Pollution Prevention Measures for Unwanted Pharmaceuticals

Sandra M. Gualtero

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Department of Earth and Environmental Engineering
Columbia University
Abstract
Studies in many countries have demonstrated the presence of pharmaceutical products at trace levels in water streams. The life cycle of a pharmaceutical product was analyzed and it was determined that the major contributor to the presence of these substances in the environment is not the manufacturing operations but the use and actions of the consumers. The amount of unwanted pharmaceuticals that could be disposed in toilets and trash in the US was estimated by using data from take back programs in other countries. Even though the environmental impact of pharmaceuticals in the environment at trace levels has not been clearly determined, the precautionary principle calls for action in the face of uncertainty.

This paper examines some of the measures that could be taken to reduce the amount of pharmaceuticals that are released into the environment due to the actions of the general public. A special analysis is made of take back programs. At the end, it is concluded that many of the pollution prevention measures proposed not only benefit the environment but also contribute to the reduction of overall health care cost. It is also determined that there is a need for a national dialogue to get agreement on some of the issues that still need to be resolved in order to implement these kinds of programs, such as regulatory compliance, funding, education and logistics.

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**Introduction**

Pharmaceutical products are used for the benefit of humanity. Their use is expected to increase in the coming years due to the fact that population is growing, and in many countries, such as the US, is aging. Also, many new drugs and therapies for otherwise non-treatable illnesses are available every year.

Several studies have demonstrated that certain pharmaceutical chemical compounds are being dispersed in the environment. It has also been established that the origin of such emissions is mainly due to consumers use and actions and not to manufacturing operations. Large amounts of pharmaceutical products are discarded as their expiration date passes or they become unwanted. At this time, the correct disposal method of waste product is not clear to the general public. Consequently, waste is discharged through sewage systems or sent to landfills in the household waste. There are a number of measures that could be taken to address this situation. These measures fall under the “pollution prevention” concept and should be applied following the established hierarchy: first, minimization/reduction; second reuse/recycle; and finally, appropriate disposal. A required element for the implementation of these initiatives is a “take back” program that would allow communities to collect these chemicals, reuse them when possible or dispose them in waste-to-energy facilities or medical waste incinerators.

The purpose of this paper is to analyze the current situation of unused/unwanted pharmaceutical products, their environmental impacts and possible solutions.

**1. Background**

**1.1 Definition of Pharmaceutical Products**

Pharmaceutical products refer to a group of chemicals used for diagnosis, treatment, or prevention of diseases and/or health conditions. Pharmaceutical products are usually classified as: Over the counter (OTC) which can be bought at supermarkets and pharmacies without any restriction and Prescription Only Medicines (POM) which, in order to be obtained, require physician’s prescription. Pharmaceutical products are usually classified according to their therapeutic purpose (e.g. antibiotics, analgesics, anti-inflammatory drugs, antibiotics, antihistaminic agents, etc).

Common pharmaceutical dosage forms are: Aerosols, capsules, creams, emulsions, gels, implants, inhalations, injections, irrigations, ointments, pastes, powders, solutions, suspensions, tablets. Approximately 70% of the drugs consumed are solid oral dosage form (tablets and capsules) (Valagaleti, 2002)

The most important constituent of a pharmaceutical product is the Active Pharmaceutical Ingredient or API (also known as drug substance). Pharmaceutical active compounds are complex molecules with different functionalities, physicochemical and biological properties. Their molecular weight typically ranges from 300 to 1000 (Kummerer 2004). Besides the API, pharmaceutical formulations include excipients, which accomplish different functions. Some, for example, are responsible for the product's delivery system. These transport the active drug to the site in the body where the drug is intended to act. Others will keep the drug from being released too early in the assimilation process. Others help the drug to disintegrate into particles small enough to reach the blood stream more quickly while others protect the product's stability so it will be at maximum effectiveness at time of use. Although technically
"inactive" from a therapeutic sense, such excipients are essential components of modern drugs. In many products, excipients make up the bulk of the total dosage form (International Pharmaceutical Excipients Council of the Americas, 2005).

1.2 Pharmaceutical Industry and Product consumption

Industry Profile
The pharmaceutical Industry is becoming an important sector in the United States economy. The PhARMA association (Pharmaceutical Research and Manufacturers of America) which represents America’s leading pharmaceutical research and biotechnology companies reported in its 2004 company profile that the domestic sales of its members increased by 10.3% compared to 2003; its total sales, including sales abroad, increased by 11.4%. According to the same report, since 1990, the domestic and total sales of these companies have increased by 306% and 318%, respectively. Some of the reasons for the growth of this economic sector include:

- Development of new and better medicines. This is related to the emphasis that the pharmaceutical industry is putting in research and development. The PhARMA association reports in its 2005 Pharmaceutical Industry profile that its members invested an estimated $38.8 billion in 2004 in the discovery and development of new medicines; this is 18 times more than what these companies had invested in 1980.
- Improvements in drug access, including growth in insurance coverage for drugs.
- Clinical guidelines recommending increased use of medications for conditions such as high cholesterol, high blood pressure, chronic asthma, and diabetes.
- Marketing strategies.
- Changes in the age and composition of the population. As it will be explained in the following section, the elderly population has increased in the last decades. This sector of the population usually requires more medical attention, including the use of drugs.

Changes in Life Expectancy and Population Age

During the 20th century, life expectancy at birth increased from 48 to 74 years of age for men and from 51 to almost 80 years of age for women. Life expectancy at age 65 years also increased during the last century (Figure 1). Among men, life expectancy at age 65 years rose from 12 to 16 years and among women from 12 to 19 years of age. In contrast to life expectancy at birth, which increased sharply early in the century, life expectancy at age 65 years improved primarily after 1950. Improved access to health care, advances in medicine, healthier lifestyles, and better health before age 65 years are factors underlying decreased death rates among older Americans (National Center for Health Statistics, 2004).
From 1950 to 2000, the total resident population of the United States increased from 150 million to 281 million, representing an average annual growth rate of 1 percent (Figure 2). During the same period, the population of 65 years of age and over grew almost twice as rapidly and increased from 12 to 35 million persons. The population of individuals 75 years of age and over grew almost three times as quickly as the total population, from 4 to 17 million persons. Projections indicate that the rate of population growth during the next 50 years will be somewhat slower for all age groups and older age groups will continue to grow more than twice as rapidly as the total population. During 1950 to 2000, the U.S. population grew older (Figure 3). From 1950 to 2000 the percent of the population under 18 years of age fell from 31 percent to 26 percent while the percent 65–74 years increased from 6 to 7 percent and the percent 75 years and over increased from 3 to 6 percent. Between 2000 and 2050, the percent of the population 65–74 years of age will increase from 7 to 9 percent and the population 75 years and over will increase from 6 to 12 percent. By 2040, the population of 75 years and over will exceed the population of 65–74 years of age. (National Center for Health Statistics, 2004)


As the older fraction of the population increases, more services, including drugs, will be required for the treatment and management of chronic and acute health conditions.
Drug Consumption

The National Health and Nutrition Examination Survey (NHANES) collects data on the prescription drug use of survey participants during in-person household interviews. Between 1988–94 and 1999–2000, NHANES data show that the percent of Americans of all ages who reported using any prescribed medication during the past month increased from 39 to 44 percent (Figure 4). During the same period, the percent of persons who reported using three or more drugs in the past month increased from 12 to 17 percent of the population. Perhaps most striking is the increase in the percent of older persons who reported taking three or more prescribed medications during a one-month period—almost one-half of those 65 and over in 1999–2000—compared with just over one-third in 1988–94. Prescription drug use is greater among middle-aged and older adults than among younger persons. Prevalence of many chronic conditions and diseases increases with age, as does use of medications designed to help control or prevent complications associated with those conditions (National Center for Health Statistics, 2004).

Figure 4. Prescription Drug Use. Source: Center for disease control and prevention. National Center for Health Statistics. National Health and Nutrition examination survey.

The increased use of medicines could be seen as a higher expenditure for the health care system. However in many cases, drugs can treat conditions that in the past were incurable or required more complicated procedures such as surgery. The new medicines prevent illness, reduce complications and disabilities from disease, avert costly hospitalizations and invasive surgeries; and decrease or delay the need for long-term care. (PhARMA, 2004).
On the other hand, there are many initiatives right now seeking to increase access to medicines for people around the world. PhARMA reports that its members support global patient assistance efforts by providing free and reduced-cost medicines to developing countries and responding to global health crises (PhARMA 2004).

### 1.3 Pharmaceuticals as Pollutants

During the last three decades, the impact of chemical pollution has focused almost exclusively on the conventional “priority” pollutants (e.g. pesticides), however this is just one piece of the larger puzzle (Daughton and Ternes, 1999). The occurrence of pharmaceutical products in the environment has gained increasingly attention since the 1980s; however its occurrence has become more widely evident since the 1990s because the continual improvement in chemical analysis methodologies (Daughton 2003).

Pharmaceuticals do not usually persist in the environment but continuous input into the environment keep concentrations relatively constant. As it will be described later, many drugs have been detected in various water streams throughout several countries. However, their concentrations are usually below the therapeutic level (e.g. ng/l, µg/l). The risks and effects of these substances in these concentrations in the environment have not been determined yet. However, this issue continues to be viewed with concern due to some of the properties that many pharmaceuticals have: biological activity, lipophilic nature and resistance to biodegradation (Valagaleti, 2002). The problem has been described by Kummerer (2004) using the terms pharmacology and ecopharmacology (Table 1).

<table>
<thead>
<tr>
<th></th>
<th>Pharmacology (Humans)</th>
<th>Eco-pharmacology (environment)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of compounds administered</td>
<td>One or only a few compounds at the same time</td>
<td>An unknown cocktail of different compounds</td>
</tr>
<tr>
<td>Desirable physicochemical properties</td>
<td>Stable</td>
<td>Readily (bio)degradable</td>
</tr>
<tr>
<td>Administration</td>
<td>Targeted, on demand, controlled</td>
<td>Diffuse i.e emissions from medical care units and community</td>
</tr>
<tr>
<td>Wanted effects/side effects</td>
<td>Active, wanted effects, side effects</td>
<td>“Wanted effects” in target organisms are often the most important “side effects” in the environment.</td>
</tr>
<tr>
<td>Metabolism/biotransformation/affected organisms</td>
<td>One type of organism</td>
<td>Various types of organisms of different trophic levels</td>
</tr>
</tbody>
</table>

### 2. Life Cycle Assessment

#### 2.1 Life Cycle of Pharmaceutical Products

The life cycle of a pharmaceutical drug product is described in Figure 5 (adapted from Valagaleti, 2002). It can be seen that there may be releases to the environment during the following stages: API synthesis, extraction and purification; commercial scale manufacture; human clinical studies and use/disposal of unwanted pharmaceuticals.
API synthesis and extraction and drug product manufacturing are pretty much within the traditional industry boundaries. Therefore, their releases are usually regulated and carefully observed. The use and disposal of unwanted pharmaceuticals will be reviewed in the following section.

Drug product raw materials, specially API, usually have a high cost, so containment procedures during the synthesis/manufacturing process of these substances are designated to ensure minimal or zero release of chemicals into the environment (Valagaleti, 2002). The more significant environmental footprint for API manufacturing (cradle to gate analysis) was found to be solvent use (Jimenez-Gonzalez et al, 2004). However, solvents may be recovered and reused in the same process or in other processes. This, along with the fact that solvent prices have gone up a lot lately, have moved pharmaceutical companies to

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Figure 5 – Life cycle of a pharmaceutical product. Adapted from Valagaleti, 2002.
review their operations involving solvents. Today almost all the major pharmaceutical companies have corporate goals related to VOC reductions.

Regarding drug products manufacturing, controls for the accountability of raw materials are required by the Good Manufacturing Practices (GMP). Again, containment procedures are put in place to ensure minimal or low release of materials into the environment. Only in the case of accidents high emissions may occur locally. Point sources for the emissions are likely to be only of minor importance (Kummerer, 2004).

2.2 Use and Input into the Environment.

In addition to the API and drug product manufacturing operations, there are two major ways in which pharmaceuticals enter the environment (Fig. 6). One is related to the metabolic excretion and the other one has to do with the disposal of unwanted medications.

- Metabolic excretion: Many pharmaceuticals are biotransformed in the body. Biodegradation modifies the chemical structure of their active molecules, which in turn often results in a change in their physicochemical and pharmaceutical properties. Metabolism may lower activity or enhance water solubility; however, metabolism is frequently incomplete. Excretion rates range from 0 to 100% (Kummer 2004). This means that in many cases, a large portion of the drugs is not assimilated by the patient’s body and it is excreted as feces, urine, vomit, etc.

- Disposal of unwanted chemicals: Getting rid of unused, unwanted, or expired medications can be a challenge. Pharmacies may send unused or expired medications back to the original manufacturer. Alternatively, they may employ a reverse distribution company to take care of manufacturer returns and incinerate those products that are non returnable. However, little is available in the way of formal guidelines on drug disposal – especially at the level of the final end user – the patient (Boehringer, 2004). It is reported that approximately one third of the total volume of pharmaceuticals sold in Germany and 25% of that sold in Australia was disposed with household waste or down the drain (Kummerer, 2004). This specific topic will be covered in detail in a following session of this paper.
Figure 6: Entry paths into the environment for most medical products when prescribed to patients. Source: Kummerer, 2004.

Waste discharged to engineering systems is subject to various levels of treatment before discharged to receiving waters. Pharmaceuticals however, display a broad range of removal efficiencies by waste and water treatment technologies; some travel through water treatment facilities with only minor reduction in concentrations (Daughton, 2003).

2.3 Occurrence and Fate

In the last few years, there have been a number of attempts to try to determine the occurrence of pharmaceuticals in the environment. A major study was conducted by the US Geological Survey in 2002. This survey used five newly developed analytical methods to measure concentrations of 95 OWC (organic waste water contaminants) in water samples from a network of 29 streams across the US during 1999 and 2000. The selection of sampling sites was biased towards streams susceptible to contamination (i.e downstream of intense urbanization and livestock production). In 80% of the samples analyzed, one or more of the pharmaceuticals were detected. The high overall frequency of detection for the OWC was likely influenced by the design of this study which placed focus on stream sites that were generally considered susceptible to contamination. Regarding the compounds, 82 of the 95 OWCs were found during this study. Again, in this study, only targeted compounds were reported with no attempt to report data on not targeted compounds. Measured concentrations for this study were generally low (in most cases less than 1 part per billion) and rarely exceeded drinking water guidelines, drinking water health advisories or aquatic life criteria. Many compounds however do not have such guidelines established. The detection of multiple OWC was common for this study; 75 percent of the streams had more than one, 50 percent had 7 or more, and 34 percent had 10 or more, with as many 38 OWCs being
detected in a given water sample. Little is known about the potential interactive effects that may occur from complex mixtures of OWCs in the environment (Kolpin et al, 2002).

Examples of pharmaceuticals found include:

- Acetaminophen was found in 24% of samples analyzed
- Steroids and hormones were also commonly found, with 17-ethyl estradiol (a hormone used in birth control pills) found in 16% of samples analyzed
- Diltiazem (blood pressure medication) was found in over 13% of samples analyzed
- Codeine was found in 11% of samples analyzed
- Antibiotics and antimicrobials were found in over 10% of samples analyzed

There have been a number of other studies that have identified pharmaceuticals in water streams in countries such as Italy, Switzerland and Canada. In general, medical substances have been detected in the effluent from medical care units, sewage and the effluent of sewage treatment plants, in surface water, ground water, and in drinking water. Pharmaceuticals have also been detected in the effluent from landfill sites (Kummerer, 2004). However it has not been possible to determine how much of these substances were due to human and animal excretion and how much to the disposal of unwanted pharmaceuticals.

2.4 Impacts and Effects:
There is very limited documentation regarding the effects of pharmaceuticals in the environment. Recent studies have focused primarily on antibiotics and strogenics steroids (hormones). For antibiotics, the question is: whether the input of antibiotics in the environment is an important source for the emergence of resistance bacteria in the environment. First results indicate that the transfer of resistance is not favored at antibiotic concentrations found in hospitals effluents or aquatic environment. (Kummerer, 2004). Regarding hormones, some studies have suggested that compounds like synthetic steroid 17α-ethinyloestradiol, (EE2) used in contraceptives, could affect certain species of fish. However other studies have shown inconclusive results. There have not been many studies on the potential risk that these substances could represent for invertebrates, even though they are important from the ecological point of view. A study done by Schulte-Oehlmann et al concluded that prosobranch snails could be affected by EE2 at the concentrations found in surface waters (Kummerer, 2004).

Other types of pharmaceuticals are also a concern among the scientific community, such as selective serotonin reuptake inhibitors (SSRIs), which are a form of antidepressants, and antiepileptic drugs. However, again, non-conclusive information is available regarding the effects of these substances on the environment.

The issues associated with potential ecological effects in particular cannot be resolved until toxicologists begin to evaluate the effects on non target organisms by simultaneous, long term exposure to multiple pharmaceuticals at low doses (Daughton 2003). Another issue that has to be assessed is the presence of pharmaceuticals in sediments and sewage biosolids.

2.5 Environmental Risk Assessments:
There are laws in the United States and Europe that require prospective Environmental Risk Assessments (ERA) as part of the drug registration process. However, meaningful effort on this front is simply not possible with the currently limited state of knowledge on environmental transport, fate, and effects of pharmaceuticals. The weakest aspect to this approach is that the toxicity of the substances is assessed from what is known for human toxicology rather than for potential nontarget organisms. Furthermore, it does not take into account possible
cumulative effects of different drugs affecting the same receptors (Daughton and Ternes, 1999).

3. Disposal of Unwanted Pharmaceuticals:
In an ideal situation, all the pharmaceuticals that are prescribed for a patient or bought by a person to treat a common illness (such as colds, etc) would totally be consumed. However this is not always the case. For many reasons, many pharmaceuticals are not consumed and they expire in the hands of the public or health care facilities. Some of the reasons why pharmaceuticals are not totally consumed are:

- Patient improvement
- Patient non compliance (e.g. patient do not complete the therapy):
  - Prescription fatigue.
  - Silent symptoms (patient does not know if his/her condition is improving or declining – patient does not have an incentive to keep taking the medication)
- Patient death
- Change in the prescription by the physician.
- Marketable presentations: medication includes more product than needed by the patients.
- Expiration date is reached before the product has been consumed completely (common for OTC medications)

With a very few exceptions, countries do not have clear and consistent guidelines on how to properly dispose unwanted pharmaceuticals, especially when it comes to the general public. Medical centers and pharmacies usually send unused or expired pharmaceuticals back to the manufacturer, in other cases they use a reverse distribution company which disposes of the products that are non returnable.

In the US, this - often contradictory - guidance varies from state to state in both formal and informal ways. As an example, this is a statement found on the Wisconsin Department of Natural Resources Web Page “If your waste is not a hazardous waste and it is a dispensed narcotic or other medication, first consider donating the medication, or if possible, return the medication to the supplier or send it to a firm specializing in accepting these wastes. This is called "reverse distribution". If you can not use reverse distribution or donation, you may flush the medications down the drain or dispose them in the trash. Do not flush medications into a septic system. Before flushing large amounts, contact your local wastewater treatment plant operator. Store dispensed narcotic medications securely before disposal”.

A survey by Kuspis and Krenzelok (Boehringer, 2004) studied expired medication drug disposal habits in 100 pharmacies and of 500 patients. Of the pharmacies surveyed, 97% had policies in place regarding disposal of expired undispensed medication, which in most cases was to return the medication to the manufacturer. However, only 5% of pharmacies surveyed had consistent recommendations for patients on drug disposal. Approximately 25% of the pharmacies indicated that the issue of drug disposal was addressed only at the customer’s request. Of the 500 patients surveyed, 1.4% returned medications to a pharmacy, 54% disposed medications in the trash, 35.4% flushed drugs down the toilet or sink, 7.2% did not dispose medications, and 2% stated they used all medication prior to expiration. In another survey performed in Canada in 1995 (Boivin, 1997), it was determined that 63% of the patients surveyed had disposed medications in the past. The methods used to dispose these medications were: 46%, toilet; 31%, trash; 17%, pharmacy; 2%, physician; 4%, other. The predominance of disposal in the trash and through the toilet is evident. It was also determined in this survey that the categories of medications that constitute the largest percentage of the overall costs of unwanted pharmaceuticals are: Cardiovascular therapies
(high blood pressure, heart and circulation): 25.7%; Analgesic and Anti-Inflammatory: 19.2%; Endocrinological and Neurological: 15.3%; Gastro-Intestinal: 12.9%

There is not much information regarding the amount of unwanted pharmaceuticals that is not properly disposed. However, there is some data available from surveys and existing take-back programs. This data is used in this analysis to estimate the amount of unwanted pharmaceuticals that could be produced annually in the US.

3.1 Amounts of Waste Disposed by Health Care Units:

King County in Washington State performed a survey on 60 drug waste generators (primary doctor’s offices, health care centers, hospitals) (Chapman, Oliver, 2003). The survey identified that Chemotherapy wastes were being disposed primarily through hazardous waste vendors, although some went to biohazardous waste containers. The “mixed” and “narcotic” wastes (DEA controlled) going to the hazardous waste vendor were reported by one reverse distributor. Otherwise, most drug wastes went into the sewer system, garbage and biohazardous waste containers. A summary of the type of waste disposal is presented in Table 2.

Table 2. Disposition of waste and quantities disposed per year. Source: pharmaceutical waste survey – King County/Washington State – 2003.

<table>
<thead>
<tr>
<th>Disposition</th>
<th>ml</th>
<th>lbs</th>
<th>pills</th>
<th>Other waste measure as items</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accumulate and wait</td>
<td></td>
<td></td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Biohazard container</td>
<td>38,961</td>
<td>80</td>
<td>517</td>
<td>2,562</td>
</tr>
<tr>
<td>Down the drain</td>
<td>10,610,644</td>
<td>6,188</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Garbage</td>
<td>4</td>
<td>40</td>
<td>93</td>
<td>36</td>
</tr>
<tr>
<td>Hazardous waste vendor</td>
<td>1,968,408</td>
<td>3,606</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>160</td>
<td></td>
<td>595</td>
<td>18</td>
</tr>
<tr>
<td>Pharmacy</td>
<td>355</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reverse distributor</td>
<td></td>
<td>256</td>
<td>6,500</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>12,618,532</td>
<td>3,982</td>
<td>13,923</td>
<td>2,616</td>
</tr>
</tbody>
</table>

Disposal methods categorized as “other” include giving wastes to charitable organizations, giving them to DEA-licensed vendors for incineration, returning them to the sales representative and putting them in the sharps container. The liquids that are disposed down the drain are: Cough syrup, injectable liquids, IV liquids, mixed (all medications in multiple forms: pills, tablets, liquids, ointments, etc), narcotics (DEA controlled substances). The major stream is the IV liquids, accounting for 10,597,500 ml, followed by injectable liquids accounting by 11,581 ml. IV fluids that provide hydration without an additional “drug” added may not be designated as dangerous waste since they consist primarily of normal saline, vitamins and minerals, dextrose, amino acids or enzymes. They may also be acceptable for sewer disposal with authorization from publicly owned treatment works (Chapman, Oliver, 2003).

In the King County survey, the results were extrapolated to Washington State taking into account the number of facilities surveyed, its type of business and the number of patients. From this extrapolation, it was determined that the pharmaceutical waste generated in Washington State by the health care industry was 1,008,395 lbs. It was also determined that
75% of this amount consists of IV fluids that are not expected to be designated as dangerous in WA. So, without IV fluids, 249,395 lbs were produced (Chapman, Oliver, 2003).

Using the extrapolation done by the King County survey, another extrapolation was done for the whole country. This was done based on the population. The US census Bureau estimates that the population for 2004 for Washington State was 5.9 million people and for the entire country was 293 millions. The results of this extrapolation are presented in Table 3 and show that about 26 metric tons of pharmaceutical waste are disposed annually down the drain (58,765 lbs) and another 26 tons are disposed annually with municipal solid waste in landfills (send with the garbage).

**Table 3.** Calculation of the amount of waste disposed annually by health care facilities down the drain and in the garbage (extrapolation taking the data from the King County survey, 2003)

<table>
<thead>
<tr>
<th>Type of disposal</th>
<th>Type of waste</th>
<th>Amount per year</th>
<th>Unit</th>
<th>Amount lbs/year</th>
<th>% in total waste</th>
<th>Extrapolation to WA lb/year</th>
<th>Extrapolation to US lb/year</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Down the drain</strong></td>
<td>IV liquids</td>
<td>10,597,500.00</td>
<td>ml</td>
<td>23,314.50</td>
<td>75.0000%</td>
<td>756,296.25</td>
<td>37,635,352.37</td>
</tr>
<tr>
<td></td>
<td>cough syrup</td>
<td>12.00</td>
<td>ml</td>
<td>0.03</td>
<td>0.0001%</td>
<td>0.86</td>
<td>42.62</td>
</tr>
<tr>
<td></td>
<td>Injectable liquids</td>
<td>11,581.00</td>
<td>ml</td>
<td>25.48</td>
<td>0.0820%</td>
<td>826.48</td>
<td>41,128.10</td>
</tr>
<tr>
<td></td>
<td>Mixed</td>
<td>1,421.00</td>
<td>ml</td>
<td>3.13</td>
<td>0.0101%</td>
<td>101.41</td>
<td>5,046.46</td>
</tr>
<tr>
<td></td>
<td>Narcotics</td>
<td>130.00</td>
<td>ml</td>
<td>0.29</td>
<td>0.0009%</td>
<td>9.28</td>
<td>461.67</td>
</tr>
<tr>
<td></td>
<td>Pills</td>
<td>6,188.00</td>
<td>pills</td>
<td>7.49</td>
<td>0.0241%</td>
<td>242.89</td>
<td>12,086.64</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>23,350.90</td>
<td></td>
<td></td>
<td>75.1171%</td>
<td>757,477.16</td>
<td>37,694,117.86</td>
</tr>
<tr>
<td><strong>Total without IV liquids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Garbage</strong></td>
<td>Narcotics</td>
<td>4.00</td>
<td>ml</td>
<td>0.0088</td>
<td>0.00%</td>
<td>0.29</td>
<td>14.21</td>
</tr>
<tr>
<td></td>
<td>Pills</td>
<td>36.11 †</td>
<td>lbs</td>
<td>36.11</td>
<td>0.12%</td>
<td>1,171.37</td>
<td>58,290.44</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>36.1188</td>
<td></td>
<td></td>
<td>0.12%</td>
<td>1,171.65</td>
<td>58,304.65</td>
</tr>
</tbody>
</table>

*Average weight: 0.55g/pill. Determined by University of Washington. (King County waste survey, 2003)*

In the King County survey, it was also clear that with the exception of large institutions as hospitals and pharmacies, health care centers are not aware of their responsibility to meet hazardous waste regulation. Lacking and understanding of proper disposal options has made these facilities come up with different methods to manage pharmaceutical waste, such as disposal down the drain or in the garbage. Besides, many of them identified the disposal of pharmaceuticals down the drain as the best way to comply with the DEA regulations for controlled substances. It is almost certain that similar observations could be found in most of the country. (Chapman, Oliver, 2003).

### 3.2 Amounts Disposed by the Public

One of the most successful pharmaceutical take back programs in the world has been one implemented in Australia. This program is described in detailed in section "5.2 – Current Programs and Initiatives". Between July 2004 and June 2005, Australia collected 315,810 kg of unwanted pharmaceuticals. Australia has a population of 20,090,437 and the United States has a population of 293,655,404 according to the US Census Bureau. So, using population as the extrapolation factor, it could be estimated that in the US there are around
4,616,089 kg (5,000 short tons) of unwanted pharmaceuticals that are either kept at people's homes representing a hazard for children or disposed in an improper manner by the public.

These calculations give us an idea of the amount of unwanted pharmaceuticals that could be collected if a program were put in place in the US. They by no means are intended to be used as a fact. It is recognized that there may be a number of factors that could impact these extrapolations.

4. Pollution Prevention Measures

The environmental impact and effect of pharmaceuticals in the environment is not clear at this moment and it seems likely that the issue would not be resolved in the near future due to the fact that science and technology required to fully assess this risk is still in earliest stages of development. However, if we follow the precautionary principle which implies that “when an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically”, there are a number of proactive measures that could be taken to reduce the amount of pharmaceuticals that is introduced to the environment due to the actions of the general public.

Humans are an integral part of the environment. It has been proven that there are inseparable connections between human health and the quality of the environment. Safety and well being of patients have to be pursued not at expenses of the safety of the communities and the ecosystems. High quality health care and environmental protection are intimately linked (Daughton, 2003).

Pollution prevention establishes a hierarchy in the type of measures that should be taken when dealing with an environmental risk. In the case of hazardous waste this hierarchy is as follows:

- First: Minimization/reduction
- Second: Reuse
- Third: Recycling
- Last: Proper disposition (incineration – waste to energy facilities)

Some of these measures have been described by Christian Daughton (2003) in two mini-monographs that have become the base for what is known as the “Green Pharmacy”.

4.1 Minimization and Reduction:

- **Healthy life style**: Preventive health measures like: exercise, stress management, nutrition, periodic physical exams are key to maintain our bodies and souls in good health. Medications should be taken when all these other measures do not work due to other factors like genetics, etc.
- **Public awareness**: Increase public's sense of environmental responsibility by showing how their actions as individuals collectively contribute to impact of pharmaceuticals in the environment.
- **Patient compliance and education**: Raise patient's awareness about the importance of complete their treatments and follow physician's directions carefully.
- **Health care practitioner's education**: Educate health care practitioners to make sure they fully understand the importance of selecting the right medication and therapy for each patient and also the implications of improper use and disposal of pharmaceuticals. These professional should be the first source of information and education to patients and public about this topic.
- **Marketing presentations**: Provide customers and patients with small presentations (package size), specially for the OTC medications.
4.2 Reuse & Recycling:
- **Donation and reuse of drugs**: Provide the legal framework and the logistics resources required to allow patients and health care facilities to return unwanted medications that could still be used by other patients. One of the key issues on this aspect is the need for the medications to include tamper evident packaging, so it can be proven that they have not been opened. Some states like Texas have redesigned their laws to allow for nursing homes to return unused drugs as long as they are sealed in unopened, tamper-evident packaging. The pharmacy or manufacturer then reimburses Medicaid or Medicare for the drugs wherever appropriate. And while there are substantial qualifications for the drugs that may be recycled (for example, controlled substances like Valium™ and Tylenol™ with Codeine must be destroyed instead of returned, and the returned drugs cannot have less than 120 days before expiration), there are many drugs that now have the potential to be rescued and returned for resale or charitable use. (Bustillos, 2005).

4.3 Proper Disposal:
- **Take Back Programs**: Provide the legal framework and the logistic resources required to allow health care facilities, patients and public in general to returned expired and unwanted pharmaceuticals so that they can be either reused or disposed safely in waste to energy or incineration facilities. Take back programs are analized in the following session.

5. Pharmaceutical Product Take Back Programs

5.1 Reverse Distribution of Pharmaceuticals:
Reverse distributors manage unwanted pharmaceuticals from pharmacies, hospitals, and clinics. Some collected pharmaceuticals are returned to manufacturers; others are packaged and sent off-site for disposal. This management service is carefully tracked both as a service to the pharmaceutical industry and to meet legal requirements for the collected controlled substances. The reverse distribution process is often viewed as a form of product stewardship, even though it only applies to drugs that are not dispensed to patients. Many pharmaceutical manufacturers offer credits for returned pharmaceuticals. These credits make the reverse distribution system work. Reverse distributors package products, send them to manufacturers, and provide manufacturer credits to pharmacies. Products that cannot be returned to the manufacturer are sorted out for disposal. While manufacturers may process returned drugs for reuse, common understanding is that most—if not all—drugs returned to manufacturers are sent off-site for disposal (Moran, 2004).

As the reverse distribution system is currently structured, reverse distributors do not have hazardous or medical waste management or transfer station permits—they are simply treated as hazardous and medical waste generators under the law. This is because unwanted pharmaceuticals that are sent to reverse distributors may have financial value—a value that is only determined by the sorting process at the reverse distributor. Pharmaceuticals sent to reverse distributors (and from reverse distributors to manufacturers) are treated as “products in commerce” because of this financial value, and thus are not subject to hazardous waste transportation and permitting requirements. For those pharmaceuticals that do not have financial value, reverse distributors become the waste generator (Moran, 2004). Reverse distributors do not process any pharmaceuticals for reuse due to the fact that, with a few exceptions, States do not allow the reuse of drug prescriptions.

On a survey by King County in Washington State in 2003 it was established that 7 out of 27 nation wide returned distributors accepted patient’s returns. However they were accepted
under certain conditions: the drug was returned through the pharmacy that dispensed it; the drug was not a controlled substances (DEA registrants may not accept controlled substances from non registrants, such as patients); patient health information subject to privacy law was protected; and the reverse distributor held the contract as the “returns department” for the manufacturer of the returned drug (Chapman, 2003). On the same survey it was determined that Reverse Distributors sent the pharmaceuticals for disposal primary to Hazardous waste incinerator and Waste to energy facilities.

5.2 Current Programs and Initiatives:

- **Australia:** Return Unwanted Medicines (RUM) Project, provides for unwanted and out-of-date medicines to be collected by community pharmacies. Commonwealth funds currently cover these costs, due to outstanding support from the pharmaceutical industry. Community pharmacies collect these medicines at no cost, and pharmaceutical wholesalers have agreed to a dramatic discount in charges for delivery and collection of containers to pharmacies. The program has established protocols on how to manage the waste. It also includes consumer awareness campaigns and media releases. The program collect around 300 ton of unwanted pharmaceuticals annually. It has a budget of 5 million Australian dollars to operate from 2001 to 2006.

- **Canada - British Columbia:** The pharmaceutical industry voluntarily established the Medications Return Program in November 1996. For the period April, 2000 to December, 2000, industry reports that over 550 retail pharmacy outlets, representing over 75% of all pharmacies in British Columbia, accepted unused and expired medications from consumers. For the nine month period April, 2000 to December, 2000, the program reports the collection of 4490.1 kg for a four year program total of 32,776 kg (Jessen, 2002).

- **European Union** (Smith, 2004): Eleven European Union member nations have pharmaceutical take-back systems, all of which allow residents to drop unwanted pharmaceuticals at pharmacies. More than half of the European nation systems are operated by the pharmaceutical industry or by pharmacies; the rest are paid for municipalities.

**Initiatives in the US** (Smith, 2005)

- **Santa Clara County** (California): Action plan under discussion (Feb 2005)
- **City of Palo Alto** (California): Palo Alto hosts take back at Senior Centers. Collected 75 lbs of pharmaceuticals during 3 day event. Only advertised at Senior Centers.
- **Los Angeles County:** Take back all consumer medications except controlled substances at HHW facilities.
- **San Francisco:** Action plan established in 2004.
- **State of Maine:** One day event with the collaboration of Police, Northeast Recycling Council, Maine EPA and Pharmacy.

- **Clark County, Washington:**
  - Have been taking back consumer drugs for about 12 years at three HHW facilities.
  - Initiated a pharmacy based take back program in 2003
  - All non-controlled drugs can be dropped off at participating pharmacies; shipped FedEx to haz waste firm.
  - All controlled substances can be dropped off at designated sheriff’s offices; stored in evidence rooms until disposed.
• **Northeast Recycling Council (NERC):** Received a grant from EPA to pilot consumer take-back programs. This project will develop and implement a replicable pilot for collecting unwanted medications at HHW collections or in other rural settings. The project will focus on Massachusetts, Maine, New Hampshire and Vermont.

• **Washington Department of Ecology:** it is coordinating a recently formed informal agency working group to address residential pharmaceutical waste management. The group includes state and local government representatives from Washington, Idaho, and Oregon. The group plans to explore options for effective collection of pharmaceuticals, including the option of returning unwanted residential pharmaceuticals to pharmacies.

**Other initiatives in the US:**

• **Hospitals for a Healthy environment (H2E):** EPA grant to H2E to develop a pharmaceutical waste management blueprint, 2004.

• **Product Stewardship Institute (PSI):** In the Spring 2005, five local government agencies provided initial funding for PSI to conduct the first phase of a potential national dialogue on unwanted/waste pharmaceuticals. PSI is in the process of interviewing key stakeholders for inclusion in its Product Stewardship Action Plan. A draft of the project summary was issued on August, 2005.

**5.3 Issues to be Addressed to Establish an Effective Take Back Program:**

The San Francisco Environmental Department (2004) did a review of the current programs, performed interviews with government and industry staff and identified a number of issues and elements that need to be addressed in order to establish a successful pharmaceutical product take back program. This is a summary of those issues:

• **Convenience:** Collection programs need to be easy to use if they are to compete with the toilet or the trash. The programs should be free to the public.

• **Safety:** Safety measures have to be taken to protect the health of the pharmacy workers receiving and managing returned pharmaceuticals.

• **Communication:** A consumer awareness campaign has to be put in place in order to communicate the procedures that have to be followed to be able to return unwanted pharmaceuticals and beyond that, to motivate people to participate in the program.

• **Privacy:** the program should comply with regulations regarding health information privacy. Current programs address privacy one of three ways: use of a secure “one way” container to hold waste; asking patients to remove labels prior to putting them into the container (this may also remove the identification of the drug in the container), or asking patients or pharmacists to empty the medication into the waste container and send the patient home with the prescription container. Sorting and repacking of waste containers with personal information on them may require procedural controls to ensure privacy.

• **Disposal methods:** The collected pharmaceutical waste should be taken to waste to energy or incineration facilities.

• **Drug abuse:** There is a real risk that collected prescription drugs could be taken for illegal re-issuance to customers or for recreational use. This risk is usually addressed with security measures or by rendering drugs unusable at the time of collection.

• **Funding:** A founding source for the take back program has to establish and maintain.
• **Identification of controlled substances**: Controlled substances are not readily identifiable by consumers. Product labels do not indicate their regulatory status. To determine if a substance is controlled, the product ingredients need to be compared to the DEA schedules of controlled substances.

• **Waste generator**: Depending on what entity is the legal “generator” of the residential pharmaceutical waste, different rules apply for the waste management.

**6. Regulatory Framework**

Event though pharmaceutical household waste (as all household waste) is not regulated by US EPA, there are some dispositions in the current regulation that have to be taken into account when designing a pharmaceutical take back program in the US.


Federal law only regulates pharmaceuticals that have been determined to be “waste.” Pharmaceuticals that can be reprocessed, reused, or otherwise have financial value—or an unsorted group of unwanted pharmaceuticals, some of which may have future use—are not covered by hazardous waste regulations because they are materials awaiting classification, rather than waste. This exemption is the basis for the reverse distribution industry. U.S. EPA has authorized reverse distribution of pharmaceuticals without hazardous waste management permits. The U.S. EPA authorization specifically requires the returns industry not to be used as a "waste management system". Any items that are inherently "waste-like" (like a broken container or contaminated prescription) cannot be shipped as products to a reverse distributor (Moran, 2004). Facilities that collect hazardous household pharmaceutical waste must obtain HHWCF permits. Each state has the authority to regulate more strictly: eg Maine applies RCRA to household waste if it is collected outside the home (Smith, 2004)

**US Drug Enforcement Administration (DEA):**
Certain Pharmaceuticals are regulated by the U.S. Drug Enforcement Administration (DEA). These are known as “controlled substances”. They are drugs that have a potential for abuse, such as narcotics or tranquilizers. Examples include codeine, Valium, anabolic steroids, Xanax, Ritalin, and Lomotil. The DEA lists controlled substances in five schedules. Schedule I drugs have no medicinal use. Schedules II through V drugs may be given to patients by prescription. The DEA does not allow pharmacies or reverse distributors to accept returns of controlled substances that have been given to patients (Moran, 2004).

**Health Insurance Portability and Accountability Act (HIPAA):** Prescription drug labels must be managed to prevent release of personal medical information. The Health Insurance Portability and Accountability Act (HIPAA) administered by the U.S. Department of Health and Human Services (DHHS) sets national standards to protect the privacy of personal health information. These standards require measures to ensure security of personal medical information, like that on prescription labels. The primary requirements are to secure personal information so that it cannot be viewed by others, and to ensure that labels will be obliterated or destroyed prior to or during prescription drug containers disposal. While HIPAA technically covers only medical care providers (such as pharmacies), it also covers their “business associates.” Under HIPAA, “business associate” could be defined to include entities that collect waste from pharmacies. If an HHW program or its waste management contractor is defined as a “business associate,” then HIPAA requires the pharmacy to enter into a written agreement with the HHW program or the waste management contractor to protect private patient information. For example, if an HHW program’s waste management contractor picked
up unwanted residential pharmaceuticals collected at a pharmacy, the waste management contractor may need to enter into a written agreement with the pharmacy to ensure protection of private patient information (Moran, 2004).

7. Cost Benefit Analysis

In the case of Australia, the Federal Budget for July 2001 allocated a total of $5 million (Australia dollars) to cover the Take Back Program expenses for four years. That is around US$3.75 million (US$ 750,800/year). There are many factors that could influence the amount of resources required to implement a take back program in the US. However, taking into account the experience in Australia and using the population as the extrapolation factor, it could be estimated that US$11,000,000 would be required annually in the US to implement a pharmaceutical product take back program.

In Australia, the pharmaceutical product take back program is supported by both government and the pharmaceutical industry. This is a schema that could be implemented in the other countries as well. Take back programs are part of what is called “product stewardship”. According to the EPA, product stewardship is a product-centered approach to environmental protection. Also known as extended product responsibility (EPR), product stewardship calls on those in the product life cycle—manufacturers, retailers, users, and disposers—to share responsibility for reducing the environmental impacts of products. Many corporations have embraced this principle. In the US, pharmaceutical industry fosters product stewardship programs through the use of reverse distributors for collection of unwanted pharmaceuticals from pharmacies and health care centers. The extension of this program to the general public could be seen as an extension of the current product stewardship approach. A dialogue between industry, government and public in general could be established to share responsibilities in this issue and to establish an integrated take back program.

On the other hand, many of the pollution preventive measures that would reduce the amount of pharmaceuticals that is discharged in the environment would also bring many benefits for both industry and consumers. One of the common criticisms usually made to the pharmaceutical industry relates to the drug prices and the cost that medications represent on the whole health care system. However, it has been determined that the cost of unwanted pharmaceuticals produced due to the lack of compliance and education, could be significant. In the survey conducted by Boivin (1997) in Canada, it was estimated that the cost of the unwanted pharmaceuticals could exceed Can$110 million annually. Other studies have estimated that for the Canadian Health Care System, the economic annual cost that could be potentially avoided by better engineering of prescribing practices and patient education (i.e. compliance) could be as high as Can$7-9 billion, which is between US$6-7.6 billion dollars (Dec 2005 exchange rate) (Daughton, 2003).

The Office of Fiscal Analysis in Connecticut estimates that recycling unused prescription drugs could save Medicaid and private insurers in the state $7 million a year. A rough estimate of the national monetary value of unused drugs in Long Term Care facilities in the US is US$ 73-378 million (Daughton, 2003). Medicare and Medicaid, government programs funded by the taxpayers, spend large sums of money on prescription drugs including those drugs that are discarded. Savings produced by increasing the efficiency of the drug distribution system could be used to expand prescription drugs benefits, lower out-of-pocket drug costs, or provide coverage for other health services. (Wang, 2000).

It can be seen that the economic benefits for establishing the different pollution prevention measures, including a take back program, exceed the cost of implementing them. This is without taking into account the environmental benefits, which at this stage would be difficult
to quantify economically. However, the health of the environment is directly linked to the health of the communities. So, we may say that every measure we take to improve the quality of our environment would represent saving in health care in the future.

8. Conclusions and Recommendations:
The occurrence of pharmaceuticals in the environment at trace levels is a fact. Reviewing the life cycle of pharmaceutical products, it can be determined that releases from manufacturing facilities are usually very low due to the fact that these processes are normally very well contained. However, it has been determined that a large amount of these substances come from the disposal of unwanted pharmaceuticals in the environment by the public.

Taking into account programs from other countries and surveys from specific areas, it was estimated that 4,600 tons of unwanted pharmaceuticals may be generated annually in the US. Part of that amount is either disposed down the sink/toilet or sent to landfills. Even though the impact of pharmaceuticals in the environment at trace levels has not been clearly determined, there are many pollution prevention measures that could be implemented in a precautionary way. These measures follow the hierarchy of: minimize/reduce, reuse/recycle and finally proper disposal. Many of these measures would also contribute to the reduction of Health Care Cost. It has been determined by many studies that the cost of unused drugs is in magnitudes of millions and perhaps billions of dollars every year.

In order to be able to reuse/recycle and to give proper disposal to unwanted pharmaceuticals there is a need of a pharmaceutical product take back program that would allow the public to return unwanted pharmaceuticals. In the US, the pharmaceutical industry currently uses reverse distributors for the collection of unwanted pharmaceuticals from Pharmacies and Health Care Centers. This system could be used as a foundation for an integrated pharmaceutical product take back program that would cover general public as well. This initiative could be also seen as an extension of the product stewardship programs already fostered by the pharmaceutical industry. A national dialogue between industry, government, the scientific community and general public is recommended in order to get agreement on issues such as regulatory compliance, funding, education and logistics. NGOs and the Academy could play a critical role as mediators in this dialogue.

9. References


