99g); fish LC ₅₀ 5.5 mg/L (Aster); 5.5 mg/L (PNN); 3.60E-002 mg/L (Neutral Organics QSAR).	MSDS; Literature: ND Predicted: Algae EC ₅₀ or LC ₅₀ 2.9 mg/L; algae chronic EC ₅₀ 5.0 mg/L (Ecosar v0.99g).	ND

Furosemide 54-31-9 Lasix®	Renal	4 (3,0,1)	Insignificant	MSDS; Literature: ND Predicted: <i>Daphnia</i> or mysid shrimp EC ₅₀ or LC ₅₀ 234 mg/L; <i>Daphnia</i> chronic EC ₅₀ 79 mg/L (Ecosar v0.99g) Wikipharma: <i>Daphnia</i> EC ₅₀ 61 mg/L 24h; <i>Ceriodaphnia</i> EC ₅₀ 84 mg/L 48h; chronic EC ₅₀ 2.4 mg/L 7d; <i>Brachionus</i> EC ₅₀ 2.5 mg/L 48h;. <i>Thamnocephalus</i> LC ₅₀ 71 mg/L 24h.	MSDS; Literature: ND Predicted: Fish LC ₅₀ 1227 mg/L (Ecosar v0.99g); fish LC ₅₀ 431 mg/L (Oasis Forecast M v1.10); 406 mg/L (Aster); 61 mg/L (PNN); 1.23E+000 mg/L (Neutral Organics QSAR); fish EC ₅₀ or LC ₅₀ 234 mg/L; (Ecosar v0.99g).	MSDS; Literature: ND Predicted: Algae EC ₅₀ or LC ₅₀ 234 mg/L; chronic EC ₅₀ 79 mg/L(Ecosar v0.99g).	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.
Haloperidol 52-86-8 Haldol®	Psy	8 (3,3,2)	Insignificant	MSDS; Literature: ND Predicted: <i>Daphnia</i> , algae or mysid shrimp EC ₅₀ or LC ₅₀ 4.0 mg/L (Ecosar v0.99g)	MSDS; Literature: ND Predicted: <i>Cyprinodon</i> LC ₅₀ 0.02 mg/L (Topkat v6.1); fish LC ₅₀ 13 mg/L (Aster); 6.0 mg/L (PNN); 2.38E-002mg/L (Neutral Organics QSAR); 4.0 mg/L; fish EC ₅₀ or LC ₅₀ 4.0 mg/L (Ecosar v0.99g).	MSDS; Literature: ND Predicted: Algae EC ₅₀ or LC ₅₀ 4.0 mg/L (Ecosar v0.99g).	ND
Hydralazine 304-20-1 Apresoline®	CVS	6 (3,0,3)	Cannot Be Excluded	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.
Ipratropium 60205-81-4	Pulmonary RCRA	6 (3,0,3)	Insignificant	MSDS: <i>Daphnia</i> EC ₅₀ >100 mg/L 48h Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	ND
Labetalol 36894-69-6 Trandate®	CVS	6 (3,0,3)	Cannot Be Excluded	MSDS: Literature: ND Predicted: <i>Daphnia</i> EC ₅₀ 1 - 10 mg/ml 48h (QSAR).	MSDS: <i>Brachydanio</i> ^{ss} LC ₅₀ 100 mg/ml 96h Literature; Predicted: ND	MSDS: moderate bioaccumulation potential; classified as dangerous to the environment. Literature: ND Predicted: Algae IC ₅₀ 1 to 10 mg/ml 72 h (QSAR).	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.
Lamotrigine 84057-84-1 Lamictal®	CNS	4 (3,0,1)	Insignificant	MSDS: <i>Daphnia</i> EC ₅₀ 56 mg/L 48h. Literature; Predicted: ND	MSDS: <i>Oncorhynchus</i> EC ₅₀ 85 mg/L 96h. Literature; Predicted: ND	MSDS: Activated Sludge LC ₅₀ >1000 mg/L 3h; algae LC ₅₀ 40 mg/L 72h. Literature; Predicted: ND	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.
Levetiracetam 102767-28-2 Keppra®	CNS	ND	Cannot Be Excluded	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	ND

Lithium 554-13-2 Lithobid®	Psy	ND	ND	MSDS: contains an active pharmaceutical ingredient that is toxic to daphnids. Literature,Predicted: ND Wikipharma: <i>Artemia</i> EC ₅₀ 4275 mg/L 24h; <i>Brachionus</i> EC ₅₀ 709 mg/L 24h <i>Daphnia</i> EC ₅₀ 33 mg/L 24 h; <i>Streptocephalus</i> EC ₅₀ 112 mg/L 24h.	MSDS: contains an active pharmaceutical ingredient that is toxic to fish Literature; Predicted: ND	MSDS; Literature, Predicted: ND Wikipharma: <i>Vibrio</i> EC ₅₀ 18,660 mg/L 5min.	ND
Methylprednisolone 83-43-2 Solumedrol®	ED	ND	Cannot Be Excluded	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS: This material is very soluble in water, not expected to enter the air. Microbes similar to those found in activated sludge are capable of biodegrading steroids completely. Highly soluble in water and poorly soluble in non-polar mediums. Expected to have a low bioaccumulative potential. Literature; Predicted: ND	Dispose of by incineration.
Metoclopramide 7232-21-5 Reglan®	GI	ND		MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	ND
Nicotine 54-11-5	CNS RCRA	3 (3,0,0)	Insignificant	MSDS: <i>Daphnia</i> EC ₅₀ 0.2 mg/L 48h. Literature, Predicted: ND. Wikipharma: <i>Artemia</i> LC ₅₀ 488 mg/L 24h; <i>Brachionus</i> LC ₅₀ 219 mg/L 24h; <i>Daphnia</i> EC ₅₀ 5.8 mg/L; 8570mM; 0.2 mg/L 24h; <i>Artemia</i> LC ₅₀ 488 mg/L; 0.6 mg/L 24h; <i>Brachionus</i> LC ₅₀ 219 mg/L; 0.5mg/L 24h; <i>Streptocephalus</i> LC ₅₀ 0.5 mg/L; 115 mg/L 24h.	MSDS: <i>Oncorhynchus</i> LC ₅₀ 4 mg/L 96h. Literature, Predicted: ND Wikipharma: <i>Oncorhynchus</i> EC ₅₀ 7252 mg/L 3h.	MSDS: Activated sludge EC ₅₀ 0.24 mg/L 48h; Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment. Literature, Predicted: ND Wikipharma: <i>Photobacterium</i> EC ₅₀ 0.38 mg/L; 38 mg/L 5min; 38 mg/L 15min.	Burn in a chemical incinerator equipped with an afterburner and scrubber.
Norepinephrine 51-41-2 Levophed®	CVS	ND	Cannot Be Excluded	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber
Olanzapine 132539-06-1 Zyprexa®	Psy	2 (0,0,2)	Insignificant	MSDS: Moderately toxic to fish and invertebrates. Literature; Predicted ND	MSDS: Moderately toxic to fish and invertebrates. Literature; Predicted ND	MSDS:Slightly toxic to green algae. Practically non-toxic to microorganisms. No volatility expected. Low potential to bioconcentrate in aquatic organisms. Persistence in the environment not expected. Literature; Predicted ND	ND
Paliperidone 144598-75-4 Invega®	Psy	4 (3,0,1)	Insignificant	MSDS; Literature; Predicted: ND	MSDS: <i>Danio</i> LC ₅₀ 18mg/L96h. Literature; Predicted: ND	MSDS:NOEC ^u Chronic Toxicity: >1 mg/l. Literature; Predicted: ND.	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.

Paroxetine 78246-49-8 PAXIL	Psy	6 (3,0,3)	Cannot Be Excluded	MSDS: <i>Daphnia</i> EC ₅₀ >17 mg/L 48 h. Literature: <i>Daphnia</i> EC ₅₀ 6.3 mg/L 48h [119]; EC50 2.5 mg/L 48h [127]; <i>Ceriodaphnia</i> LC ₅₀ 0.6 mg/L 48h [120]. Predicted: ND.	MSDS: <i>Oncorhynchus</i> LC ₅₀ >16 mg/L 96h. Literature; Predicted: ND	MSDS: ND Literature: <i>Pseudokirchneriella</i> EC ₅₀ 0.1 mg/L 48h [192]. Predicted: ND. Wikipharma: <i>Xenopus</i> (egg) LC ₅₀ 5.1 mg/L 96h; EC ₅₀ 4.1 mg/L 96h.	ND
Phenytoin 57-41-0 Dilantin®	CNS	ND	Cannot Be Excluded	MSDS: ND Literature: <i>Ceriodaphnia</i> IC ₅₀ 7.8 mg/L 6-8d [122]; Predicted: <i>Hyallela</i> LC ₅₀ 18 mg/L 96h(OPPTS); <i>Daphnia</i> EC ₅₀ >39 mg/L 48h; <i>Daphnia</i> EC ₅₀ 16.5 mg/l (Topkat v6.1); <i>Daphnia</i> or mysid shrimp EC ₅₀ or LC ₅₀ 246 mg/l (Ecosar v0.99g).	MSDS: ND Literature: <i>Danio</i> IC ₅₀ >16.4 mg/L 5d [122]; Predicted: <i>Pimephales</i> LC ₅₀ >23 mg/L 96h (OPPTS) LC ₅₀ 8.8 mg/l (Topkat v6.1); fish LC ₅₀ 52 mg/l (Oasis Forecast M v1.10); LC ₅₀ 157 mg/l (Aster); LC ₅₀ 122 mg/l (PNN); LC ₅₀ 1.32E+000 mg/l (Neutral Organics QSAR); fish EC ₅₀ or LC ₅₀ 246 mg/l (Ecosar v0.99g)	MSDS: ND Literature: <i>Pseudokirchneriella</i> IC ₅₀ 28.3 mg/L 72h [122]. Predicted: algaeEC ₅₀ or LC ₅₀ 246mg/l (Ecosar v0.99g);algae EC ₅₀ 148 mg/L Ecosar (Johnson et al. 2007).	ND
Pilocarpine 92-13-7 PILOPINE HS®,	Optho	6 (3,0,3)	Cannot be excluded	MSDS: <i>Daphnia</i> EC ₅₀ 13.1 mg/l 48h. Literature; Predicted ND	MSDS; Literature; Predicted: ND	MSDS: Activated sludge > 1000 mg/l 3 h. Not easily biodegradable. No bioaccumulation is to be expected. Literature; Predicted: ND	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.
Promethazine 60-87-7 PHENERGAN®	Pulmonary	ND	ND	MSDS; Literature: ND Predicted: <i>Daphnia</i> or mysid shrimp EC ₅₀ or LC ₅₀ 0.2 mg/l (Ecosar v0.99g)	MSDS; Literature: ND Predicted: <i>Cyprinodon</i> LC ₅₀ 0.1 mg/l (Topkat v6.1); fish LC ₅₀ 2 mg/l (Ecosar v0.99g); LC ₅₀ 2.5 mg/l (Aster); LC ₅₀ 28 mg/l (PNN); LC ₅₀ 9.62E-003 mg/l (Neutral Organics QSAR); EC ₅₀ or LC ₅₀ 0.2 mg/l (Ecosar v0.99g).	MSDS; Literature: ND Predicted: Algae EC ₅₀ or LC ₅₀ 0.2 mg/l (Ecosar v0.99g).	ND
Quetiapine 111974-72-2 Seroquel®	Psy	5 (3,0,2)	Insignificant	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS: Harmful to aquatic organisms. Green algae NOEC (growth rate) 2.5 mg/L14d; NOEC(cell density) 2.5 mg/L14d; blue-green algae NOEC (growth rate) 2.5 mg/L14d.	Dissolve or mix material with a suitable combustible solvent and incinerate in a chemical incinerator equipped with an afterburner and scrubber.
Risperidone 106266-06-2 RISPERDAL®	Psy	5 (3,0,2)	Insignificant	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.

Sertraline 79559-97-0 Zoloft®	Psy	6 (3,0,3)	Moderate	MSDS: <i>Daphnia</i> EC ₅₀ 0.6 mg/L48h Literature: <i>Daphnia</i> EC ₅₀ 0.9 mg/L 48h [119]; <i>Ceriodaphnia</i> LC ₅₀ 0.1 mg/L 48h [120]. Predicted: ND WikiPharma: <i>Artemia</i> EC ₅₀ 4.1 mg/L 48h; <i>Ceriodaphnia</i> LC ₅₀ 0.1 mg/L and 0.4 mg/L 48h; <i>Daphnia</i> EC ₅₀ 0.9 mg/L, 3.1 mg/L 24h; 1.2 mg/L and 1.3 mg/L 48h; 0.07 mg/L 21d; LC ₅₀ 0.1 mg/L 21d; <i>Hydra</i> EC ₅₀ 1.8 mg/L 96h; <i>Thamnocephalus</i> LC ₅₀ 0.6 mg/L 24h	MSDS: <i>Oncorhynchus</i> LC ₅₀ 12,900-15,300 mg/L 96h; <i>Pimephales</i> LC ₅₀ 0.3 mg/L 96h. Literature: LC ₅₀ @ pH 6.5 0.5 mg/L 7d; EC ₅₀ (growth) @ pH 6.5 0.54 mg/L 7d; @ pH 7.5 0.13 mg/L 7d; & @ pH 8.5 0.05 mg/l 7d; EC ₅₀ (feeding rate) @ pH 6.5 0.2 mg/L 7d; @ pH 7.5 0.15 mg/L 7d; @ pH 8.5 0.08 mg/L 7d [128]. WikiPharma: <i>Oncorhynchus</i> LC ₅₀ 0.38 mg/L96h; <i>Pimephales</i> LC ₅₀ 1.9, 2.3 and 2.7 mg/L 48h; EC ₅₀ 0.05 -0.5 mg/L 7d	MSDS: <i>Pseudokirchneriella</i> NPDES EC ₅₀ 0.03 mg/L 96h; <i>Skeletonema</i> NPDES EC ₅₀ 0.03 mg/L 96h; <i>Pseudokirchneriella</i> TAD NOEC 0.033 mg/L 12d. Toxicity to wastewater treatment microorganisms may occur. In the environment, the active ingredient in this formulation is expected to remain in water or migrate through the soil to groundwater. Releases to the environment should be avoided. Literature: <i>Chlorella</i> IC ₅₀ 0.8 mg/L 96h [127]. Predicted: algae EC ₅₀ 118 mg/L Ecosar.. WikiPharma: <i>Chlorella</i> IC ₅₀ 0.8 mg/L 96h; <i>Crassostrea</i> EC ₅₀ 1.1 mg/L 24h; 0.07 mg/L 36h; <i>Haliotis</i> EC ₅₀ 0.7 and 4.4 mg/L 48h; <i>Pseudokirchneriella</i> EC ₅₀ 0.04 mg/L 48h; 0.1 and 0.2 mg/L 72h; IC ₅₀ 0.01 mg/L 96h; <i>Scenedesmus</i> IC ₅₀ 0.1 and 0.3 mg/L 96h; <i>Skeletonema</i> EC ₅₀ 0.07 mg/L 72h; <i>Vibrio</i> EC ₅₀ 11 mg/L 5min; 9.2 mg/L 15min and7.3 mg/L 30min; <i>Xenopus</i> EC ₅₀ 3.3 mg/L 96h; LC ₅₀ 3.9mg/L 96h.	ND
Terbutaline 23031-32-5	Pulmonary	3 (3,0,0)	Insignificant	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.
Tetracaine 136-47-0	LA	ND	ND	MSDS; Literature: ND Predicted: <i>Daphnia</i> or mysid shrimp EC ₅₀ or LC ₅₀ 1.4 mg/L(Ecosar v0.99g).	MSDS; Literature: ND Predicted: <i>Cyprinodon</i> LC ₅₀ 1.2 mg/l (Topkat v6.1); fish LC ₅₀ 11.4mg/L(Ecosar v0.99g); 69,317 mg/L (Oasis Forecast M v1.10); 2.5 mg/L (Aster); 3.4 mg/L (PNN); 2.15E-001 mg/L(Neutral Organics QSAR);EC ₅₀ or LC ₅₀ 1.4mg/L (Ecosar v0.99g).	MSDS; Literature: ND Predicted: Algae EC ₅₀ or LC ₅₀ 1.4 mg/L(Ecosar v0.99g).	ND
Timolol 26839-75-8 Blocadren	CVS	ND (ND,0,ND)	Cannot Be Excluded	MSDS: <i>Daphnia</i> LC ₅₀ 161 mg/L 48 h Literature; Predicted: ND	MSDS: <i>Pimephales</i> LC ₅₀ 411 mg/L 96 h Literature; Predicted: ND	MSDS: Does not have significant aquatic toxicity. Based on ASRIT results, concentrations must be >1000 mg/L to inhibit an unacclimated sludge system in a sewage treatment plant. Literature; Predicted: ND. WikiPharma: <i>Eisenia</i> LC ₅₀ >2000 mg/L 14d.	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.

Topiramate 97240-79-4 TOPAMAX®	CNS	4 (3,0,1)	Insignificant	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS; Literature; Predicted: ND	ND
Tramadol 22204-88-2 36282-47-0 53611-16-8 ULTRAM(R)	CNS	ND(ND,0,ND)	Cannot be excluded	MSDS; Literature; Predicted: ND	MSDS: <i>Carassius</i> ^{uu} LC ₀ 5 mg/l 96 h; LC ₅₀ 6.2 mg/l 96 h; LC ₁₀₀ 7.5 mg/l 96 h Literature; Predicted: ND	MSDS; Literature; Predicted: ND WikiPharma: <i>Pseudomonas</i> ^{vv} EC ₅₀ >4000 mg/L 16h.	Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.
Trazodone 25332-39-2 DESYREL®	Psy	ND	Not Rated	MSDS; Literature: ND Predicted: <i>Daphnia</i> , or mysid shrimp EC ₅₀ or LC ₅₀ 1.5 mg/l(Ecosar v0.99g)	MSDS; Literature: ND Predicted: fish LC ₅₀ 0.4 mg/l (Ecosar v0.99g); LC ₅₀ 5.7 mg/l (Aster); LC ₅₀ 31mg/l (PNN); LC ₅₀ 2.01E-001 mg/l (Neutral Organics QSAR); fish, EC ₅₀ or LC ₅₀ 1.5 mg/l(Ecosar v0.99g).	MSDS; Literature: ND Predicted: algae EC ₅₀ or LC ₅₀ 1.5 mg/l(Ecosar v0.99g).	ND
Triamcinolone 76-25-5 Kenalog®	ED	4 (3,0,1)	Cannot be excluded	MSDS:Acute Toxicity to aquatic invertebrates: EC ₅₀ > 100 mg/l 48h20 - 25°C. Literature; Predicted: ND	MSDS; Literature; Predicted: ND	MSDS: Not Readily Biodegradable. Literature; Predicted: ND	Disposal by incineration is recommended.

A total of 12,345 drug records for dispensing and waste collection were reviewed; 4,889 records from the 630 bed Albany Medical Center Hospital and 7,257 records from the 20 bed South Clinical Campus of Albany Medical Center. The contents of 199 pharmaceutical waste collection containers placed at SCC were sorted by hand and the results tabulated by location, medication form and weight of units discarded. Weights are for active ingredient, e.g. a 1 g dose of acetazolamide was recorded as 1 g regardless of the total weight of the drug formulation.

N.b. MSDS = Material Safety Data Sheet (Safety Data Sheet –Global Harmonization). WikiPharma = WikiPharma database (<http://www/WikiPharma.org>) is a compilation of publicly available ecotoxicity data for human pharmaceuticals available in Sweden.

a. Class – pharmaceutical is used to treat disease (e.g., Ophtho = eye; Pulmonary – lung function; Psy = mood altering; CVS = cardiovascular; CNS = central nervous system; ED = endocrine; Mus = musculo-skeletal; NS – nervous system, GI – gastrointestinal; Renal – kidney; Radiology – imaging, LA = local anesthetic).

b. Ecotoxicity: from material safety data sheets (MSDSs).

c. CAS# - Chemical Abstracts Services unique chemical identification number.

d. PBT : persistence, bioaccumulation, and toxicity (0 – 3 range for each, with zero being the most benign).

e. Risk: defined as - cannot be excluded, insignificant, low, moderate, and high

f. Disposal – from MSDSs - n.b., does not apply to consumers or end users – refer to US FDA guidelines and office of national drug control policy (ONDCP, 2007).

g. ND = no data available or not determined.

h. *Daphnia*: crustacean, water flea.

i. *EC50*: concentration of a material which is expected to cause an adverse biological effect on 50% of the test organisms – acute toxicity.

j. *LC50*: lethal concentration that kills 50% of the test organisms – acute toxicity.

k. *Oncorhynchus*: rainbow trout, fish.

l. *Cyprinodon*: minnow, fish

m. *Ceriodaphnia*: invertebrate, crustacean

n. *Pseudokirchneriella* (AKA: *Synechococcus*):unicellular cyanobacteria

o. *Scenedesmus*:green algae.

p. *Desmodesmus*:green algae.

q. *ErC50*:is theEC50 of growth rate reduction in 72 hours, acute toxicity.

r. *Artemia*: brine shrimp, invertebrate, crustacean.

s. *Brachionus*: rotifer, invertebrate.

t. *Streptocephalus*:fairy shrimp,invertebrate, crustacean.

u. *Hydra*:Cnidarian, invertebrate.

v. *Photobacterium*:bioluminescent, gram-negative bacteria.

w. *Spirostomum*: ciliated protozoan.

x. *Tetrahymena*:ciliated protozoan.

y. *Thamnocephalus*:fairyshrimp, crustacean.

z. *Oryzias*: ricefish.

aa. *Vibrio*: gram-negative bacteria.

bb. *Pimephales*:fathead minnow, fish.

cc. *Danio*: zebrafish, fish.

dd. *IC50*: concentration of a material in water which is expected to cause an inhibitory effect on 50% of the test organisms – acute toxicity.

ee. *Leuciscus*: orfe,fish.

ff. *Eisenia*: common earthworm.

gg. *Eisenia*: common earthworm.

hh. *EbC50*: is the EC50 of the reduction in biomass growth in 72 hours, acute toxicity.

ii. *Chironomus*: midge, arthropod.

jj. *Hyalella*:amphipod crustacean.

kk. *Plationus*: rotifer, invertebrate.

ll. *Gambusia*: mosquitofish.

mm. *Chlorella*: green algae.

nn. *Crasostrea*: oyster, shellfish.

oo. *Dunaliella*: green algae.

pp. *Haliotis*: abalone, shellfish.

qq. *Lemna*: snail.

rr. *Skeletonema*: diatom.

ss. *Xenopus*: clawed frog.

tt. *Brachydanio*: fish.

uu. NOEC: no observable effect concentration, concentration of a material that causes no observable effect on test organisms – acute toxicity.

vv. *Carassius*: goldfish.

ww. *Pseudomonas*: common environmental bacteria.

xx. *Rasbora*: harlequin fish.

Table 2: Summary of Metabolism and Excretion of the Most Frequently Wasted and Discarded Pharmaceuticals at an Academic Medical Center Hospital and a Surgical Care Center in Albany, NY					
Pharmaceutical – Drug Class ^a		Metabolism - Excretion ^b			
Generic Name (CAS # ^c -Trade name [®])	Drug Class	Metabolism ^d	Active Metabolites ^e	Excretion of Parent Compound ^f	Drug Conjugates (glucuronides) Excreted ^g
Acetazolamide 59-66-5 Diamox [®]	Ophtho	N ^h	N	Y90% ⁱ	N
Albuterol 51022-70-9 Proventil [®]	Pulmonary	Y ^j	ND ^k	Y	ND
Albuterol and Ipratropium 66985-17-9 and 51022-70-9 Combivent [®]	Pulmonary	Y	ND	Y50%(Ipra.) Y10.2-30.8%(Alb.)	ND
Dexamethasone 50-02-2 Decadron	ED	Y	ND	Y65%	ND
Diatrizoatemeglumine 131-49-7 Gastrografin [®]	Radiology	N	N	Y95-100%	ND
Gadodiamide 131410-48-5 Omniscan [®]	Radiology	N	N	Y95%	ND
Glycopyrrolate 596-51-0 Rubinol [®]	Ophtho	N	N	Y80%	ND
Ibuprofen 15687-27-1 Advil [®]	NSAID	Y100%	N	Y	ND
Insulin 160337-95-1 Lantus [®]	ED	Y	N	N	N
Iopamidol 60166-93-0 Isovue [®]	Radiology	N	N	Y90% (Urine) 1% (Fecal)	ND
Ketorolac 74103-07-4 Toradol [®]	Mus	Y40%	N	Y60% (Urine) 6% (Fecal)	N
Mepivacaine 1722-62-9 Polocaine [®]	LA	Y90%	N	Y5-10%	ND

Metoprolol 83-43-2 Lopressor®,	CVS	Y	N	Y~5%	ND
Neostigmine 59-99-4 Prostigmin®	Ophtho	Y30%	N	Y50%	ND
Nicardipine 54527-84-3 / 55985-32-5 Cardene IV®	CVS	Y 99%	N	Y <1%	Y
Nitroglycerine 55-63-0 Nitrostat®,	CVS	Y	Y	N	ND
Ondansetron 99614-02-5 Zofran®	GI	Y95%	N	Y05%	Y
Oxymetazoline 2315-02-8 Afrin®	NS	N	N	Y	ND
Phenylephrine 61-76-7 Neo-Synephrine®	CVS	Y ^g	N ^h	Y12% ⁱ	ND ^j
Prednisone 53-03-2 Deltasone®	ED	Y	Y	Y	Y

A total of 12,345 drug records for dispensing and waste collection. There were 4,889 records at the 630 bed Albany Medical Center Hospital and 7,257 records for the 20 bed South Clinical Campus of Albany Medical Center. The contents of 199 pharmaceutical waste collection containers placed at SCC were sorted by hand and the results tabulated by location, medication form and weight of units discarded. Weights are for active ingredient, e.g., a 1g dose was recorded as 1g regardless of the total weight of the drug formulation.

a. Class – pharmaceutical is used to treat disease (e.g., Ophtho = eye; Pulmonary – lung function; Psy = mood altering; CVS = cardiovascular; CNS = central nervous system; ED = endocrine; Mus = musculo-skeletal; NS – nervous system, GI – gastrointestinal; Renal – kidney; Radiology – imaging, LA = local anesthetic).

b. Metabolism — Excretion: data are summarized from official government drug monographs and labels Drugs@FDA (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>); DailyMed (<http://dailymed.nlm.nih.gov/dailymed/about.cfm>), RxList (http://www.rxlist.com/drugs/alpha_a.htm), Drugs.com (<http://www.drugs.com/>) and the Hazardous Substances Data Bank, United States National Library of Medicine TOXNET Toxicology Data Network (<http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>). Where data were insufficient, a search of the primary literature was conducted.

c. CAS# - Chemical Abstracts Services unique chemical identification number.

d. Metabolism: indicates the drug undergoes change in the body.

e. Active Metabolites: indicates the drug is changed in the body to pharmacologically active compounds prior to excretion, thus the risk to the environment from the excreted drug may reside in its metabolites and not in the parent compound.

f. Excretion of Parent Compound: indicates that the drug, or a portion of the dose, is excreted unchanged.

g. Drug Conjugates (glucuronides) Excreted: indicates excretion (urine or feces) of drug as conjugate.

h. N: no.

i. Value within parentheses: the percent of the drug that is excreted unchanged or the percent of the drug that is metabolized unchanged. Y (fecal and 10 – 40% urine) indicates that some fraction of the drug is excreted in the feces unchanged and from 10 to 40% of the drug is also excreted in the urine unchanged. Y (<5%) indicates that less than 5% of the drug is metabolized, more than 95% is not].

j. Y: yes.

k. ND: not determined, no data available.

Supplemental Table 2: Summary of Metabolism and Excretion of Wasted and Discarded Pharmaceuticals at an Academic Medical Center Hospital and a Surgical Care Center in Albany, NY.

Pharmaceutical –Drug Class ^a		Metabolism - Excretion ^b			
Generic Name (CAS # ^c -Trade name®)	Drug Class	Metabolism ^d	Active Metabolites ^e	Excretion of Parent Compound ^f	Drug Conjugates (glucuronides) Excreted ^g
Acetylcholine 60-31-1 Miochol ®	Ophtho	Y ^h	N ⁱ	N	N
Alprazolam 28981-97-7 Xanax ®	Psy	Y	N	Y	ND ^j
Amiodarone 1951-25-3 Cordarone	CVS	Y	Y	Y	ND
Benztropine 132-17-2	CNS	ND	ND	Y	ND

Betamethasone 378-44-9 Celestone ®,	ED	Y	ND	Y	ND
Brimonidine 59803-98-4 Alphagan ®	Ophtho	Y	N	Y	N
Bupivacaine and Epinephrine 14252-80-3 and 51-43-4 Marcaine®	LA	Y	N	Y(5%) ^k	N
Clozapine 5786-21-0 Clozaril®,	Psy	Y	N	Ytrace	N
Cyclopentolate 512-15-2 Cyclogyl®)	Ophtho	ND	ND	ND	ND
Dantrolene 14663-23-1 Dantrium IV	Mus	Y	ND	Y	ND
Diphenhydramine 58-73-1 Benadryl ®	Pulmonary	Y55%	ND	Y45%	ND
Dorzolamide hydrochloride and Timolol maleate 130693-82-2 and 26921-17-5 COSOPT®	Optho	Y	Y	Y	N
Esmolol 1161-17-3 BREVIBLOC	Ns	Y	N	Y2%	N
Esomeprazole 119141-88-7 Nexium®	GI	Y	N	Y<1%	N
Flurbiprofen 5104-49-4 Ocufen	Ophtho	Y	Y	Y3%	Y
Furosemide 54-31-9 LASIX®	Renal	Y	Y	Y	Y
Hydralazine 304-20-1 Apresoline®	CVS	Y	N	Y	N
Labetalol 36894-69-6 TRANDATE®	CVS	Y	N	Y	Y
Methylprednisolone 83-43-2 SOLU MEDROL®	ED	Y	Y	Y	Y
Metoclopramide 7232-21-5 REGLAN®	GI	Y	ND	Y85%	Y
Pilocarpine 92-13-7 PILOPINE HS®,	Optho	Y	N	Y	ND
Promethazine 60-87-7 PHENERGAN®	Pulmonary	Y	Y	N	N
Terbutaline 23031-32-5	Pulmonary	Y	N	Y60% (Urine) 6% (Fecal)	Y
Tetracaine 136-47-0	LA	Y	N	N	N
Triamcinolone 76-25-5 Kenalog®	ED	Y	N	Y40% (Urine) Y 60% (Fecal)	ND
Tropicamide 1508-75-4 MYDRIACYL®,	Ophtho	ND	ND	ND	ND
Vasopressin 24564-52-1 Pitressin	CVS	Y	N	Y5%	N

Verapamil 152-11-4 CALAN®	CVS	Y	ND	Y3-4%	ND
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A total of 12,345 drug records for dispensing and waste collection were reviewed. These were 4,889 records at the 630 bed Albany Medical Center Hospital and 7,257 records for the 20 bed South Clinical Campus of Albany Medical Center. The contents of 199 pharmaceutical waste collection containers placed at SCC were sorted by hand and the results tabulated by location, medication form and weight of units discarded. Weights are for active ingredient, e.g. A 1 g dose of acetazolamide was recorded as 1 g regardless of the total weight of the drug formulation.

xx. Class – pharmaceutical is used to treat disease (e.g., Ophtho = eye; Pulmonary – lung function; Psy = mood altering; CVS = cardiovascular; CNS = central nervous system; ED = endocrine; Mus = musculo-skeletal; NS – nervous system, GI – gastrointestinal; Renal – kidney; Radiology – imaging, LA = local anesthetic).

yy. Metabolism — Excretion: data are summarized from official government drug monographs and labels Drugs@FDA (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>); DailyMed (<http://dailymed.nlm.nih.gov/dailymed/about.cfm>), RxList (http://www.rxlist.com/drugs/alpha_a.htm), and Drugs.com (<http://www.drugs.com/>). Where data were insufficient, a search of the primary literature was conducted.

zz. CAS# - Chemical Abstracts Services unique chemical identification number.

aaa. Metabolism: indicates the drug undergoes change in the body.

bbb. Active Metabolites: indicates the drug is changed in the body to pharmacologically active compounds prior to excretion, thus the risk to the environment from the excreteddrug may reside in its metabolites and not in the parent compound.

ccc. Excretion of Parent Compound: indicates that the drug, or a portion of the dose, is excreted unchanged.

ddd. Drug Conjugates (glucuronides) Excreted: indicates excretion (urine or feces) of drug as conjugate.

eee. Y=yes.

fff. N=no.

ggg. ND=not determined, no data available.

hhh. Value within parentheses: the percent of the drug that is excreted unchanged [e.g., Y (5%) indicates that 5% of the drug is excreted unchanged, 95% is not].

Drugs Dispensed, Wasted or Discarded by Therapeutic Class

As depicted in the pie chart (Figure 2), a total of 84 drugs were wasted from 14 separate therapeutic classes. Drugs affecting the cardiovascular system (CVS) were the most numerous (20), followed by psychiatric drugs (PSY) at 17, drugs used in ophthalmology (Ophtho) at 10, central nervous system drugs (CNS) at 9, regulated hazardous drugs (RCRA) at 7 and endocrine disrupting (ED) drugs at 5. Other therapeutic classes each had but 1 to 3 drugs wasted (Figure 2).

Figure 2: Wasting of 84 Drugs by 14 Therapeutic Classes

Total wasting by therapeutic class is depicted in the bar graph (Figure 3). Almost 2.3 kg of drugs were wasted with 5 classes accounting for nearly 80% of the waste (Ophtho, Radiology - Imaging, CVS, RCRA and local anesthetics - LA). In each therapeutic class one drug contributed the majority of waste: neostigmine – Ophtho; gadodiamide – Radiology-Imaging; phenylephrine – CVS; insulin – RCRA; mepivacaine – LA (local anesthetic); oxymetazoline – PNS (peripheral nervous system); dexamthasone – ED;

ondansetron – GI (gastro-intestinal); diphenhydramine – Pul (pulmonary); ketorolac – NSAID (anti-inflammatory); esmolol – CNS; alprazolam – PSY (psychiatric); furosemide – Renal; dantrolene – NUS/MR (muscle/muscle

Figure 3: Weight of Drugs Wasted by Therapeutic Class.

relaxant).

Nearly 2.3 kg of 84 individual drugs representing 5 therapeutic classes were wasted or discarded. Twelve drugs (Figure 4) accounted for over 80% of the drug waste. The remaining 72 drugs or drug combinations (e.g., albuterol and ipratropium) contributed only 20% of the wasting.

Overall, drug wasting averaged 3% but was not uniform, varying from over 57% for insulin to about 0.2% for vasopressin (Figure 5).

As depicted in the bar graph (Figure 6), almost 56 kg of drugs were dispensed with 5 therapeutic classes (NSAID, CVS, GI, RCRA and ED) accounting for almost 80% of the drug dispensed. In each therapeutic class, one drug contributed the majority of the waste.

As depicted in Figure 7; 56 kg of 85 drugs were dispensed. Fifteen drugs accounted for over 80% of the total weight of drug dispensed while

Figure 4: Bar graph of cumulative drug waste (in grams) from two healthcare facilities

A total of 12,345 drug records for dispensing and waste collection were reviewed. There were 4,889 records at the 630 bed Albany Medical Center Hospital and 7,257 records for the 20 bed South Clinical Campus of Albany Medical Center. The contents of 199 pharmaceutical waste collection containers placed at SCC were sorted by hand and the results tabulated by location, medication form and weight of units discarded. Weights are for active ingredient, e.g., a 1g dose was recorded as 1g regardless of the total weight of the drug formulation. In this study, 12 drugs accounted for over 80% of the drug waste.

Figure 5: Bar graph of drug wasting as a percentage of drugs dispensed from two healthcare facilities

A total of 12,345 drug records for dispensing and waste collection were reviewed. There were 4,889 records at the 630 bed Albany Medical Center Hospital and 7,257 records for the 20 bed South Clinical Campus of Albany Medical Center. The contents of 199 pharmaceutical waste collection containers placed at SCC were sorted by hand and the results tabulated by location, medication form and weight of units discarded.

Figure 6: Weight of Drugs Dispensed by Therapeutic Class

A total of 12,345 drug records for dispensing and waste collection were reviewed; 4,889 records from the 630 bed Albany Medical Center Hospital and 7,257 records from the 20 bed South Clinical Campus of Albany Medical Center. The contents of 199 pharmaceutical waste collection containers placed at SCC were sorted by hand and the results tabulated by location, medication form and weight of units discarded. Weights are for active ingredient, e.g. a 1 g dose of acetazolamide was recorded as 1 g regardless of the total weight of the drug formulation.

Class – pharmaceutical is used to treat disease (e.g., Ophtho = eye; Pulmonary – lung function; Psy = mood altering; CVS = cardiovascular; CNS = central nervous system; ED = endocrine; Mus = musculo-skeletal; NS – nervous system, GI – gastrointestinal; Renal – kidney; Radiology – imaging, LA = local anesthetic).

Figure 7: Bar graph of cumulative drugs dispensed (in grams) from two healthcare facilities

A total of 12,345 drug records for dispensing and waste collection were reviewed from 2008 and 2009. There were 4,889 records for a one week period in April, 2009 at the 630 bed Albany Medical Center Hospital and 7,257 records from August, 2008 through February, 2009 for the 20 bed South Clinical Campus of Albany Medical Center. The contents of 199 pharmaceutical waste collection containers from August, 2008 through February, 2009 placed at SCC were sorted by hand and the results tabulated by location, medication form and weight of units discarded. Weights are for active ingredient, e.g., a 1g dose was recorded as 1 g regardless of the total weight of the drug formulation. In this study, 15 drugs accounted for over 80% of the drug dispensed.

68 drugs comprised the remaining 20% (note one drug was dispensed but not wasted).

Cost of Wasting

Based on pricing data provided by the participating pharmacy

department, the value represented by the wasted and discarded drugs exceeded \$111,000. As depicted in Figure 8, the most costly drug wasting was associated with neostigmine, which accounted for nearly 30% of the discarded value (\$31,692). Acetazolamide, dexamethasone,nitroglycerine, ondansetron, phenylephrine and tetracaine accounted for the rest of the

Figure 8: Bar graph of the cumulative cost of drug wasting from two healthcare facilities

Values were based on pricing data provided by the participating pharmacy department. A total of 12,345 drug records for dispensing and waste collection were reviewed; 4,889 records from the 630 bed Albany Medical Center Hospital and 7,257 records from the 20 bed South Clinical Campus of Albany Medical Center. The contents of 199 pharmaceutical waste collection containers placed at SCC were sorted by hand and the results tabulated by location, medication form and weight of units discarded. Note that seven drugs accounted for over 80% of the costs of drugs wasted.

top 80% of drugs wasted, for an aggregate total of almost \$91,000.

PBT and Environmental Risk Ratio (PEC/PNEC) of Healthcare Pharmaceuticals

Five of the top 12 wasted and dispensed drugs have PBT scoring values, with ondansetron a 6 of 9, oxymetazoline a 5 of 9, albuterol and mepivacaine a 4 of 9 and gadodiamide a 3 of 9. All 5 are considered very persistent (P value of 3 of 3; not readily biodegradable) and none were bioaccumulative (B value of 0 of 3, no bioaccumulation). Ondansetron is considered "very highly toxic" (T value of 3 of 3; EC50, IC50 or LC50<1.0 mg/L), oxymetazoline is "highly toxic" (T value of 2 of 3 EC50, IC50 or LC50 of 1.0 to 10 mg/L), albuterol and mepivacaine are "moderate toxicity" (T value of 1 of 3; EC50, IC50 or LC50 of 10 to 100 mg/L), and gadodiamide was "low toxicity" (T value of 0 of 3; EC50, IC50 or LC50>100 mg/L). The environmental risk ratio (PEC/PNEC) for gadodiamide and ondansetron is "Insignificant" (PEC/PNEC <0.1) and neostigmine, mepivacaine, oxymetazoline, albuterol, and dexamthasone are considered "Cannot Be Excluded" (no data for environmental risk ratio; Table 1).

For the other drugs amongst the top 80% most dispensed, (Table 1), the PBT index values ranged from 6 of 9 for ipratropium, 4 of 9 for albuterol, ketorolac, and metoprolol; and 2 of 9 for ibuprofen. Albuterol and ipratropium, ketorolac and metoprolol are "very persistent" while ibuprofen is not. None are "bioaccumulative" (B value 0 of 3). Ipratropium

is "very highly toxic" (EC50, IC50 or LC50<1.0 mg/L), ibuprofen "highly toxic" and albuterol, ketorolac and metoprolol are "moderately toxic". The environmental risk ratio for ibuprofen, ipratropium, ketorolac and metoprolol are "Insignificant" while albuterol and prednisone are considered "Cannot Be Excluded".

Ecotoxicity of the Most Frequently Wasted and Discarded Drugs

Invertebrates

As depicted in Table 1, four drugs (dexamethasone, ibuprofen, neostigmine and nitroglycerine) are very highly toxic to invertebrates (EC50, IC50 or LC50 values of <1.0 mg/L). Dexamethasone has the greatest chronic toxicity to Ceriodaphnia of 0.05 ppm (or mg/L; 7 d EC50). Ibuprofen is extremely chronically toxic (28d EC50 of 0.0007 mg/L) to the crab (Carcinus) and very highly toxic (96hr EC50 of 0.4 mg/L) to zebra mussel (Dreissena). Ibuprofen toxicity was variable from high to moderate (96 hr EC50, IC50 and LC50 of 1.7 mg/L to 22 mg/L) to Hydra. Neostigmine is very highly acutely toxic to Daphnia with a 24 hr EC50 of less than 1 mg/L. Nitroglycerine is predicted to be very highly toxic to Daphnia (EC50 of 0.0000156 mg/L, Topkat software program). Mepivacaine, metoprolol, neostigmine and prednisone are highly toxic (acute and chronic) to Daphniaor Hydrawith EC50 or LC50 values of from >1 mg/L to 10 mg/L. Metopropol is highly toxic to Ceriodaphnia (24 and 48 hr LC50

of >1 mg/L to <10 mg/L). Metoprolol toxicity is variable, ranging from a low of 2.6 mg/L (24hr, 48hr EC50) for Daphnia; 8.8 mg/L (48hr LC50) for Ceriodaphnia and Hyalella; 45.3 mg/L (48hr EC50) for Ceriodaphnia; 64 – 76 mg/L (48hr EC50) for Daphnia; and to >100 mg/L (48hr EC50) for Daphnia, Hyalella and Thamnocephalus. Prednisone is chronically highly toxic to Ceriodaphnia (7 d IC50>2.0 mg/L). Dexamethasone is moderately toxic to Brachionus (rotifer) and Thamnocephalus (fairy shrimp) with a 24 hr LC50 of 48 or 60 mg/L, respectively. Ibuprofen was moderately toxic to the freshwater snail Planorbis (48hr LC50 of 17 mg/L). Metoprolol was moderately lethal to Thamnocephalus after 24 hr of exposure (LC50 of 78 mg/L) but of low toxicity after only 1 hr (EC50>100 mg/L). Nitroglycerine is acutely and chronically toxic (EC50 or LC50>10 mg/L to <100 mg/L) to Daphnia. Oxymetazoline, ondansetron and dexamethasone are also acutely toxic to Daphnia with EC50 values (>10 mg/L to <100 mg/L reported in the MSDS/SDS). Phenylephrine, the most wasted drug, is acutely toxic to Daphnia, with a predicted EC50 or LC50 of 58 mg/L. Prednisone was also toxic to Brachionus (24hr LC50 of 55 mg/L). Acetazolamide, albuterol, ipratropium, insulin and ketorolac are of low toxicity to Daphnia (EC50 or LC50 values >100 mg/L). Diatrizoate meglumine, gadodiamide, glycopyrrolate, iopamidol and nicardipine have no toxicity data available for aquatic invertebrates.

Fish

Acetazolamide is very high toxicity to fish (<1 mg/L) with a value of 0.001 mg/L for 120hr LC83, but is predicted to be of low toxicity (LC50 value of >1000 mg/L, Ecosar, Aster, PNN and Neutral Organics QSAR computer programs). Ibuprofen is predicted to be very highly toxic to fish (LC50<1 mg/L, Neutral Organics QSAR in the ECOSAR computer program). However, the 96 hr LC50 for ibuprofen was variable from moderately toxic (89 mg/L) for Oryzias to low toxicity (>100mg/L) for Lepomis. Mepivacaine, ondansetron are highly toxic to fish (EC50 or LC50 values of <10mg/L). Nitroglycerine is highly toxic to fish with a LC50 of 1.4 mg/L as reported by the MSDS/SDS and predicted by Neutral Organics QSAR (LC50 of 4.8 mg/L) but is essentially non-toxic (LC50>100 mg/L) as predicted by Aster, Ecosar, Oasis Forecast and PNN computer programs. Ketorolac, metoprolol, oxymetazoline and phenylephrine are essentially non toxic to fish with EC50 or LC50 values >100 mg/L, despite one value for metoprolol reported at 31 mg/L for a 72hr EC50. Albuterol, dexamethasone, diatrizoate meglumine, gadodiamide, glycopyrrolate, insulin, iopamidol, ipratropium, neostigmine and nicardipine have no ecotoxicity data available for fish as depicted in Table 1.

Other

Ondansetron is very highly toxic to green algae (Pseudokirchneriella) with a 24 hr IC50 of less than 1 mg/L (Table 1). Insulin is moderately toxic (EC50 10-100 mg/L) to algae (72 h EC50 of 19 to 33 mg/L). Ibuprofen had high to low toxicity values for algae and other organisms ranging from a high toxicity (7d EC50 of 1.0 mg/L) for the vascular plant duckweed (Lemna); moderate toxicity (5d EC50 of 40 mg/L) for the algae Skeletonema and bacteria Vibrio (15 min EC50 values of 11 to 19 mg/L) to low toxicity (96 h EC50 of >100 mg/L) for the algae Pseudokirchnerella and Desmodesmus (3d EC50). Ibuprofen was moderately toxic to African clawed frog Xenopus tadpoles 3 (96h EC50 of 40 mg/L and 57 mg/L). Mepivacaine is predicted to be highly toxic (EC50 or LC50 of 5.3 mg/L, Ecosar) to algae. Metoprolol

was high to moderately toxic to Desmodesmus (3d EC50 of 7.3 mg/L; 48 h EC50 of 7.9 mg/L; and 24 h EC50 of 40 mg/L) or green algae (72 h ErC50 value of 58.3 mg/L); moderate (EC50 value of 14.5 mg/L) to low toxicity (30 min EC50 value of >100 mg/L) to Vibrionibacteria; and low toxicity to Lemna (7 d EC50 value of >100 mg/L or >320 mg/L). Nitroglycerine is predicted to have moderate chronic toxicity (EC50 21 mg/L, Ecosar) and low acute toxicity EC50 or LC50>100 mg/L, Ecosar) to algae. Prednisone was moderately toxic to algae (Pseudokirchnerella with a 72h IC50 of 31 mg/L) while acetazolamide (Ecosar, acute and chronic EC50 or LC50>100 mg/L), dexamethasone (Pseudokirchnerella 72 h EC50>100 mg/L) and ketorolac (Chlorella EC50>1000 mg/L) had low toxicity to algae. Activated sludge toxicity was extremely low and recorded at >1000 mg/L for insulin and ondansetron. Albuterol, diatrizoate meglumine, gadodiamide, glycopyrrolate, iopamidol, ipratropium, neostigmine and nicardipine have no ecotoxicity data available for algae or other aquatic organisms.

Recommended Disposal

Incineration was recommended by the MSDS/SDS for dexamethasone, insulin, nicardipine and prednisone. Iopamidol is accompanied by a warning in the MSDS/SDS not to dispose in household garbage or into the sewer system. No method of disposal was recommended by the MSDS/SDS for 15 of the top wasted or dispensed pharmaceuticals (Table 1).

Metabolism and Excretion

As depicted in Table 2, all but 2 (insulin and nitroglycerine) of the “wasted”, discarded or dispensed pharmaceuticals were excreted as parent compound in the urine and or feces of human patients, at levels from 5 to 100% of the administered dose. Fourteen of these underwent metabolism in vivo but active metabolites were formed from only two (nitroglycerine and prednisone). Nicardipine, ondansetron and prednisone formed potentially reversible drug conjugates (predominantly glucuronides) which were excreted in the urine, feces or underwent enterohepatic recirculation (Table 2).

Discussion

The present communication found that over 56 kg of 84 drugs from 14 therapeutic classes were dispensed in two Albany, New York hospitals. Of this 56 kg, only 2.3 kg of drug (as active ingredient) worth in excess of \$111,000 was discarded. Others have reported detectable levels of drug waste in effluents of healthcare facilities [16, 60, 74]. Sim et al. [16] assayed twenty-four (24) different drugs in Korean wastewater finding ug/L levels of pharmaceuticals in hospital effluent. Olivera et al. [71] measured 185 pharmaceutical and personal care products by liquid chromatography – mass spectroscopy (LC-MS) in hospital effluent and wastewater in Suffolk County, USA finding very low levels ranging from undetectable (most) to 1.4 ug/L for erythromycin.

In previous studies [71, 72], wasting of propofol, other injectable drugs, and controlled substances (CS) was generally higher (4.1%) at the same facilities as reported herein. For example; Mankes [71] found that 41 liters of propofol emulsion and other liquid injectable surgical drugs were wasted of 150 liters dispensed. Mankes and Silver [72] reported that 8.5 kg of CS were wasted of 38 kg dispensed and 2.3 kg wasted of 56 kg dispensed in the present study. This contrasts to much lower (1.7%) wasting of antibiotic/antimicrobial drugs (Ab), found to be 1.3 kg

wasted of 77 kg dispensed [73]. This disparity between Ab wasting and other pharmaceuticals [71-74] may be due to the longstanding process of antibiotic stewardship [75].

Others [76] have concluded hospitals are not the main source of pharmaceutical waste in municipal sewage in Germany, with community use reported to be 70-75%, (on a defined daily dose or DDD basis). Application of the Pareto Principle (or 80-20 rule [77]) has been previously reported for propofol, controlled substances [71, 72] and other hospital processes [78-80]. For example, a process improvement team consisting of representatives from nursing, anesthesiology, and pharmacy could be charged with targeting the wasting of the top drugs as illustrated by “Lean-Six Sigma” [81]. Reduction in dispensing, sizes and strengths stocked, etc. could be enforced with a reduction in wasting [41, 71, 79].

In the present study, all but two of the wasted, discarded or dispensed drugs were excreted in whole or in part as active drug [18] or drug conjugates [3]. Kummerer [76] found that nearly 70% of drugs evaluated were excreted unchanged. We previously reported that injectable drugs [71], CS [72], or Ab [73] were metabolized in vivo or were highly biodegradable (e.g., propofol). In the case of Ab [73], the total drug discharged was representative of the total drug dispensed (77 kg) rather than just that which was wasted, thus complicating estimations of hospital discharge of drugs [82].

Others have assumed drug loads in hospital wastewater to be proportional to total dispensing [12] while Escher et al. [9] have advocated more complex computer simulations. In this report, Escher et al., [9] evaluated 100 drugs expected to occur in 2 hospitals’ wastewater. One was a 338 bed general hospital and the second a 211 bed psychiatric center. In the general hospital, the top-100 drugs dispensed totaled 1137 kg consumed and 777 kg excreted. X-ray contrast media was 58% of the excreted load, 19% from laxatives, 16% from antibiotics, and 8% from others.

As seen in our earlier studies, drug waste, although an overall average of 3%, was not uniform and varied from 0.2% (vasopressin) to as high as 57% (insulin). In previous studies, wasting of injectable surgical drugs varied from 12 to 48% of dispensed drug [71]; wasting of CS ranged from less than 0.1% to 49.5% of drug dispensed [72]; and wasting of Ab varied from 0.1% to 45% [73]. In the present study, the highest percentage of wasted drugs were not among those with the greatest absolute wasting (in grams). For example: insulin at 57.4% wasting accounted for only 140g of 2.3 kg wasted, while phenylephrine accounted for the most (329g) drug wasted but only 8.75% of the phenylephrine dispensed.

As noted, the costs of drug wasting in the present study exceeded \$111,000 and were primarily due to seven of 46 pharmaceuticals (acetazolamide, dexamethasone, neostigmine, nitroglycerine, ondansetron, phenylephrine and tetracaine). Others [83-86] have found that costs of drug wasting can be significant, ranging from \$185,000 for 543 surgical cases [83] up to \$30 billion annually [87]. In an earlier study, Mankes [71], found eliminating larger vial sizes of propofol, by stocking only 20 mL size had a significant reduction in propofol waste. Others also have advocated: reductions in vial sizes [84, 86, 88]; mandating drug take back and reissue programs [84]; use of prefilled syringes for surgical cases

[83]; use of sophisticated drug management software to increase reuse of anti-cancer drugs [85] or better managed short-stability and titratable products [89]. In any event, it is clear that small changes in pharmaceutical waste management can have a significant impact on pharmaceutical waste costs.

PBT, Environmental Risk Ratio and Ecotoxicity Analysis

As noted earlier, the PBT Index was developed in 2003 by the Stockholm County Council to rank the environmental impact of pharmaceuticals (<http://www.janusinfo.se/Beslutsstod/Miljo-och-lakemedel/About-the-environment-and-pharmaceuticals>). The PBT (persistence, bioaccumulation and toxicity) and environmental risk ratio system of drug comparison [90] is used by European governments (REACH - http://ec.europa.eu/environment/water/water-dangersub/pri_substances.htm) [91] as well as adopted by one US State (Oregon) [92-95]. One of our objectives is to determine if such data provides the hospital environmental professional with a method of ranking damaging drug wastes.

Persistence (as determined by OECD Test 301) [96] is important when evaluating the environmental impact of a contaminant. In the present study, we found eight drugs were considered “not readily biodegradable” or highly persistent (3/3) while only one (ibuprofen) was rated “readily biodegradable” (0/3 for persistence) and thus would not be expected to be long lived in the environment. Similarly, bioaccumulation (OECD Tests 107 and 111) [97-98] is a function of amplification within the environment and is seen with increasing concentrations (generally Log KOW or the log oil/water partition coefficient). None of the top wasted / dispensed drugs in the present study were considered potentially bioaccumulative.

The REACH PBT toxicity designations are based upon OECD Tests 201, 202 and 203 [99-101]. Four drugs (ibuprofen, ipratropium, ondansetron and oxymetazoline) were “very high” or “high” toxicity. Five drugs were considered “moderate” or “low” toxicity. In contrast, the toxicity values derived from the laboratory test results for crustaceans (*Daphnia*, *Ceriodaphnia*, *Thamnocephalus*, etc.), fish (*Cyprinodon*, *Oryzias*, *Lepomis*, etc.) and other (*Pseudokirchneriella*, *Desmodesmus*, *Lemna*, *Xenopus*, etc.) revealed that only 2 (neostigmine and ondansetron) were very highly toxic to *Daphnia* (neostigmine) or algae (ondansetron). Dexamethasone is very highly toxic to *Ceriodaphnia* (0.05 ppm or mg/L) after 7 days, while ibuprofen is very highly toxic to *Dreissena* (EC50 0.4 mg/L). Four drugs (ibuprofen, mepivacaine, nitroglycerine and ondansetron) are highly toxic to fish. Thus there appears to be poor correlation between the laboratory toxicity test results and the REACH PBT toxicity scoring. Recently, Mendoza et al. [102] analyzed 25 drugs and radiocontrast agents in effluents from a hospital. PBT and environmental risk values from the Stockholm County Council were presented. These values were not correlated to the results of the ecotoxicity reviews regardless of species. As noted in our previous communications for controlled substances and antimicrobial drugs [72-73], we recommend more complete laboratory derived aquatic toxicity data (e.g., EC50 or LC50 values for *Daphnia*, fish, algae and bacteria) be included in manufacturer MSDSs/SDSs for the most frequently wasted drugs, rather than an over reliance on PBT or the environmental risk ratio.

In general, toxicity values for pharmaceuticals are determined by

laboratory testing or predicted by models. Some sources of toxicity values such as MSDSs/SDSs, Wikipharma, and literature reviews [59] present both lab test and predicted data. In some instances lab testing results are dissimilar and appear contradictory. For example, acute lab data results for *Daphnia* (magna) for ibuprofen range from 31 mg/L to 132.6 mg/L [51, 103-105], an order of magnitude different. In other instances, lab data and predicted data can be dissimilar. Using ibuprofen as an example again, the acute laboratory toxicity result for fish (*Oryzias*) is 89 mg/L, while the predicted acute data for fish is 0.0318 mg/L (Neutral Organics QSAR in Ecosar), a difference of almost 2,800. These wide ranges can be problematic when applying a toxicity scale of <1 mg/L to indicate that a pharmaceutical is very highly toxic, 1-10 mg/L as very toxic, 11-99 mg/L as moderately toxic, and >100 mg/L as not toxic. Pharmaceuticals in this paper other than ibuprofen that present these potential data interpretation issues include insulin, metoprolol and nitroglycerine. We recommend more complete laboratory derived aquatic toxicity data rather than relying solely upon modeled data.

Metabolism and Excretion

Excretion of drugs has been considered a major source of pharmaceuticals in wastewaters [30, 40]. Hospital effluents are recognized as major sources of drugs [2, 60, 74, 102]. For most of the drugs studied herein, the official (FDA) manufacturer label provided adequate insight into the urinary and fecal excretion of the drug and its metabolites. For the top drugs that were both wasted and dispensed, 18 were excreted in urine and feces, 3 (nicardipine, ondansetron and prednisone) formed drug conjugates, while 2 (insulin, nitroglycerine) were not excreted, in whole or in part.

As noted by others [30, 40], our data suggest that for these 18 pharmaceuticals, excretion from patients, with or without direct hospital wasting, would be a major source in hospital effluent. Unfortunately, little data are available in the open literature for wastewater concentrations of these 18 pharmaceuticals [12, 45, 82]. Albuterol levels varied from 0.08-0.28 ug/L in hospital wastewater systems from Suffolk County, New York [74] while an average of 23 ng/L (range of 3.7-110 ng/L) was reported by Bernot et al. [106]. Santos et al. [60] found dexamethasone levels in hospital effluents ranging from undetectable to 352 ng/L. Ibuprofen is commonly detected in hospital effluents at ng/L levels (119 to 7090) [13, 102], or at ug/L levels (3.11)[107]. Metoprolol was found at levels from 1.57 to 32.8 ug/L in Suffolk County, NY [74] to 11.4 to 37.8 ng/L [3] or 35.6 ng/L to 830 ng/L [102].

Disposal and Destruction

The traditional method for “left over” drug disposal is to squirt any remaining liquid drug into a waste receptacle, sink or toilet [27, 68, 108]. The first federal (US) guidance for consumer disposal of drugs, issued in 2007, recommended discarding them in the household trash [108]. US consumers have been offered scheduled national “Drug Take Back Days” by the US Drug Enforcement Administration where excess drugs may be dropped off with drug enforcement officials prior to the drugs being disposed of responsibly. In healthcare facilities, pills are usually crushed and mixed with water and flushed or put into sharps containers [109]. Excluding disposal in a sharps container [110], these procedures increase

the likelihood that drugs will be released into the environment, as WWTP do not fully remove them [61, 62]. Recently, Phillips et al. [111] found septic systems in New York and New England contribute a wide variety of micropollutants, including pharmaceuticals, to shoreline wells. In the present study, drugs were discarded into pharmaceutical waste containers which were then sorted and shipped via commercial waste transporter to a secure incineration facility.

Recommendations for disposal methods are confusing and conflicting [27, 31, 112]. In the present study, only 5 of the twenty frequently wasted or discarded drugs had disposal recommendations provided by the MSDSs/SDSs. Incineration was recommended for 4 drugs (dexamethasone, insulin, nicardipine and prednisone) and one drug (iopamidol) it is not to be disposed of in the trash nor in the sewage. The MSDS/SDS for the other fifteen drugs provide no guidance regarding disposal. Seehusen and Edwards [113] surveyed disposal of medication practices and found incineration to be the best disposal option currently available. In any event, clear and detailed disposal recommendations are needed and should be included in a manufacturer’s MSDS/SDS. This would provide guidance and clarity to healthcare environmental professionals and pharmacy staff alike in designing and implementing pharmaceutical waste programs. In the study reported herein, all residual drugs were disposed offsite, in a permitted hazardous waste incineration facility and appropriate documentation was maintained throughout.

Conclusions

Pharmaceutical wasting in healthcare facilities, represented by two hospitals in Albany, New York, USA, can be identified and quantified by drug class, individual drug and costs of wasting. The 80-20 rule is applied to the data to focus remediation efforts upon the drugs accounting for the greatest waste in weight and costs. Potential for ecological damage by wasted drug is assessed by using MSDS/SDS, WikiPharma and open literature data for ecotoxicity, drug metabolism and bioaccumulation. We find that information on drug ecotoxicity should be more readily available to pharmacists and healthcare environmental personnel in MSDS/SDS provided by drug suppliers. We also find that wasted drugs should be centrally collected for destruction by incineration and not disposed in sinks or toilets.

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Supplemental Data

Supplemental Table 1 summarizes the ecotoxicity data available for the other wasted, discarded or dispensed drugs. Supplemental Table 2 depicts the human pharmacokinetic data available for the other wasted, discarded or dispensed drugs.

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