Disposal and Treatment of CONTROLLED SUBSTANCES from the O.R.

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Environmental contamination by pharmaceuticals is well-documented worldwide.[1-6] The environmental burden of a pharmaceutical generally correlates with the amount that is dispensed, and therefore the most commonly utilized medications (birth control, antihypertensives, antibiotics, anti-epileptics, mood stabilizers and over-the-counter analgesics) are those most frequently found in the environment.[3] Propofol is the medication most frequently wasted in the O.R. by volume,[7] and although it is not currently regulated by the Drug Enforcement Administration (DEA), it was recommended by the DEA in 2010 to be added as a schedule IV drug like fospropofol.[8] Propofol has been treated as a controlled substance in Alabama, Georgia and North Dakota as well as by certain health care systems. Midazolam, acetaminophen-codeine and fentanyl contributed nearly 90 percent by weight to the total controlled drug waste from two hospitals in one study.[9] Proper disposal of controlled substances, including propofol, would prevent both environmental contamination as well as unlawful diversion.

What exactly constitutes "proper disposal"? Federal, state and local governmental entities, as well as non-governmental public interests and facilities themselves, have rules or recommendations that enter into the discussion, so there is no "one size fits all" answer. There are regulations from a veritable alphabet soup of agencies, including the DEA, Environmental Protection Agency (EPA), Department of Transportation (DOT), Occupational Safety and Health Administration (OSHA), state EPAs, state pharmacy boards, and local publicly owned treatment works (POTW, i.e., wastewater treatment plants). The EPA classifications, under the Resource Conservation and Recovery Act (RCRA), are the most widely known and include "hazardous substances" (U-list) and "acutely hazardous" (P-list).[10] Of note, these lists have not been updated in many years. In addition to the P and U lists, drugs may exhibit a characteristic of hazardous waste, such as ignitability or toxicity, based on their specific formulations; however, these drugs are generally not used in anesthesia. Since no drugs should be disposed down the drain without the specific permission of the local POTW, some health care facilities have provided containers for disposal of either hazardous or non-hazardous pharmaceutical waste in the O.R. setting, although this is not always the case. Anesthesia medications, including controlled substances, are often referred to as "non-P/non-U listed" and do not carry regulatory obligations for hazardous waste disposal. Regulations from the DEA focus solely on potential of diversion, mandating that controlled substances be "non-retrievable" or unable to be recovered for use/abuse. In contrast to unused expired medications, which must be disposed of by the pharmacy via a reverse distributor, medications charged out to a patient are required only to be managed in such a way as to prevent diversion.[11] States, health systems or individual hospitals therefore have created their own policies for wasting controlled substances and

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non-controlled substances from the O.R. **Historically, controlled substances have been wasted down the drain**, witnessed, in order to comply with the DEA's diversion requirements. This practice directly contaminates the environment, as wastewater treatment plants are not designed to remove medications or their potentially harmful degradation products.[12,13]

An alternative to disposal of controlled drugs into the sink is use of a medication disposal system, which is a receptacle for pharmaceuticals that uses either a binding agent or denaturing agent that solidifies liquids to render them unrecognizable and unrecoverable. Examples of approved systems include Stryker's Cactus Smart Sink® and Pharma Lock® O.R., and Rx Destroyer™. The contents of these containers should then be disposed through incineration unless specifically permitted into the local landfill. However, termination of the solidified drug into landfills ultimately leads to contamination of groundwater due to leaching into the environment.[2]

Stryker's Cactus Smart Sink® and Pharma Lock® O.R. Controlled Substances Waste Management Systems.
Photo courtesy of Stryker Corporation.

Guidance from a drug's manufacturer could be helpful in determining its ecotoxicity and best disposal practices. However, the safety data sheets (SDSs) in the U.S. don't include details of ecotoxicity, and the section of the SDS titled "Disposal Considerations" is frequently nonspecific, suggesting only to follow federal, state and local regulations.[14,15] European SDSs disclose far more information, even stating that a medication should not be disposed of down the drain[16] or that incineration is recommended for destruction.[17]

Virtually all medications drawn up from vials will end up in the environment in some form. Direct disposal into wastewater is least preferable, but disposal into landfilled trash only delays the inevitable migration of the pharmaceutical into groundwater. Toxic byproducts of incineration have been identified, particularly when plastic is combusted; however, incineration in an approved facility is the only method that will prevent the majority of aquatic pollution due to pharmaceutical waste disposal. All incinerators must meet appropriate Maximum Achievable Control Technology standards, which reduces the emissions released during incineration.[18]

O.R. Controlled Substances

In anesthesia practice, propofol is the most wasted medication by volume, while emergency drugs (succinylcholine, atropine, epinephrine, ephedrine) have the highest waste fractions (percent of opened drug that is not used and must be wasted).[7] Though the full environmental impact of these medications is not known, there is legitimate concern for the bioaccumulation of propofol. It is not biodegradable in water or anaerobic conditions, and incineration is required for its destruction.[7]

Ecotoxicity literature on pharmaceuticals is both substantial and insufficient. Propofol and morphine are considered toxic to aquatic life (the established surrogate marker of ecotoxicity).[5] Of all the controlled substances commonly used in anesthesia, morphine has the most established experimental ecotoxicity data.[6] Diazepam, the most studied of the benzodiazepines, has been found in surface and groundwater worldwide[19] and is resistant to degradation in the environment. Low levels have been shown to affect aquatic species' behavior,[19,20] and there is growing concern for the effects of chronic low-level exposure on ecosystems and on humans. Ketamine is not susceptible to microbial degradation or hydrolysis, and its phototransformation results in byproducts that are similar to human metabolites, demonstrating that analysis of metabolites in the environment is even more lacking than analysis of the parent pharmaceuticals themselves.[21]

Chloral hydrate, a class IV controlled substance used for sedation primarily in pediatric anesthesia, is a U-list medication and must be disposed of into the appropriate receptacle as it is regulated by the EPA. Physostigmine salicylate (though not a controlled substance and whose use in anesthesia is only for diagnosis and treatment of central anticholinergic syndrome) is worth mentioning because it is P-listed. For all medications not regulated by the EPA, the DEA edict of "non-divertible" is the main federal guidance that applies to clinicians. For this reason, the sink or trash has historically been the preferred route of disposal for clinicians due to simplicity.

One alternative to sink or "regular" trash disposal is the sharps container. While the sharps container is theoretically a "non-divertible" location, there are numerous examples

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to prove otherwise.[22] A fatality was recently described when a narcotic-dependent woman drained out the liquid from a sharps container in her employer's emergency department and injected the contents. This liquid contained not only narcotics but also rocuronium.[23] Sharps containers are not designed to sequester wasted controlled substances and should not be used for this purpose due to risk of diversion as well as the possibility of environmental contamination if the sharps container is landfilled rather than incinerated.

> *"Virtually all medications drawn up from vials will end up in the environment in some form. Direct disposal into wastewater is least preferable, but disposal into landfilled trash only delays the inevitable migration of the pharmaceutical into groundwater."*

The recent introduction of the medication disposal systems previously discussed are likely the best means for disposal of controlled substances currently available as they render the medications unusable, provided the medications are ultimately incinerated. Unfortunately, their cost can be significant, and the motivation of a health care facility to change to a new disposal practice can be low. Despite these challenges, such systems are rapidly gaining in popularity, especially as medication waste practices are receiving greater scrutiny from The Joint Commission and their accreditation alternatives, such as DNV GL.

Waste Prevention and Other Solutions

All unused prepared medications that leave their vials will end up in the environment in some form. These medications must be disposed of, and therefore judicious use will decrease environmental contamination. Propofol waste was significantly reduced at Cincinnati Children's Hospital by using the chart in Table 1 for propofol infusions. Additionally, avoidance of unnecessarily large vials of medication decreases the waste fraction.[7] Pre-filled syringes of small quantities of fentanyl decreased the waste fraction at a pediatric institution.[24] Generally, outsourced pre-filled syringes have a relatively long shelf life and can be re-stocked if not opened, reducing waste.[25]

Table 1: How Much Propofol Do I Need?

Chart shows ml of propofol needed, assuming 250mcg/kg/min (includes priming two extensions)

Weight (kg) ↓ / Time (minutes) →	15	30	45	60	90	120
10	15	20	20	25	35	40
15	15	20	25	35	45	55
20	20	25	35	40	55	70
25	20	30	40	50	65	85
30	20	35	45	55	80	100
35	25	35	50	65	90	115
40	25	40	55	70	100	130
45	25	45	60	80	110	145
50	30	50	65	85	125	160
60	35	55	80	100	145	190
70	35	65	90	115	170	220
80	40	70	100	130	190	250

Red line indicates 50ml threshold

The list of "hazardous waste drugs" that fall under EPA jurisdiction should be updated to reflect controlled substances and propofol. Finally, federal and state laws should be brought into alignment to reduce confusion for policymakers.

A comprehensive plan to reduce the environmental burden of pharmaceuticals must include proper disposal. Disposal into sinks, toilets and trash must be discouraged, while incentivizing proper disposal by incineration. Commercial medication disposal systems, like those mentioned earlier, are a new, industry-borne solution for simplicity, compliance, diversion avoidance and environmental protection.

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Conclusions

Among the many responsibilities of the anesthesia provider, attention to the environmental impact of our practice must not be forgotten. Controlled substances, like other anesthetic medications, will contaminate the environment if not properly destroyed by incineration. Drug waste can be minimized through careful planning of case requirements and through reliance on pre-filled syringes. Reduction of the amounts of unused drugs coupled with proper disposal will minimize water contamination for future generations. Pharmaceuticals are nearly ubiquitous in freshwater worldwide, and we all (quite literally) live downstream. O.R. pharmaceuticals are one piece of a large puzzle, but it is a piece that all anesthesia providers handle every day.

The authors would like to thank Charlotte A. Smith, R.Ph., M.S., Kathleen A. Skibinski, R.Ph., M.S., Monica Livingston and Russell F. Mankes, Ph.D., for their expertise and assistance with this manuscript.

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