

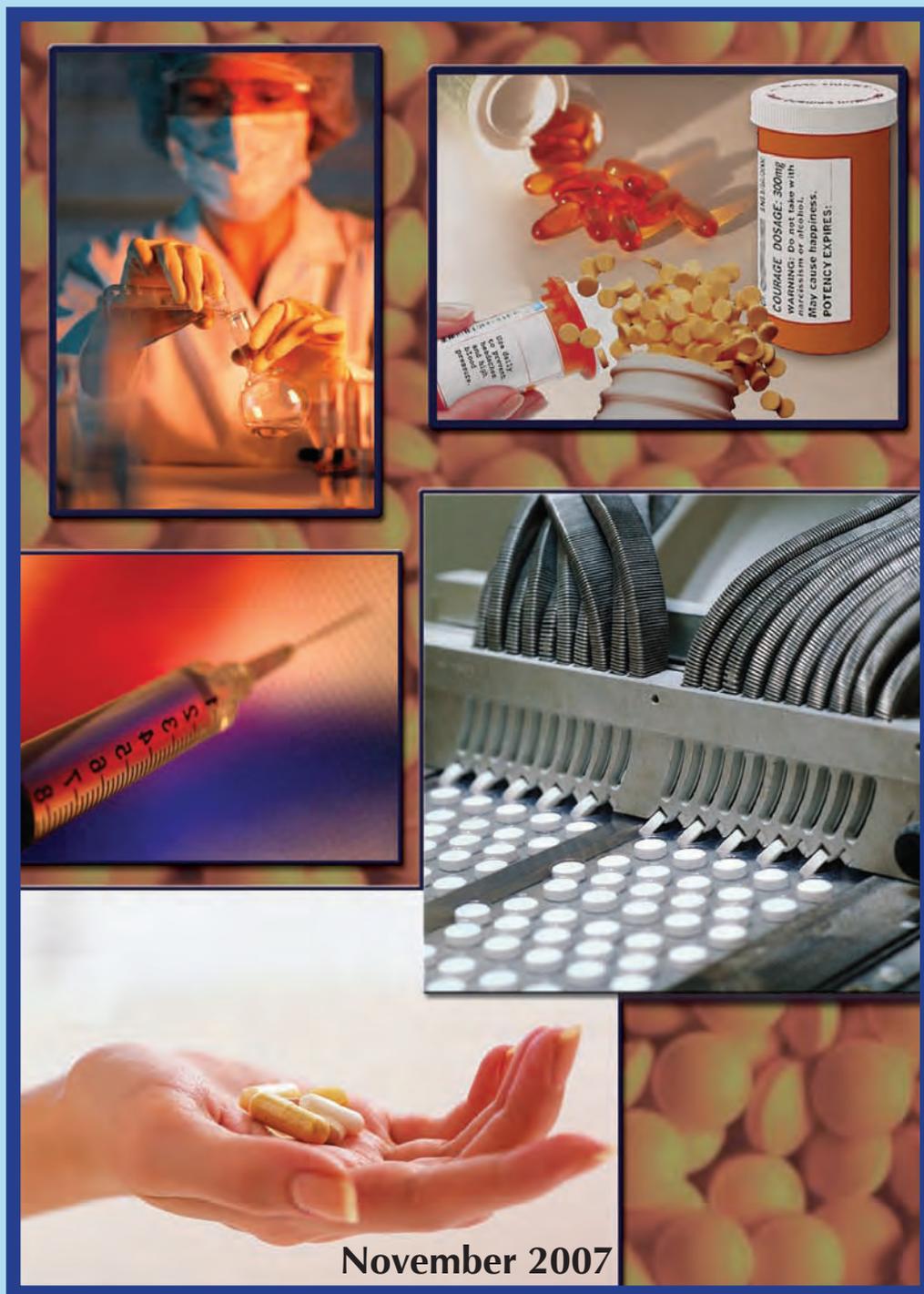
California Pharmaceutical Industry Hazardous Waste Source Reduction 2002 Assessment Report



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November 2007

**CALIFORNIA PHARMACEUTICAL INDUSTRY
HAZARDOUS WASTE SOURCE REDUCTION
2002 ASSESSMENT REPORT**

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REPORT OVERVIEW

This is the first assessment of the California pharmaceutical industry's (Standard Industrial Classification (SIC) 2833, 2834, 2835 and 2836) efforts to reduce its hazardous waste under the Hazardous Waste Source Reduction and Management Review Act of 1989 (the Act or SB 14).

SIC 2833, (medicinals and botanicals) refers to manufacturers that make or extract bulk materials-barrels or jars of materials.

SIC 2834, (pharmaceutical preparation), manufacturers make pills, powders, potions, etc., combinations of active and inactive ingredients in forms suitable for dosing patients.

SIC 2835, (In Vitro and In Vivo diagnostics substances), In Vivo manufacturers make products like x-ray dyes and radioactive tracers that are used in the body for testing. In Vitro manufacturers make test kits.

SIC 2836 manufacturers make serums, vaccines, blood plasma, and various similar substances.

This report addresses the period from 1999-2006. It discusses California pharmaceutical industries' hazardous waste source reduction achievements during 1999-2002 and source reduction projections for 2003-2006. This assessment is based on a review of the 2002 source reduction documents prepared by the California pharmaceutical industry as mandated by SB 14. DTSC's review of the 2002 plans was done during 2006.

DTSC initially contacted all the California pharmaceutical facilities that appeared to be subject to SB 14, and requested each to submit their 2002 SB 14 Source Reduction Plan (Plan) and Hazardous Waste Management Performance Report (Performance Report). Upon receipt of these documents, DTSC reviewed the Plans and Performance Reports for completeness and notified the facility if further information was needed. Once DTSC had complete information for a facility, staff reviewed the documents for their technical content, to extract information regarding waste generation, waste management techniques, and source reduction measures in the industry. The review process also entailed frequent telephone conversations with the facility representatives to clarify or augment the information the facilities provided. Furthermore, DTSC staff visited a number of pharmaceutical facilities, to get a hands-on knowledge of the manufacturing and waste-generating processes of the industry.

Based on the review of this industry 2002 Source Reduction (SB 14) documents, DTSC prepared an assessment report with 28 profiles representing 26 companies. Each profile was sent to the respective facility for review. Each

profile may have information on one individual site or multiple sites for each company. The profile contains site information, its reduction accomplishments for major waste streams from 1999 to 2002, and their projections for further reducing these major waste streams from 2003 to 2006. The report provides an overall data review and summary of the industry-wide accomplishments for reducing hazardous waste.

Based on our SB 14 document reviews and site visits, we found that a large portion of pharmaceutical facilities' hazardous wastes are collected and sent off-site for incineration. In order to learn more about the industry's overall waste management practices, we requested general waste information from the reporting facilities. Table 1 provides a compilation of data from those facilities that chose to respond.

Facilities subject to SB 14 reported a total manifest hazardous waste generation of 19 million pounds in 1998, and about 39 million pounds in 2002. The total reported waste avoidance through source reduction by this industry sector was 3.1 million pounds/year from 1998-2002.

I. BACKGROUND

The Hazardous Waste Source Reduction and Management Review Act of 1989 (SB 14) is codified in Health and Safety Code Sections 25244.12 to 25244.24. This law applies to large quantity generators that produce more than 12,000 kilograms (13.2 tons) of hazardous waste, or 12 kilograms (26 pounds) of extremely hazardous waste, in 1990 and every four years thereafter. The law requires these generators to:

- Conduct a source reduction evaluation of their facilities and prepare the following source reduction documents:
 - (1) Source Reduction Evaluation Review and Plan (Plan)
 - (2) Hazardous Waste Management Performance Report (Report)
 - (3) Summary Progress Report (SPR)
- Implement feasible methods for reducing the quantity and/or the hazardous characteristics of routinely generated hazardous waste.

The main purpose of requiring generators to review and implement source reduction practices is to reduce the quantity of hazardous waste generated in California and thereby to promote public health and safety and to improve environmental quality. However, source reduction can also help large quantity generators avoid future liabilities and become more efficient in their use of resources. In short, source reduction is a win/win proposal for environmental protection and business improvement.

The Plan, which is directed toward the future, must include information about the facility's operations, and provide waste generation data for the reporting year (i.e. 2002). The Plan must also include a list of potential source reduction measures for major waste streams, and describe the efforts taken to evaluate these measures. Major waste streams are defined as those waste streams that exceed five percent of the total weight of routinely generated hazardous wastes. Major waste streams are separately categorized¹ for both Category A and Category B wastes.

¹ Major waste streams can fall under one of three categories:

- Category A: hazardous wastes that are processed through an on-site wastewater treatment unit prior to discharge to a publicly owned treatment works (POTW) or to a receiving water under a National Pollution Discharge Elimination System (NPDES) permit.
- Category B: all other hazardous wastes that is not processed in a wastewater treatment unit.
- Category C: all wastes that are classified as extremely hazardous wastes.

Please refer to the "Guidance Manual for Complying with the Hazardous Waste Source Reduction & Management Review Act of 1989" (December 2002) for a more detailed discussion in determining major wastes.

To develop and screen source reduction measures, generators must indicate in their Plan that they considered, at a minimum, the five approaches mandated by SB 14:

- (1) Input Changes, which include raw material or feedstock changes to reduce, avoid, or eliminate the use of hazardous materials in the production processes. This reduces the generation of hazardous waste within the production process.
- (2) Operational Improvement, which includes loss prevention, waste segregation, production scheduling, maintenance operations, and overall site management.
- (3) Production Process Changes, which includes changes in production methods or techniques; equipment modifications; changes in process operating conditions such as temperature, pressure; process or plant automation; or the return of materials or their components for reuse within existing processes.
- (4) Product Reformulations, which includes changes in design, composition or specification of final or intermediate products.
- (5) Administrative Steps, which includes inventory control, employee continued improvement programs, and good operating practices that apply to the human aspect of conducting day-to-day operations at the facility. These steps include employee training, procedures, incentives, bonuses and other such programs that encourage employees to focus on preventing the generation of hazardous waste.

The Report discusses past source reduction activities and management practices of major waste streams, production and other factors that affected routine waste stream generation since the baseline year (previous reporting year: 1998).

The SPR summarizes key data and major waste stream information spanning eight years. The current 2002 SPR covers the 1999-2006 period. Source reduction accomplishment and projection data are entered into the SPR directly from the generators' previously prepared Plans and Reports. The SPR also summarizes generators' total hazardous waste quantities for year 1998, and 2002. Starting September 1, 1989, and every four subsequent years, SB 14 generators are required to submit their completed SPR to DTSC. Out of the three SB 14 documents, the SPR is the only SB 14 document that must be submitted to DTSC.

SB 14 requires DTSC to select two categories of generators by Standard Industrial Classification (SIC) code every two years for source reduction planning

assessment. For this fourth SB 14 cycle, generators subject to SB 14 were required to prepare documents by September 1, 2003, for the 2002 reporting year. As part of this assessment, during 2005, letters were sent to the California industries operating under SIC code 2833 (medicinals and botanicals), 2834 (pharmaceutical preparations), 2835 (diagnostic substances), and 2836 (biological products, except diagnostic) requesting SB 14 documents submittal to DTSC for a technical and completeness review.

II. INTRODUCTION

A. General Industry Background

The pharmaceutical industry includes the manufacture, extraction, processing, purification, and packaging of chemical materials to be used as medications for humans or animals. The principal manufacturing steps are: (a) preparation of process intermediates; (b) introduction of functional groups; (c) coupling and esterification; (d) separation processes such as washing and stripping; and (e) purification of the final product. Additional steps include granulation; drying; tablet pressing, printing and coating; filling and packaging. [1]

Each of these steps may generate air emissions, liquid effluents, and solid wastes. This assessment report focuses on the hazardous wastes generated by this industry. One type of waste that is generated by the pharmaceutical industry, but regulated by the Department of Health Services is medical waste. Pharmaceutical wastes are managed as follows:

- Hazardous waste: recycled or shipped offsite for land disposal, treatment, or incineration.
- Medical waste:
 - solids: shipped offsite for incineration
 - liquids: discharged to POTW following inactivation of biological/biohazardous components

This report focuses on four SIC codes:

1) Medicinals and Botanicals (SIC 2833)

Facilities in this category are primarily engaged in: (1) manufacturing bulk organic and inorganic medicinal chemicals and their derivatives and (2) processing bulk botanical drugs and herbs. This category includes industries that manufacture products of natural origin, hormonal products, and basic vitamins, as well as those that isolate active medicinal principals such as alkaloids from botanical drugs and herbs.

2) Pharmaceutical Preparations (SIC 2834)

This category includes facilities primarily engaged in manufacturing, fabricating and processing raw materials into pharmaceutical preparations for human and veterinary uses. Finished products include tablets, capsules, liquids, etc. These are intended for distribution as prescription and over-the-counter (OTC) drugs.

3) In Vitro and In Vivo Diagnostic Substances (SIC 2835)

This category includes facilities engaged in the manufacturing of chemical, biological, and radioactive substances used in diagnosing or monitoring human and animal health by identifying and measuring normal and abnormal constituents of body fluids or tissues. Diagnostics substances manufactured In Vivo (tested inside a living organism) and In Vitro (tested outside a living organism)

4) Biological Products, except Diagnostics Substances (SIC 2836)

This category includes facilities engaged primarily in the production of bacterial and virus vaccines, toxoid and analogous products, serums, plasmas, and other blood derivatives for human and veterinary use.

The pharmaceuticals industry also receives extensive regulatory oversight by the U.S. Food and Drug Administration (FDA). When a pharmaceutical company discovers a compound that may have medical potential, the company usually applies for a patent. Patents are valid for 20 years from the date of application. Any drug may be marketed only after approval by the FDA. The drug development process averages 15 years, beginning with initial toxicology testing, followed by clinical trials for safety and effectiveness, and review of the application by the FDA. [2] Figure 1 shows a schematic of the drug development and approval process.

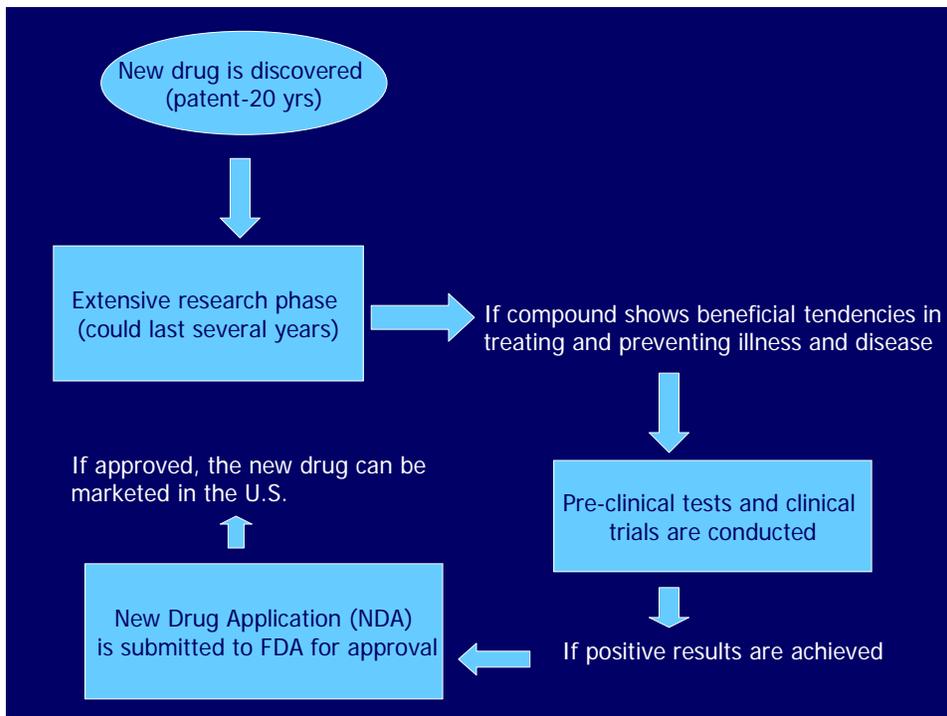


Figure 1. Schematic of the process from discovery to application for approval

Industrial Process Description[2]

The production of pharmaceutical products can be broken down into three main stages: a) research and development; b) the conversion of organic and natural substances into bulk pharmaceutical substances or ingredients through fermentation, extraction, and/or chemical synthesis; and c) the formulation of the final pharmaceutical product.

The pharmaceutical production process starts with an extensive research stage, which can last several years (see above stage characterization).

The three most common manufacturing methods include chemical synthesis, natural product extraction, and fermentation.

- (1) Chemical synthesis consists of four steps-reaction: reaction, separation, purification, and drying.
- (2) Natural product extraction, involves isolating an active ingredient from natural sources, such as plants, roots, parasitic fungi, or animal glands. Blood fractionation, used to produce plasma, is also part of the natural product extraction process.
- (3) In fermentation, microorganisms are typically inoculated in a liquid broth supplemented with nutrients that are acclimated to an environment conducive to rapid growth. These microorganisms produce the desired product as a by-product of normal metabolism. Fermentation involves three main steps:
 - (a) Inoculum and seed separation, where spores from a master stock are activated with water, nutrients, and heat. As the mass grows, it is transferred to a seed tank with a typical capacity of 100-2,000 gal, where further growth occurs.
 - (b) Fermentation, where the seeds from the foregoing step are combined with raw materials in a fermentation vessel, typically 5,000 to 100,000 gal. Air is sparged through the vessel to help sustain growth, and the action of the microorganisms on the raw materials results in the desired product. At the end of this step, filtration may be used to separate the microorganisms from the product. Fermentation typically requires a period of 12 hours to 1 week for completion and
 - (c) Product recovery and purification, which are usually achieved through solvent extraction, direct precipitation, ion exchange, or adsorption.

Formulation processes convert bulk chemicals into refined products that include: tablets, capsules, liquids, patches and ointments. Typical formulation operations include mixing, blending, granulating, drying, coating, polishing, tablet pressing, capsule filling, sorting, and packaging.

B. Overall Pharmaceutical Industry Wastes

This report focuses primarily on hazardous wastes, but will also provide a general overview of the other types of wastes generated by the pharmaceutical industry. Based on our SB 14 document reviews and site visits, we found that a large portion of pharmaceutical facilities' hazardous wastes are collected and sent off-site for incineration. In order to learn more about the Pharmaceutical industry's overall waste management practices, we requested general waste information from the reporting facilities. Table 1 provides a compilation of data from those facilities that chose to respond. While Table 1 includes all wastes identified by our responders, the results for individual facility vary with no facility producing all of the wastes noted.

Disposal of pharmaceutical products is regulated by both hazardous waste laws and state medical waste laws. A correspondent from the industry stated that the medical waste rules address only final products, and do not include product intermediates. If a product intermediate does not meet hazardous waste definitions, rules governing disposal are frequently prescribed by the local POTW and solid waste vendor. Product intermediates meeting the definition of hazardous waste in California are regulated as hazardous waste.

The FDA (Food and Drug Administration) requires companies to conduct environmental assessments of the impact that their drug can have in the environment due to manufacturing related releases and also via human use. There are categorical exclusions addressed online. See "Guidance for industry Environmental Assessment of human drug and Biologics Applications" at <http://www.fda.gov/cder/guidance/index.htm>

Table 1. Overall Pharmaceutical Industry Wastes

Waste type	Source	Waste Description	Management Approach
Solid	General business activities	Trash including office waste, food wastes, non-recyclable plastic/paper/cardboard/metals	Consolidated then shipped for disposal at a solid waste landfill
Recyclable	General business activities	Aluminum, mixed paper, cardboard, other scrap metal, plastic, styrofoam	Consolidate and shipped to Recycler
Aqueous	General business activities, R &D,	Industrial process wastewater (includes liquid product intermediates), non-process wastewater, utility wastewater,	Discharged to POTW in compliance with local ordinance and industrial discharger

	Manufacturing	sanitary wastewaters, equipment wash water	permit.
Hazardous	General business activities, R &D, Manufacturing, lab clean outs, quality control	Liquid and solid hazardous chemical wastes, non-hazardous chemical wastes, universal wastes, chemical based pharmaceutical compounds, excess and expired lab chemicals	Shipped off-site for land disposal, treatment, recycling and/or incineration at a permitted hazardous waste facility.
Medical - solid	R&D, Manufacturing of biologics	Solid wastes containing biological/biohazardous materials (blood contaminated articles, e.g. plastic bottles, gloves). Solid biotech pharmaceutical waste (final dosage/form product intermediates), APIs (Active Product Ingredients), solid debris, sharps	Shipped off-site for incineration at a licensed medical waste facility
Medical - liquid	R&D, Manufacturing of biologics	Liquid wastes containing biological/biohazardous materials. Liquid biotech pharmaceutical waste (not in final dosage/form and packaging)	Biological/biohazardous materials are inactivated prior to discharge to the local POTW under local discharge requirements.
Radioactive -liquid	R&D	Liquid radioactive materials	Measured for activity, decayed when possible then discharged to POTW under local discharge requirements
Radioactive -solid	R&D	Solids contaminated with radioactive materials	Shipped off-site for burial at a licensed radioactive waste facility.
Universal	Computers, lights, small electronic devices	CRTs, fluorescent bulbs, batteries	Recycled, reclaimed or scrapped offsite.

C. WASTE PHARMACEUTICALS

In the past ten to fifteen years, there has been an increasing concern about waste pharmaceuticals in environmental media, particularly surface and ground waters. This is due less to the sudden appearance or increase of pharmaceuticals or their metabolites in the environment, as to the development

of more sensitive analytical methods that now allow greater identification and measurement of these compounds, as well as to the results of ecological investigations that were previously not recognized.

The escalating growth of new pharmaceutical products is adding exponentially to the already large array of chemical classes we have introduced to the environment. [3] Human pharmaceuticals include prescription and over-the-counter drugs, diagnostic agents, and “nutraceuticals” (bioactive food supplements). Therapeutic drugs include hormones, antibiotics, blood lipid regulators, analgesics and anti-inflammatory drugs, beta-blockers, antidepressants, antiepileptics, antineoplastics, tranquilizers, and retinoids, among others [4] In addition, the proliferation of large-scale animal farming has resulted in the widespread use of animal drugs and feed additives, including antimicrobials, antiprotozoals, ecto- and endo-parasiticides, and hormones. [5] Farmers administer the drugs and additives to their animals for therapeutic, growth, and nutritional purposes.

It appears to be generally accepted that the main source of pharmaceuticals in the environment is from human and farm animal excretions of drugs or their active or inactive metabolites. Other sources include: disposal of unused pharmaceuticals, particularly to sewage systems; disposal of product from the supply chain; and releases of waste from pharmaceutical manufacturers. A brief discussion of each follows.

1) Excretion of pharmaceuticals to environmental media:

In countries where we have detected and measured pharmaceuticals in the environment, humans excrete pharmaceuticals to sewage systems which discharge primarily to wastewater treatment facilities, or in some cases to septic systems. Wastewater treatment facilities discharge treated effluent to surface waters, while septic systems generally leach wastewaters directly to subsurface soils.

Cattle, swine, poultry, and fish excrete pharmaceuticals into the soil and water. Manure and litter is also often spread on the land, resulting in the drug contaminants leaching and running off into ground and surface waters. Wash-off of topical treatments also results in environmental discharges. While pet treatment and disposal of unused medicines may also contribute to the problem, farm animals (including those in aquacultures) are probably the largest source of environmental contamination from animal drugs. [4]

2) Disposal of unused pharmaceuticals.

Individuals as well as medical institutions can dispose of unused pharmaceuticals into their sewage systems or solid waste stream. Data from

some countries suggest that patients dispose 25% to 33% of the volume of drugs sold.

3) Disposal of product from the supply chain.

The disposition of unsold product along the supply chain is tightly controlled. Companies maintain accounting procedures, and expired products, for example, are commonly returned to the manufacturer. Typically, companies use destructive processes such as incineration to dispose of unsold pharmaceuticals. For these reasons, this is an unlikely source of pharmaceutical contamination of the environment. [5]

4) Releases of waste from pharmaceutical manufacturers.

Our study focuses on hazardous wastes generated by the pharmaceutical facilities in California, but discharges from manufacturing facilities are not believed to be the source of widespread detection of human pharmaceuticals in the aquatic environment on the basis of several lines of evidence and reasoning. In general, manufacturers avoid disposal of active pharmaceutical ingredients (APIs), which are extremely valuable products, from a purely business perspective. APIs are commonly synthesized and purified in organic solvent-based media. Spent solvents are recovered or treated and disposed via incineration. Losses of APIs to the environment should be relatively small. Solid wastes that contain APIs are commonly incinerated.” [5] Furthermore, it is unlikely that drug manufacturing wastes contribute significantly to environmental contamination, as these wastes are highly regulated. This was verified in the course of this industry assessment.

With regard to the environmental impact of pharmaceuticals, there is a great deal of uncertainty. Some of the problems include: the ability of current environmental effect tests to address effects caused by bioactive pharmaceuticals; the paucity of chronic ecotoxicity data on pharmaceuticals; the relevance of acute toxicity test data in an area where experts suspect the more damaging effects may be chronic; and, following on the last point, the value of predicting chronic ecotoxicity potential from acute toxicity data; and the value in using information we already have from studying industrial chemicals in assessing the behavior of pharmaceuticals, whose physiochemical properties differ significantly. [5]

That said, there appear to be some disturbing data which indicate that waste pharmaceutical environmental contaminants are having some effect on the living organisms. A recent review of the effects of animal pharmaceuticals in the environment noted both acute toxicity and chronic developmental and reproductive effects on certain microorganisms. [4] Leading scientists have noted disquieting effects or potential effects from human and animal pharmaceuticals or their metabolites in the environment. Some examples include: [3]

- the endocrine disruptive action of hormone contaminants – feminization of fish in sewage treatment lagoons and outlets was first noted in the mid-1980s
- the alarming pathogen resistance and genotoxicity probably resulting from the widespread use of antibiotics, in both human and animal treatment
- the reproductive interference on aquatic organisms of antidepressants and other neuron-regulators
- the highly genotoxic activity of antineoplastics (used for chemotherapy), which have the potential to act as either acute or long-term stressors (acting as mutagens, carcinogens, teratogens, and/or embryotoxins)

It is clear that a great deal of work remains in assessing the threat of waste pharmaceuticals in the environment – from identifying and measuring the waste pharmaceuticals and their metabolites, to developing effective risk assessment and risk management methods.

III. PHARMACEUTICAL INDUSTRY PROFILES

This assessment report contains information on 28 pharmaceutical industry profiles, representing 26 companies. Each profile may have information on one individual site or multiple sites for one company. This information is uniformly reported based on the categories listed below. Readers can evaluate like information categories across the profiles, and gain some insight into industry operations and their accomplishments and projections to reduce hazardous waste for the eight year span (1999 to 2006). Readers are cautioned against making strict comparisons between facilities due to differences in feedstocks, processes, products, and other industry-specific factors. The categories listed in each profile include:

- (1) Site Information—Contains general site-specific information such as location, principal products, number of employees, years of operations and other descriptive information.
- (2) Major waste streams—Contains a table with information on the major waste streams by California Waste Code (CWC) generated by the facility for 1998 and 2002, if the facility was subject to SB-14 both years. If the facility was subject to SB-14 only in 2002, then information is listed for that year only. Note that some facilities provided updated information for more recent years for comparison.
- (3) Accomplishments—This section discusses for each site, the overall hazardous waste reduction of their SB-14 waste production for the reporting years 1998 and 2002. Included is information on the source reduction progress of all measures selected in 1999 for major generated waste streams. For each of the major waste streams, information was presented on the waste stream source.
- (4) Projections—This section discusses each site's selected source reduction measures for their major waste streams from their 2002 source reduction documents.
- (5) Remarks—This section includes any information about facility name changes and/or any factor affecting the generation of waste.

**Profile #1
Aerojet Fine Chemicals
Rancho Cordova
EPA ID: CAR000069153
SIC: 2834**

Site Information

[In November 2005, American Pacific (Ampac) acquired the Aerojet Fine Chemicals Rancho Cordova facility. However, this assessment report addresses *Aerojet Fine Chemicals*, which owned the facility in 2002.]

Aerojet Fine Chemicals (AFC) primarily produces bulk chemicals for pharmaceutical applications, specializing in high hazard chemistry and new technologies. AFC manufactures Active Pharmaceutical Ingredients and bulk pharmaceutical intermediates. Also, the facility provides process research and development services on a contract basis. As of 2003 AFC had approximately 150 employees.

Major Waste Streams in 1998-2002

Waste Stream	CWC	Pounds (1998)	Pounds (2002)	Description/Waste Generating Processes
Aqueous solutions with organic residue > 10%	133	4,383,870	4,970,000	
Unspecified solvent mixture	214		13,969,191	These include methanol, isopropyl alcohol and acetone. Generates from reactions, wash product and equipment cleaning.
Phosphorous Oxychloride	791	NA	4,500	Manufacturing process
Chloroform*	741		725	Manufacturing process

*this wastestream was replaced by phosphorous chloride after 2002.

Accomplishments

Measures taken consist of:

- Inventory control. Expired materials are sent back to vendor as a first attempt. If the original vendor does not accept the material, the next approach is seek a vendor that can still use the material, such as a college, broker, or other chemical company. The final option is disposal as hazardous wastes.
- Production scheduling and loss prevention. AFC uses batch records to keep track of each kilogram used at every step during production.
- Training. AFC also provides training to encourage waste minimization activities. Annually AFC provides Good Manufacturing Practice (GMP) and hazardous waste generator trainings, where waste segregation and avoidance of spills are emphasized.

Projections

CWC 214 (Unspecified solvent mixture)

This stream is generated from the use of raw solvents to start and complete reactions, transport chemicals during reaction, wash product, and to clean equipment after a program has finished. The amount of solvent used is not randomly determined since programs (which are contracted to AFC by a customer), are validated by the Food and Drug Administration (FDA). A possible reuse of solvents has to be addressed at the very start of negotiations for a contract.

CWC 133 (Aqueous solutions with organic residue > 10%)

Measures that are currently taken but have room for improvement are operational improvements. One opportunity would be to separate the organic even further from the aqueous by reducing the amount of hazardous waste by introducing a carbon filter or steam stripper prior to the waste tank.

CWC 791 (Phosphorous Oxychloride)

The measure proposed to this stream is to reuse the first process stream of Phosphorous Oxychloride (POCL) in the manufacturing process. This would result in a 25 % waste reduction. This measure would require safety controls. Assuming the generation of POCL would be the same; this would mean a \$1700 savings in material cost.

Profile #2

Alza Corporation

EPA IDs: CAD982475964

CAD981694961

CAD061622783

CAD982503534

CAD981973712

CAR000016782

SIC: 2834

Site Information

The Alza Corporation has six facilities which are located in Palo Alto, Mountain View (headquarters), Menlo Park, Redwood City and Vacaville. It conducts research, development and manufacturing of controlled rate drug delivery systems ("therapeutic systems"). Alza documented in its SB 14 Plan that their facilities are engaged in similar operations using similar processes that generate similar waste streams. In 2002-2003, Alza's California workforce was comprised of approximately 2400 people. The following is a brief overview of the activities conducted in each of their six facilities.

(1) Vacaville Site (Building V): Alza produces essentially four types of therapeutic systems. These four types include Oral Osmotic Systems (OROS), Transdermal Therapeutic System (TTS), Implant Technology known as DUROS, and Liposomal Technology. The OROS system generated relatively large volume of hazardous waste. Three types of raw materials are required to produce therapeutic systems: (a) active drug medium (b) excipients (non-active filler substances added to a drug medium to give it more consistency) and (c) solvents. Active drug medium and excipient are initially blended together. A non-hazardous lubricant is added to the mixture to avoid sticking during die pressing. The mixture is then run through a tablet compression machine. The next step is to provide the tablet with a membrane coating. Membrane processes delay drug release until the tablet enters the stomach and are proprietary. Alza has four tablet coaters: two are operated using chlorinated solvents and the other two with non-chlorinated solvents. Essentially all solvents are evaporated from the applied coatings following the coating application process. The OROS systems are drilled using a laser and then dried to remove any residual solvents. An aqueous based overcoat is then applied. Finally the coating is printed with product name, or symbol, and packaged. Alza Vacaville also produces three types of transdermal products: an extruded product, a form-fill-seal (FFS) product, and a solvent cast product. Contacts at the Vacaville facility indicated that approximately 70% of waste management concerns are related to the OROS solvent coating process. The remaining waste management concerns center around "nicotine contaminated process waste".

(2) Redwood City (RC1) site: This site performs commercial manufacturing of ORTHO EVRA, a contraceptive transdermal (TTS) system. This manufacturing operation was initiated in 2002. TTS systems are produced using the process used at Vacaville site. Waste solvents are stored in drums for disposal through a hazardous waste disposal contractor that picks up stored wastes at the facility.

(3) Palo Alto site (PA11): Research and Development (R & D) activities are performed at this site. In addition to R & D, a small scale manufacturing of DUROS (implant system for treatment of advanced prostate cancer) occurs at this facility. The hazardous waste generated through the R & D and manufacturing activities is limited. The major waste stream at the facility is wastewater containing a non-hazardous disinfectant generated from cleaning the aseptic (sterile) facility.

(4) Mountain View facility (M1): The M1 facility is engaged in the development, analytical testing, and pilot scale operation of products using OROS technology, and the membrane coating of ALZET. ALZET is a device (pump) that is used to control the amount of a drug administered during research and development activities. The Pan-Coating step (typical of that used for coating OROS tablets) in which the membrane material, dissolved in a solvent, is sprayed onto the subassembly. This is the only ALZET process step that generates hazardous waste. Hazardous waste ALZET solvents are drummed and disposed through professional disposing contractor. ALZA sold its ALZET product line in 2003.

(5) Mountain View facility (Site M3): This site consists of one building, which contains offices, R & D facilities and analytical laboratories. The most significant analytical research activities occurring at this site is the High Pressure Liquid Chromatography (HPLC) analytical function. Chlorinated and non-chlorinated wastes are generated at this facility.

(6) Menlo Park Facility (Site MP): The Menlo Park facility conducts R & D and pilot scale operations for transdermal and liposomal technologies, as well as laboratory analytical operations. The hazardous waste streams generated from this site include (a) process waste water containing a small quantity of flammable solvent, (b) wastewater from facility cleaning and disinfecting operations (c) small amount of cytotoxic drug compound (d) mobile phase solvent waste (e) expired laboratory and chemical feedstocks and (f) empty reagent bottles.

Major Waste Streams in 1998-2002

Vacaville Site (Building V)

EPA ID: CAD982475964

Waste Stream	CWC	Pounds 1998	Pounds 2002	Description/Waste Generating Processes
Spent halogenated solvents	211	970,397	935,847	Tablet Coating Operations
Non-halogenated solvents	212	57,637	464,576	Tablet Coating Operations
Nicotine containing wastes	P075	123,222	267,985	Pharmaceutical Manufacturing Operations
Active Pharmaceutical (drug) waste	311	173,577	0	Pharmaceutical Manufacturing Operations

Site RC1 (Redwood City)

EPA ID: CAD981694961

Waste Stream	CWC	Pounds (1998)	Pounds (2002)	Description/Waste Generating Processes
Active Pharmaceutical (drug) process waste	311	----	120,794	Pharmaceutical Manufacturing Operations
Non-halogenated solvents	212	----	39,421	Pharmaceutical Manufacturing Operations
Empty bottles previously contained solvents	513	----	7,508	Pharmaceutical Manufacturing Operations

Major Waste Streams in 1998-2002

Site PA11 (Palo Alto)

EPA ID: CAD061622783

Waste Stream	CWC	Pounds (1998)	Pounds (2002)	Description/Waste Generating Processes
Unspecified aqueous solution	135	----	32,784	Generated from aseptic manufacturing operations. Contains disinfectant and corrosive detergent.
Spent oxygenated solvents	212	10,493	4,800	Generated from research and analytical testing process.
Other organic solids	352	----	3,873	IPA wipes generated from aseptic manufacturing operations
Off-specification, aged, or surplus organics	331	4,224	2,174	Generated from Aseptic manufacturing operations.
Aqueous soln. with total organic residue <10 percent	134	1275	0	
Empty containers < 30 gallons and empty one gallon glass reagent bottles	513	4,300	0	

Major Waste Streams in 1998-2002

Site M1 (Mountain View)
EPA ID CAD982503534

Waste Stream	CWC	Pounds (1998)	Pounds (2002)	Description/Waste Generating Processes
Oxygenated solvents	212	68,013	66,960	Research and Development Activities and analytical equipment
Unspecified aqueous solution	135?		10,640	corrosive aqueous solution generated from analytical laboratory processes
Active Pharmaceutical (drug) process waste	311	75,573	755	Research and Development Activities and analytical equipment
Halogenated spent solvents	211	1,917	3,604	Previous manufacturing of equipment used to conduct research (ALZET)
Other empty containers 30 gallons or more (previously contained solvents)	512	5,000	990	Research and Development Activities and analytical equipment
Off-spec., aged, or surplus organics	331	7,926	1,804	Research and Development Activities and analytical equipment

Major Waste Streams in 1998-2002

Site MP (Menlo Park)

EPA ID CAD981973712

Waste Stream	CWC	Pounds (1998)	Pounds (2002)	Description/ Waste Generating Processes
Unspecified aqueous solution	135	----	17,466	Facilities cleaning and disinfecting
Oxygenated solvents	212	8,600	9,169	Research and Development Activities and analytical Equipment
Aqueous soln. with total organic residues less than 10 percent	134	35,640	5,080	R & D Activities
Off-spec., aged, or surplus organics	331	1,529	1,821	Research and Development Activities and analytical Equipment

Site M3 (Mountain View)

EPA ID CAR000016782

Waste Stream	CWC	Pounds (1998)	Pounds (2002)	Description/Waste Generating Processes
Spent oxygenated solvents	212	21,600	23,500	Research and Development Activities and analytical Equipment
Unspecified aqueous solution	135		5,720	Corrosive aqueous solution generated from laboratory analytical processes
Off-spec., aged, or surplus organics	331	960	4,299	Research and Development Activities and analytical Equipment
Empty containers less than 30 gallons	513	1,640	1,185	Research and Development Activities and analytical Equipment

Accomplishments

In 1998, Alza's Waste Minimization committee evaluated routinely generated major hazardous waste streams. Alza identified twelve source reduction measures as potentially viable waste reduction methods. Four out of the twelve measures were selected for implementation and are discussed below:

- (1) Computerized tracking system for research chemicals: Alza purchased a license to use the Environmental Management Software (EMS) to track laboratory chemicals use at its Mountain View facility. This measure entailed the use of software at the Palo Alto and Vacaville facilities as well. The EMS system has a networking capability to interface with Alza's existing systems such as its inventory of research chemicals and its computerized purchase order system.
- (2) Review requests for raw materials purchases: This measure involves a process to review requests for raw materials purchases against a criteria designed to reduce waste generation. Alza's purchasing department and Environmental Health and Safety department review all chemical acquisition requests to determine if the quantity requested is appropriate and can be used within the allowable time. This enables Alza to minimize the generation of unused and/or outdated chemicals and drugs, excipients, and packaging materials which were previously disposed of as hazardous waste.
- (3) Replace disposable glass solvent bottles: This measure consists of elimination of one gallon reagent glass bottles by replacing them with reusable plastic containers.
- (4) Recycle oxygenated solvents: Oxygenated solvents are used in Alza's analytical laboratories. Many of the analyses involve the use of liquid chromatography (HPLC) processes. The HPLC process is used to extract drug molecules from the liquid chromatographic column. Oxygenated solvents and water are used to recondition the column after the analysis to ensure that no residual drug or contaminant molecules remain in the column. Alza installed Alltech recycler to interface with the HPLC systems to reduce mobile phase consumption.

Projections

Based on the review of Alza's 2002 Source Reduction Plan and SPR, it appears that all the measures selected during 1998 SB 14 evaluation and planned for 1999-2002 implementation were also selected in 2003 and implementation continues during the 2003-2006 cycle. However, one of the on-going initiatives

that results in future waste reduction benefits currently being implemented by ALZA takes place during the research and development (R & D) of new pharmaceuticals. At the R & D stage, ALZA designs the product formulation and production process to avoid use of chlorinated material.

While it is difficult to quantify the success of the program, ALZA believes that it has significantly reduced the volume and toxicity of hazardous waste generated. Since implementation of the program, there have been no new processes developed by ALZA that use chlorinated material.

ALZA is in a process of validating a procedure that will reduce the amount of waste generated during die cutting.

Miscellaneous—

- (1) During 1999-2002 period, Alza was operating four coaters—two using chlorinated and the other two using non-chlorinated solvents in their OROS product line. Alza is planning to substitute nonchlorinated coater for its use of chlorinated solvent, resulting in a total of three non-chlorinated and one chlorinated coater. This will result in reduction of waste chlorinated solvents.
- (2) Alza is also planning to reduce its membrane coating solution overspray at its Vacaville plant. This will result in reduction of 220 pounds per batch of product.
- (3) Alza has identified additional tentative measures that are currently being tested for feasibility.

Remarks

Based on a review of the ALZA SPR, it appears that most of the measures selected during 1998 and planned for implementation during 1999-2002 were also selected in 2003 and implementation is continuing during the 2003-2006 cycle.

Profile #3
Amgen Inc.
Thousand Oaks
CAD981450893
SIC Code: 2836

Site Information

Amgen Thousand Oaks operations consist of the research, development and manufacture of pharmaceuticals. Activities include the fermentation and purification of products, equipment maintenance, quality control and assurance, research and development of new product candidates, and administrative functions. In 2002, Amgen manufactured two commercially available biopharmaceuticals, Aranesp™ and Neulasta™. The facility currently employs approximately 7,000 people and has been operating for over 26 years.

Major Waste Streams

Waste Stream	CWC	Pounds 1998	Pounds 2002	Description/Waste-Generating Process
Dilute cyanide	135	0	180,385	25 ppm aqueous cyanide waste; from manufacturing process (protein modification and purification) in production of Neulasta™
Ethanol*	214	102,582	180,990	From production purification process

* Facility ceased to manufacture product which generated this waste stream in 2002.

Accomplishments

Participation in chemical exchange programs kept more than 24,500 pounds excess raw materials from going to landfills in 2002. (Although this may not appear as source reduction in the table above, excess raw material can become a hazardous waste if not reused.)

Projections

CWC 135 (Dilute cyanide)

By implementing waste segregation in the purification process, non-hazardous buffers loaded during equilibration can be discharged to industrial wastewater. Citrate buffer will be discharged with industrial wastewater, with an expected ten percent hazardous waste reduction, per run.

Remarks

Changes in product manufacture have resulted in changes in the types and quantities of hazardous waste generated. Amgen Thousand Oaks ceased producing Aranesp™ in 2003, thereby eliminating one waste stream. From a review of the facility's source reduction measure evaluations, it became clear that the major barrier to source reduction is the requirement for FDA approval for use of a new process or material.

Current hazardous waste management approaches include engineering controls, evaluation of pollution prevention opportunities prior to FDA approval, participation in chemical exchange programs, onsite recycling of excess raw materials, waste segregation where possible, and offsite treatment. Changes in product lines have affected hazardous waste management practices.

Profile #4
AnaSpec Inc.
San Jose
EPA ID: CAL000137397
SIC: 2834

Site Information

AnaSpec Inc. (AnaSpec) conducts business in the areas of custom peptide synthesis, antibody production, and reagent manufacturing. AnaSpec started its operations at San Jose in 1993 and employs 70 full time people. Their primary function is to manufacture peptides and reagents primarily amino acids according to customer's specifications. Peptide antibody and reagents are used as tools for drug discovery. AnaSpec provides support for researchers on biotech industries for peptide and reagent manufacturing. Manufacturing peptides and reagents involve chemical synthesis and purification.

Hazardous wastes are generated during the synthesis process and purification. The solid phase peptide synthesis comprise of five major steps: (1) Deprotection (2) Washing (3) Coupling (4) Washing and (5) Cleavage.

In peptide purification, a reverse phase High Pressure Liquid Chromatograph (HPLC) technique is used. The major steps are as follows: (1) Dissolve peptide (2) Separation by HPLC and (3) Lyophilization.

Major Waste Streams in 1998-2002

Waste Stream	CWC	Pounds (1998)	Pounds (2002)	Description/Waste Generating Processes
Methylene Chloride, DCM	211	1,133	3,365	Washing step during peptide manufacturing
N,N-Dimethylformamide	311	17,588	52,236	Washing, Coupling and Deprotection
Acetonitrile	133	2,835	8,419	HPLC Purification process
Wastewater	133	14,152	42,031	HPLC Purification process

Accomplishments

Based on data provided in one page summary, AnaSpec mentioned that considering 20 to 30% growth each year, it reduced from 5126 lbs of waste per pounds of peptide produced in 1998 in comparison to 2,932 in 2002.

Projections

CWC 211 (Organic solvent waste from peptide synthesis)

AnaSpec concluded that only practical option is to reduce the number of washing cycle in the peptide synthesis. It has proposed to reduce washing cycles from 6 to 4. AnaSpec intended to start experimental test to reduce washing cycle from 6 to 4, immediately (June 2004). If the results are positive, company wide change will be implemented. AnaSpec is projecting over 6,000 kg reduction in 2006.

CWC 133 (Aqueous waste containing low organics from peptide purification)

During peptide purification, this company maintains solvent flow rate of 15 ml/minute. The company is considering reducing this flow rate to 10 to 12 ml/minute. The company has concerns: (1) it will result in a longer run time requiring more solvent and (2) the productivity will be reduced. AnaSpec is projecting nearly 5,000 kg reduction in 2006.

Remarks

AnaSpec is projecting a 30% increase in production during 2004-2007 period.

Profile #5
Baxter Bioscience, Los Angeles Facility
EPA IDs: CAD 042236844
SIC: 2836

Site information

The Baxter Bioscience, Los Angeles facility is engaged in manufacturing of purified blood derivatives through fractionation of human plasma. This site employs 1000 people and the company has been in business for 51 years.

The Baxter Bioscience Los Angeles Plant is a plasma manufacturing facility. Plasma is separated into different “fractions” using various chemical and physical methods to promote the concentration of the desired product and the removal of unwanted contaminants. Precipitation and solvent extraction methods are used to separate desired compounds from feedstock. Once fractions are separated, each fraction undergoes further purification and filtration.

Major Waste Streams in 1998-2002

Waste Stream	CWC	Pounds (1998)	Pounds (2002)	Description/Waste-Generating Processes
Aqueous alkaline waste		36,617	36,617	Filtron and Pelican filter units Cleaning operations, as well as the pumps, cleaning of piping and tanks associated with the Albumin processing
Sodium Hydroxide	122	12,713	0	Sodium hydroxide is used to decontaminate tanks and associated lines to prevent bio-burden cross contamination
Hydrochloric acid	791	9,096	0	Hydrochloric acid is used to decontaminate tanks and associated lines to prevent bio-burden cross contamination
Alcohol contaminated rags	352	9,044	14,844	Rags containing 70 % ethanol used to sanitize table tops, benches and equipment. Ethanol rags are generated in manufacturing
Waste oil	221	8,258	6,360	vacuum pumps on freeze-drying operation

Accomplishments

The facility generated 36,000 pounds of category A waste for both 1998 and 2002. The facility has explored the possibility of replacing sodium hydroxide used as a cleaning/sanitizing agent for filtration equipment. The facility reported that this is a FDA validated cleaning process and a drastic process change would have a significant effect on this FDA validated process. The facility generated 21,204 pounds of category B waste in 2002, versus 39,111 pounds in 1998, a 46 % reduction. The category B waste streams generated in 1998 were alcohol rags from general manufacturing (CWC 352), Waste oil from Drying (CWC 222), sodium hydroxide waste (CWC 122) and Hydrochloric acid waste (CWC 791). As part of the Pollution Prevention program, Baxter is always looking for ways to decrease or totally eliminate sources of hazardous waste.

CWC 352 (Alcohol rags from manufacturing)

This waste stream increased from 1998 to 2002. The measure implemented since 1998 was to reuse the alcohol rags by incorporating these rags in the biohazardous bin clean up procedure.

CWC 122 (Sodium hydroxide waste)

In 2002, the facility discontinued the use of sodium hydroxide for processes not affected by bioburden or coliform.

CWC 791(Hydrochloric acid waste)

In 2002, the facility discontinued the use of hydrochloric acid for processes not affected by bioburden or coliform.

CWC 221 (Waste oil)

Baxter LA reported a 23% reduction for this waste stream (see Table). The measure implemented since 1998 was to replace pumps with "oil less" vacuum pumps.

Projections

Baxter has projected the following measures to continue to be implemented:

CWC 352 (Alcohol rags from manufacturing)

Re-use alcohol rags for cleaning bio-hazardous waste bins.

CWC 221 (Waste oil)

- Carefully analyze and segregate waste oil from the Drying department to ensure that all oil goes to recycling.
- Replace old vacuum pump dryers with new “oil less” vacuum pump type dryers to eliminate waste oil generation.

Remarks

In 2000, Baxter launched its Quality Management VOICE (Visions of Involved Caring Employees) and 2002 its VIP (Value Improvement Project) programs. These initiatives promote awareness among employees and offers opportunities to submit suggestions focusing on quality improvement ideas that will help eliminate product defects, waste generation and non-valued added activities.

Profile #6
Baxter Biosciences, Thousand Oaks Facility
EPA ID: CAR 000010207
SIC: 2836

Site information

Baxter International, Inc is a global health care company that, through its subsidiaries, provides critical care therapies for people with life-threatening conditions. The Thousand Oaks facility manufactures therapeutic proteins derived from human plasma or recombinant technology to treat hemophilia. The Thousand Oaks facility is made up of three major manufacturing departments: Cell culture, Purification, Formulation and Finishing, and a Laboratory. This facility was built in 1992, and began production in 1995/96. This site employs more than 500 people.

Major Waste Streams in 2002

Since 2002 was the first year that the Baxter Thousand Oaks facility was subject to SB-14, 2002 was chosen as both baseline and reporting years. All of the wastes generated in 2002 were disposed off site.

Waste Stream	CWC	Pounds	Description/Waste-Generating Processes
Acetone/Methanol	212	4860	Lab assays, filter testing and cleaning procedures
Thimerosal	343	6030	Used to preserve columns in the purification step
Rags with alcohol	352	14800	Aseptic area cleaning
Contaminated containers	513	1395	Laboratory and manufacturing area chemical containers

Accomplishments

N/A. 2002 was both baseline and reporting years.

Projections

The Baxter Thousand Oaks facility projects 23.62 % waste reduction by using the following source reduction measures:

CWC 212 (Acetone/Methanol solvent)

The source reduction measure projected focused on teaching employees to use chemicals carefully and conservatively, thus reducing generated waste. The facility is also planning to implement an inventory control and JIT (just in time) systems. The expected change in hazardous waste generation using this measure is expected to be about 200 pounds/year. This would result in a waste management savings of about \$200.

CWC 343 (Thimerosal)

Baxter plans to replace its existing use of thimerosal with a less toxic chemical. This measure would employ a combination of BAK/EDTA (benzalkonium chloride/ethylenediamine tetracetic acid). The expected change in hazardous waste generation using this measure is estimated to be 6,000 pounds annually. This would result in a waste management savings of about \$10,000. The unit drum disposal cost for this waste stream is \$475.

CWC 352 (Debris/Rags with Alcohol)

The proposed source reduction measure is to reuse alcohol rags. The expected hazardous waste generation change using this measure is expected to be about 1,000 pounds annually. This would result in an estimated \$1,100 in waste management savings.

CWC 513 (Contaminated containers)

The company proposes to train employees on effective chemical handling practices and on the reuse of glass/drum containers as waste containers. The implementation of this measure is expected to reduce hazardous waste generation by about 100 pounds annually.

Remarks

The facility mentioned that FDA regulatory requirement and the need to get FDA approval for process changes are barriers to implement the above proposed measures.

Profile #7
Bayer HealthCare, Pharmaceuticals
Berkeley Site
EPA ID: CAD 009126 418
SIC: 2836

Site information

Bayer HealthCare LLC (Bayer) is a part of the Bayer group, a worldwide chemical and pharmaceutical company with large facilities located throughout the world. The Berkeley site houses the global headquarters of the Hematology/Cardiology Division and is dedicated to the development and manufacturing process of biologically based pharmaceuticals. This profile refers to Bayer HealthCare located at the Berkeley site. The activities at this site include biological product research and development, biological product manufacturing, production ancillary laboratory activities, and utilities. The last two activities routinely generate hazardous waste and are subject to SB-14. The facility's primary product is Kogenate, a protein used in the treatment of hemophilia. This site employs more than 1,500 employees and regular contractors.

Major Waste Streams in 2002-2005

Bayer was first subject to SB-14 in 2002. The facility used 2002 its baseline year and updated its SB-14 information up to 2005. In 2002, this facility generated about 29,000 pounds of Category B wastes.

Waste Stream	CWC	Pounds (2002)	Pounds (2005)	Description/Waste-Generating Processes
Waste oil	221	7,300	8,900	Vacuum pumps
Excess Chemicals*	331	30,000	26,000	Laboratory research and quality control

* Due to a change in tracking the origins of waste chemicals at the site, this figure includes Category B waste plus non-routinely generated waste that is normally exempt from SB 14 reporting.

Accomplishments

CWC 221 (Waste oil)

No source reduction measures were identified for CWC 221. There was an increase of 22 percent in the generation of this waste stream from 2002-2005.

However, because of the rate of production increase over this same period, waste oil generation actually decreased relative to the production rate.

CWC 331 (Excess Chemicals)

Source reduction steps included to limit direct purchases and to train employees about source reduction. The company's reduction in excess chemicals represents an even more significant reduction, considering that production increased for this same period.

Projections

CWC 221 (Waste oil)

The facility reported it did not identify applicable source reduction activities for CWC 221 due to operating constraints associated with complying with FDA cGMP (Food and Drug Administration Good Manufacturing Practices) regulations. The site is however continuing to investigate alternatives, including conversion to dry vacuum systems eliminating the need for oil-based vacuum systems. Dry vacuum systems are however currently unable to meet vacuum requirements for the process. The site is also investigating ways to extend the life of the oil used in the vacuum process.

CWC 331 (Excess Chemicals)

The facility projected the following administrative measures to reduce the CWC 331 waste stream:

- Inventory control for limiting excess quantities ordered.
- Improved central purchasing systems. Streamline the purchasing process thereby eliminating piecemeal purchasing.

Bayer believes that a 25% reduction in the amount of excess chemicals requiring disposal is very achievable by implementing these measures.

Profile #8
Beckman Coulter, Inc.
Carlsbad Facility
EPA ID: CAD 072 518 517
SIC: 2835

Site information

Beckman-Coulter, Carlsbad facility, produces primarily in-vitro diagnostic reagents for use in clinical and medical applications. The facility has been at this site for 31 years and employs 265 employees. The business activities that are associated with hazardous waste generation are clinical diagnostic product manufacturing; manufacturing support; lab operations; and general facility and maintenance operations.

Major Waste Streams in 1998-2002

Waste Stream	CWC	Pounds (1998)	Pounds (2000)	Pounds (2002)	Description/Waste-Generating Processes
Product Rinsate	331/343	23,567	30,220	22,895	Rinses from manufacturing cleaning activities, excluding corrosive liquids.
Lab-Pack	551	7,461	34,544	26,260	Assorted waste streams from laboratory and manufacturing activities (e.g. expired or unused lab reagents)
Solid waste	181	NA	NA	22,130	Reagent manufacturing activities.
Waste Buffer Solutions	141	1,600	6,640	6,000	Reagent manufacturing activities (e.g. line flushing, tank washes)
Alkaline solutions	122	NA	17,220	14,400	Reagent manufacturing activities (e.g. line flushing, tank washes)
Corrosive liquid, Acidic	791	1,158	18,160	13,840	Laboratory/Production
Sodium azide	551	429	NA	2,250	Production

Accomplishments

Due to the additions of product lines in the reagent manufacturing area, the waste generating activities were monitored and evaluated through 2000 to allow for the establishment of a 'new' normal operating baseline. Both 1998 and 2000 are shown on the Table. 2000 and 2002 presented a similar production level and the waste streams generated in those years showed 10-24 % reduction from 2000-2002. All of the waste streams in the Table were treated off-site.

Projections

The Carlsbad facility projects an overall reduction in its hazardous waste generation by an additional 6-10 %. For the Product Rinsate waste stream (CWC 331/343), the most effective measurement would be production process changes especially in the areas of equipment modifications and plant automation.

The facility presented a few general source reduction measures that are in place and are being implemented for all of the waste streams:

- The loss prevention approach currently in place for the reagent manufacturing operations uses just-in-time management (JIT), which is based upon having the least amount of inventory available to complete the requested job orders. This approach avoids wastes generated from expired chemical feedstock.
- Preventative maintenance operations are evaluated to minimize process down time by anticipating needed maintenance prior to failure. This lowers total overall process costs while avoiding wastes generated by failure events.
- Employee award programs are currently practiced throughout the company's Continual Process Improvement (CPI) program and Performance Sharing Award Program. Employees are recognized for their efforts to identify and recommend process operation improvements.

Profile #9
Chiron Corporation (Novartis)
Emeryville
EPA ID: CAD 046866463
SIC: 2834

Site information

Chiron focuses on ways to diagnose and treat cancer and infectious diseases. Chiron also builds on its pioneering research directed toward the hepatitis C virus (HCV) and the human immunodeficiency virus (HIV) to develop vaccines. The Chiron site covered on this report is located in Emeryville. This site is the global corporate headquarters for Chiron and home to its administrative, research, development and manufacturing operations. Current manufacturing operations at this site include producing biopharmaceuticals, vaccines and diagnostic kits using fermentation biotechnology methods. Chiron was founded and began operations in 1981 and in 1994 unveiled an expansion plan to solidify Chiron's presence in Emeryville. Chiron has over 6,000 employees worldwide, 2400 employees in the U.S, with 2000 of these employees in Emeryville. Major products include Betaseron®, Proleukin®, antigens, Men C, RIBA® qualitative tests and Quantiplex® quantitative test kits.

Major Waste Streams in 1998-2002

Raw materials used in the production process vary depending upon the specific product being manufactured. However most raw materials are non-hazardous and include salts, acetates, sulfates, sugars and water. Acids and bases are used to adjust pH during the process. Solvents are sometimes used in fermentation and product purification to isolate the protein (the active drug ingredient). Copper solutions are also used in some processes to help isolate the protein through chelating methods. Other hazardous materials are used to clean equipment, facilities and to perform maintenance. The major SB-14 waste streams for 1998 and 2002 are listed on the following table:

Waste Stream	CWC	Pounds (1998)	Pounds (2002)	Description/Waste-Generating Processes
Aqueous waste	122	2,000,387	NA*	Industrial process wastewater
Isopropyl Alcohol Solution	212	24,625	44,421	Preparation for column packing/unpacking and protein purification
Copper Chelate solution	132	1,480	NA	Purification process

*The facility reported that streams that are treated on the neutralization unit operate under the HSC 25201.15 exemption.

Accomplishments

CWC 212 (Isopropyl Alcohol Solution)

Chiron reported an 80 % increase (see Table) in the CWC 212 waste stream from 1998 to 2002. The facility reported that changes in production schedule and the decision to co-mingle non-RCRA, non-California wastes into this waste stream can explain its generation increase. The facility mentioned that the following measures have been implemented to help to minimize the generation of CWC 212 hazardous waste:

- Centralized purchasing of raw materials
- Inventory control
- Use of large raw material storage tank, minimizing the generation of excess raw materials if individual containers were used.

This waste stream was disposed off-site.

CWC 132 (Copper Chelate Solution)

The copper chelate solution waste stream generation has been affected by the production schedule. Only one production process contributes to this waste stream. The process generating this stream was not operated in 2002 and therefore none of this waste was generated. This waste stream was disposed off-site.

Projections

The only major waste stream generated in 2002 was isopropyl alcohol. The process generating the copper solution was not operated in 2002.

CWC 212 (Isopropyl Alcohol Solution)

Chiron stated that none of the selected source reduction measures evaluated were chosen for implementation, because the positive benefits of each measure did not outweigh the costs and/or negative consequences of implementation. The considered measures included:

- Using caustic instead of 20% ethanol for column storage
- Purchasing additional columns in order to minimize the need for unpacking and re-packing column resins, therefore minimizing the frequency of 20 % ethanol waste stream generation.
- Building new facilities so that each product could have its own production room. This would enable the use of stationary columns. Columns only require re-packing when moved.
- Additional segregation of hazardous and non-hazardous wastes

Chiron also considered other measures, but these were rejected due to the Food and Drug Administration (FDA) regulations.

Remarks

In 2006, Chiron Corporation was acquired by Novartis and Novartis Vaccines and Diagnostics, Inc became the new owner of the facility. Since this report is based on the 1998-2002 SB-14 cycle, the Chiron corporate name was retained as the facility's name used in this report.

Profile #10
Dade Behring Inc.
Cupertino
EPA ID: CAD000099259
SIC: 2835

Site Information

Dade Behring Inc. (DBI) Cupertino facility's primary business activities consists of manufacturing diagnostic reagents for use in clinical diagnostic instruments and drugs of abuse analytical instruments. Operations at this facility in Santa Clara County began in 1977. DBI has owned and operated this facility since 1998. The average number of personnel at this facility including temporary and contract workers is approximately 280. The major manufacturing processes include reagent formulation, liquid filling, lyophilization and quality control of raw materials and final products. DBI manufactures biochemical analytical reagents and reference solutions. The manufacturing area is operated under U.S. Food and Drug Administration Good Manufacturing Practice protocols.

Major Waste Streams in 1998—2002

Waste Stream	CWC	Pounds (1998)	Pounds (2002)	Description/Waste generating Processes
Mercury-containing liquid waste	725	9,540	30,440	Batch production of analytical reagents. Thimerosal used as product preservative contains mercury.
Mercury-containing solid waste	331	19,165	32,876	Off-specification, aged, or surplus organic waste.
Mercury-containing aqueous waste	132	6,940	1,200	
Azide-containing aqueous waste	134	2,675	1,800	

Accomplishments

DBI identified the following four major waste streams in its 1998 Source Reduction Plan:

- (1) Mercury-containing liquid wastes produced during batch production process (CWC 725);
- (2) Mercury-containing aqueous wastes from reagent quality control testing (CWC 132);
- (3) Mercury-containing solid waste from disposal of quality control sample retains and analytical instrument cuvettes (CWC 331); and
- (4) Azide-containing aqueous waste (CWC 134).

DBI in its 2002 revised Performance Report mentioned that the generating processes and waste characteristics of these four major waste streams are outlined in detail in its 1998 Source Reduction Plan.

DBI successfully reduced three out of four waste streams mentioned above. DBI provided waste generation data for 1998 and 2002 and factored in production data (normalization) to calculate percent reduction or percent increase in its hazardous waste generation. It used an average annual growth of 30% during four year cycle (1999 to 2002). A total of seven hazardous waste source reduction measures were implemented during 1999-2002 period; one of these seven measures was applicable to all the four major waste streams mention above. The discussion follows:

All Hazardous Waste streams: Improve solid waste determinations by re-evaluating profiles of the hazardous characteristics and concentrations of wastes so they are managed appropriately and consistently. This measure is applicable to all four major waste streams. DBI consolidated two waste streams under the Mercury-Containing Liquid Waste category. The effect of this consolidation on the quantity, hazardous properties, and management of wastes is not known. DBI plans to conduct additional waste characterization re-evaluations.

CWC 725 (Mercury-Containing Liquid Waste)

Measure (1): Reduce use of Thimerosal as a preservative: Since 1998, DBI has not introduced any new product formulations containing Thimerosal, and continues to reformulate existing products with preservatives that do not contain mercury.

Measure (2): Change batch mix procedures to match production quantity to final

product: requirements, DBI instituted a company-wide manufacturing optimization initiative to increase resource use efficiency.

By applying all these measures and 30% annual increase in production during 1999-2002 period, DBI realized a 6.1% reduction in mercury-containing liquid waste.

CWC 132 (Mercury –Containing Aqueous Waste)

Measure: Conduct Statistical analysis to determine if number of QC analyses can be reduced. DBI started a company-wide manufacturing optimization initiative to increase resource use efficiency. By applying these measures, DBI reduced mercury-containing waste by more than 40 percent.

CWC 331 (Mercury-Containing Solid Waste)

Measure (1):

Conduct statistical analysis to determine if number of batch sample retentions can be reduced. DBI started a company-wide manufacturing optimization initiative to increase resource use efficiency.

Measure (2):

Provide training and oversight of container labeling to confirm that non-hazardous materials are not inadvertently disposed of as hazardous waste. DBI continues to implement an ongoing hazardous waste minimization training program.

By applying these measures, DBI reduced mercury-containing solid waste by more than 65 percent.

CWC 134 (Azide-Containing Aqueous Waste)

Measure: Change batch mix procedures to match production quantity to final product: DBI started a company-wide manufacturing optimization initiative to increase resource use efficiency. This wastestream actually increased by approximately 2 percent, while mercury-containing wastes decreased due to changed batch mix procedures.

Projections

DBI reported that it did not generate any Category A waste during 2002. DBI reported 14 waste stream totaling more than 75,000 pounds during calendar year

2002. Two of these 14 qualified as major waste streams: (1) Off specification organic waste or Mercury-containing solid waste (cwc 331) and (2) Product remainders or Mercury-containing liquid waste (cwc 725).

CWC 725 (Product remainders or Mercury-containing liquid waste)

This waste stream includes liquids with mercury concentrations equal to or greater than 20 parts per million. Mercury-containing liquids are routinely generated during batch production of analytical reagents. The mercury originates from the use of thimerosal as a preservative. The amount generated during 2002 was more than 30,000 pounds, approximately 40 percent of the total SB 14 applicable wastes.

DBI's main manufacturing process involves batch mixing of various raw materials to make reagents and calibrators. Analytical reagents are prepared by mixing raw materials in steel vessels, which are then emptied into polyethylene or glass bulk containers. Materials from these bulk containers are then dispensed into 1 to 5 milliliter glass vials, which are then lyophilized to produce a solid product within the vials. Generally during the batch-mixing processes, excess product is manufactured.

DBI evaluated five source reduction measures to reduce this waste stream and selected three of these five measures. They are:

- (1) Review existing hazardous and solid waste profiles to verify waste determinations and identify waste reduction opportunities;
- (2) Reduce thimerosal use as a preservative; and
- (3) Change batch mix procedures to match production quantity to final product.

CWC 331(Off specification organic waste or Mercury-containing solid waste)

This waste stream includes off-specification, aged, or surplus organic waste. There are several different origins of this waste stream including off specification products and raw materials, quality control samples, and waste equipment. This off-specification organic waste quantity during 2002 was nearly 33,000 pounds or nearly 44 percent of the total SB 14 applicable waste.

DBI considered six source reduction measures for evaluation and selected all six measures for implementation during 2003-2006 period:

- (1) Review existing hazardous and solid waste profiles to verify waste determinations and identify waste reduction opportunities

- (2) Develop written protocols to include steps to confirm that non-mercury containing vials and bottles are not being disposed of as hazardous waste
- (3) Conduct statistical analysis to determine if number of batch sample retentions can be reduced;
- (4) Reduce batch sample size
- (5) Provide training and oversight of container labeling to confirm that non-hazardous materials are not disposed as hazardous waste; and
- (6) Develop inventory-tracking system that is capable of improving inventory management and reduce production of expired product and raw materials.

Remarks

DBI's overall goal is to reduce its waste for the 2003-2006 period by 10%.

Profile #11
Depomed
Menlo Park
CAR000096040
SIC code: 2834

Site Information

Depomed specializes in using oral drug delivery technologies for the development of new oral medications. The company has developed a proprietary drug delivery platform, which is based on polymer technology, and provides targeted drug delivery solutions for a wide range of compounds. Depomed also has developed drugs for the treatment of diabetes and urinary tract infections. The Menlo Park facility employs approximately 90 employees and has been in business at this location for over six years.

Major Waste Streams in 2002

Waste Stream	CWC	Pounds 2002	Description/How Generated
HCl dissolution liquids	791	21,558	0.1 N HCl (pH=1-1.2), with traces of pharmaceuticals, generated by QC and R&D processes (dissolving drugs in hydrochloric acid solution)
Flammable liquids	331	2,035	Methanol, acetonitrile, phosphate buffer solution, and perchlorate buffer solution from mobile phases in HPLC analysis
Decontamination solutions	551	1,376	Aqueous Alconox® detergent, with traces of pharmaceuticals, used to decontaminate equipment

Accomplishments

N/A Baseline and reporting years are the same – therefore there is no previous hazardous waste generation data.

Projections

CWC 791 (0.1 N HCl Dissolution Waste)

Depomed plans to reduce this waste stream by 2,156 lbs (10%) in the next four years, by segregating pH>2 and pH<2 wastes.

CWC 551 (Decontamination Solutions)

Depomed projects a reduction of 138 lbs (10%) of CWC 551 in the next four years, through the segregation of first and final decontamination rinses (and managing the latter as non-hazardous).

Remarks

Barriers to source reduction include FDA-mandated best management practices for USP methodology and HPLC methodology. The facility managed its hazardous waste through offsite treatment and disposal.

Profile #12
Dey, L.P.
Napa
EPA ID: CA0000921544
SIC: 2834

Site information

Dey is a specialty pharmaceutical company focused on the development, manufacturing, and marketing of prescription drug products for the treatment of respiratory diseases and respiratory related allergies. This company has been in business for twenty-eight years. It employs 900 people at its Napa facility. The major products include Duoneb, Ipratropium Bromide, Accuneb (albuterol sulfate inhalation solutions 0.63 and 1.25 mg) and Cromolyn Sodium inhalation solution 20 mg/2 ml.

Major Waste Streams in 2002-2004

Dey became subject to SB-14 in 2002. The facility therefore used 2002 as its baseline and reporting years and provided 2004 data for comparison.

Waste Stream	CWC	Pounds 2002	Pounds 2004	Description/Waste-Generating Processes
Lab liquid	212	19,620	20,525	Laboratory analysis
Isopropyl alcohol (IPA)	212	13,455	8,764	Manufacturing
Hydraulic oil	221	5,063	6,930	Maintenance
Lab and manufacturing wipes	352	5,350	2,560	Laboratory and manufacturing
Dry powder inhaler*	352	2,252	NA	Manufacturing

*This product line was terminated in the development phase

Accomplishments

CWC 212 (Oxygenated solvents):

- **Laboratory liquid waste (HPLC solvent)**

This waste stream is generated by the laboratory's High Performance Liquid Chromatography (HPLC) systems. There was a 5% increase in CWC 212 waste generation from 2002-2004. The amount of HPLC waste generated fluctuated considerably due to shifts in product development and production activities.

Based on existing laboratory procedures; mobile phase (HPLC solvent) must be used within 7 days or be disposed as hazardous waste. It was determined that the shelf life of mobile phase could be extended to 14 days. In addition, the facility determined that the practice of running a mobile phase through the HPLC equipment to keep it ready for the next run, is unnecessary and it will be phased out.

- **Isopropyl Alcohol (IPA)**

There was a 35% reduction of the IPA waste stream from 2002-2004. This reduction is likely the result of reducing the numbers of batches/lots. Dey is currently investigating the feasibility of changing its procedures to extend the IPA solution's life time.

CWC 221 (Waste oil):

There was an increase in CWC 221 waste stream from 2002-2004. This waste stream is hydraulic oil used in the Form Fill and Seal (FFS) machines. Currently this oil is changed twice a year regardless of whether the oil is actually spent. Dey is reviewing a change to the maintenance approach by changing the oil based on the actual machine usage and oil quality testing rather than on a fixed schedule.

CWC 352 (Other Organic Solid Waste)

Manufacturing wipes (Oil/IPA)

This waste stream includes oil soaked wipes, paper towels, sterile wipes and oil absorbent pads. There was a 52% reduction of this waste stream from 2002-2004. The facility is implementing waste segregation by using special colored bags for the collection and segregation of oil soaked wipes, thereby reducing the amount of oil soaked wipes generated. Dey is also implementing a program designed to track and analyze hydraulic oil consumption on some of their machines.

Projections

Dey will continue to implement the following measures for the following waste streams:

CWC 352 (Other Organic Solid Waste)

- **Manufacturing wipes (Oil/IPA)**
 - Implement the use of colored waste bags for the collection and segregation of oil soaked wipes in an effort to ensure that normal

waste materials are not mixed with oil soaked wipes thereby reducing the amount of oil soak debris generated.

- Dey's Manufacturing Maintenance group will implement a program designed to track and analyze hydraulic oil consumption on the machines. This information will be used to track the trend of oil consumption and prioritize maintenance activities in an effort to identify leaks early thereby reducing the amount of oil soaked wipes generated

Using the above measures, the facility projects a reduction of this waste (52 %) to 2300 pounds per year by the end of 2006. This waste is disposed of as recyclable solid waste costing \$ 555 per cubic yard. This measure would represent more savings on waste disposal, since less waste would be generated and need to be disposed of.

CWC 212 (Oxygenated solvents)

- **Laboratory liquid waste (HPLC solvent)**

The company projects making:

- Procedure changes to increase the shelf life of the solution.
- Decrease flow rates on HPLC equipment where possible to minimize waste generation.

Dey anticipates that the HPLC solvent waste will be reduced (5 %) to approximately 18500 pounds per year by the end of year 2006. This waste is disposed of as blended fuel costing \$ 1.20 per gallon. This measure would represent more savings on waste disposal, since less waste would be generated and need to be disposed of.

- **Isopropyl Alcohol (IPA)**

Dey projects extending the useful life of the IPA solution by testing and analysis to determine IPA exhaustion. Dey is examining the 24 hour rule (maximum useful life) on an attempt to extend the useful life of IPA solution within its operating specifications. If the solution is tested and deemed to be within operating specification, the solution may continue to be used. Once it fails, it will be disposed of as hazardous waste. By implementing this measure, Dey anticipates this waste stream will be reduced (35 %) to 7900 pounds per year by the end of 2006. This waste is disposed of as blended fuel costing \$ 1.20 per gallon. This measure would represent more savings on waste disposal, since less waste would be generated and need to be disposed of.

CWC 221 (Waste oil)

Dey projects making a procedure change to replace hydraulic oil based on the machine operation hours and oil quality testing as opposed to change out based on a fixed calendar schedule. By implementing this measure, Dey anticipates this waste stream will be reduced to 6200 pounds per year by the end of 2006. This waste is disposed of as recyclable lubricating oil costing \$ 0.35 to 0.58 to recycle. This measure would represent more savings on waste disposal, since less waste would be generated and need to be disposed of.

Remarks

By the end of 2002 Dey, L.P. had abandoned its product development operations and terminated its dry powder inhalers project. Both of these decisions eliminated the inhaler powder waste stream. During 2005, Dey has decommissioned three of its fourteen machines using hydraulic oil. This is expected to reduce the amount of hydraulic oil used and recycled.

Profile #13
EMD Biosciences Inc.
San Diego
EPA ID: CAD 983660689
SIC: 2836

Site information

EMD develops biochemical products for research and development. The EMD facility is located in San Diego. The major products manufactured or services provided by EMD include: antibodies, cancer/cell cycle/apoptosis, disease related pathways, high-throughput purification, peptide synthesis, signal transduction, solid phase organic synthesis and solution phase organic synthesis. A generic process would consist of taking raw materials, designing a reaction with organic solvents, quenching the reaction with organic and aqueous solvents followed by extraction using inorganic substances, followed by concentration and purification using silica gel or recrystallization to yield the final product. EMD has been in business for 9 years and employs 158 people.

Major Waste Streams in 1998-2002

EMD's major waste streams consist of halogenated solvents, laboratory waste chemicals, oxygenated solvents, other organic solids, and other inorganic solid waste.

Waste Stream	CWC	Pounds 1998	Pounds 2002	Description/Waste-Generating Processes
Halogenated solvents	211	2,620	2,160	Reaction Processes
Lab Waste Chemicals	551	180	16,622	Reaction Processes
Organic solvents	212	13,520	8,040	Reaction Processes
Other inorganic solid waste	181	600	5,175	Extraction Processes
Other Organic solids	352	NA	1,965	Purification Processes
Waste and mixed oil*	221	9,970	1,720	Vacuum pumps use

*not a major waste stream in 2002

Accomplishments

Hazardous waste management approaches for the following streams since 1998, include

CWC 211 (Halogenated solvents)

This waste stream was reduced by 18 % from 1998-2002 (see Table). This reduction is primarily a consequence of the facility focusing on the reduction of chlorinated solvents used in purification processes.

CWC 551 (Laboratory waste chemicals)

There was a large increase of this waste stream since 1998-2002 (see Table). This waste was mainly disposed off-site.

CWC 212 (Organic solvents)

There was a 41 % decrease in the quantity of this waste stream from 1998-2002. EMD implemented a chemical inventory system enabling the purchase of only the required amount of chemicals when needed.

CWC 181 (Other inorganic solid waste)

There was a large increase in the generation of CWC 181 waste stream from 1998-2002 (see Table). This increase is due to the facility collecting silver oxide waste on-site for recycling.

CWC 221 (Waste and mixed oils)

There was an 83 % reduction in CWC 221 from 1998 to 2002. This waste has been recycled off-site to be burned as an alternate fuel source or refined into a usable product.

Although recycling is not source reduction, it is a valid hazardous waste management approach.

Projections

EMD has projected the following measures for implementation:

For all of the major waste streams (see Table):

- Substitution of hazardous chemicals with less hazardous alternatives;
- Eliminate MTBE from the detergent recrystallization process by 90 %;
- Implement a chemical inventory;
- Collect silver oxide waste for recycling;
- Order bulk solvents in reusable, stainless steel dispensing containers instead of disposable 55 gallon drums.

Remarks

The increase in waste generation noted from 1998 to 2002 on some of the waste streams presented on the Table is due to an increase in production. A few waste streams that were generated in 1998, CWCs 551, 213, 343 and 791 were eliminated in 2002.

**Profile #14
Genentech
South San Francisco
CAD080129000
SIC Code: 2834**

Site Information

Genentech uses biotechnology to produce complex proteins designed to treat specific diseases. Its primary operations include research and development, bacterial and mammalian cell manufacturing, quality assurance and control, and commercial product filling and packaging. The manufacturing process involves the growth of cells which have been genetically engineered to produce specific therapeutic proteins. The proteins are recovered, purified and formulated into a therapeutic product, which is dispensed into vials and packaged for distribution.

The South San Francisco facility employs approximately 8,000 people, and has been in operation at this location since 1976.

Major Waste Streams in 1998-2002

Waste Stream	CWC	Pounds 1998	Pounds 2002	Description
Basic corrosive wastewater	791		929,384	Aqueous solutions containing 2%-5% potassium hydroxide or sodium hydroxide – from flushing/rinsing of vessels and piping.
Acidic corrosive wastewater	122		866,630	Aqueous solutions containing 2%-5% phosphoric acid – from flushing/rinsing of vessels and piping, and chromatography column.
Combined corrosive wastewater	791	52,368,656*		In 1998, the two waste streams above were reported as one waste stream.
Product recovery solutions	134	1,120,818	1,516,923	Aqueous solutions containing 6% tetramethylammonium chloride, 3%-5% unwanted proteins, trace salts and sugars – from rinsing chromatography column.

*In 1998, Genentech apparently estimated its quantities of corrosive wastewater based on total volumes of acidic and basic cleaning solutions purchased, with no

direct measurement of wastewater volumes with pH values less than 2 and over 12.5. Thus the amount of corrosive wastewater reported may be considerably higher than the actual hazardous wastewater generated.

Accomplishments

CWC 791 and 122 (wastewater)

Genentech reduced corrosive wastewater by changing the water purification system: the facility replaced a resin bed system requiring periodic regeneration with acid to a reverse osmosis system whose maintenance does not generate corrosive wastewater. It is not possible to measure actual reductions because of the installation of new data capture devices on the elementary neutralization system.

CWC 134 (Product recovery solutions)

Genentech reduced their product recovery solutions by 38% due to:

- Operational improvements in the titer and yield of the biochemical manufacturing processes, and
- A new portfolio of products that do not generate hazardous product recovery solutions.

Projections

CWC 791 and 122 (wastewater)

The facility plans to reduce corrosive wastewater per pound of commercial product by increasing productivity through titer improvement – i.e., each run will yield more protein. Currently, titer improving is scheduled for two products with anticipated improvements of 30% to 50%. Genentech South San Francisco projects 2% reduction of corrosive wastewater per pound of product.

CWC 134 (Product recovery solutions)

The facility is considering substituting a non-hazardous product-recovery solution for the current product-recovery solution. Genentech's Environmental Health and Safety (EHS) department has begun participating in the evaluation of materials and processes from the research lab to clinical production, allowing EHS to evaluate and influence the safety and environmental aspects of production. As new processes require FDA approval, new alternatives for recovery solutions would only be developed for new products.

Remarks

A one hundred forty six percent increase in total marketed product manufactured during the reporting period resulted in increased waste generation. As with other pharmaceutical companies, Genentech, South San Francisco, reported FDA approval or validation for new materials and processes as a barrier to source reduction.

Profile #15
Genentech
Vacaville
CAR000017004
SIC: 2834

Site Information

Genentech, Vacaville, is a biotechnology facility that manufactures the human pharmaceutical products Herceptin®, Rituxan®, Xolair, and Avastin. Its activities include cell fermentation, equipment maintenance, quality control and assurance, and administrative functions.

Genentech’s high-purity solution product requires a series of complex steps, including: DNA introduction; cell culture, harvest and separation; recovery and purification; and maintenance. The facility manufactures one product at a time, using batch processes for a three to six month campaign. Consequently, Genentech’s hazardous waste streams generated from manufacturing vary throughout the year. Hazardous waste streams subject to SB 14 are generated primarily by the facility’s manufacturing and maintenance operations.

Genentech’s Vacaville facility has been operating since 1999, and employs approximately 600 people.

Major Waste Streams

Waste Stream	CWC	Pounds 2002	Description/Waste-Generating Process
Column rinse, and column regenerator liquids	134	2,141,487	Column rinsing agents, column regenerating agents, various salts, and various cell proteins
Corrosive wastewater	122,791	104,958	94-99% water and 6% or less corrosives (both acids and bases); from equipment cleaning, water filtration resin regeneration, and product recovery

Accomplishments

N/A. Genentech Vacaville began manufacturing operations in 1999, and was not subject to SB 14 in 1998.

Projections

CWC 134 (Column rinse and regenerating solution)

Genentech Vacaville plans to explore the following approaches to reduce this waste stream:

- Substituting column regenerator with an acid ;
- Eliminating column rinse; although the column rinse removes unwanted proteins from the recovery column, several product solution filtration and recovery steps following removal of the solution from the recovery column could sufficiently reduce protein contaminants, thus eliminating need for a prior column rinse;
- Using a special, combined recovery step in the recovery process. This new technology could be used before the column recovery step to create a cleaner protein mixture to be passed through the column;
- Using a different column resin, that eliminates non-specific binding. This would eliminate the column rinse;
- Developing a process economics model to determine the value of the column rinse and column regenerator to the recovery process.

Based on these measures, the facility hopes to reduce column rinse and regenerator by 15 percent

Remarks

Barriers to Source Reduction: costly FDA revalidation process.

Profile #16
Gen-Probe
San Diego
EPA ID: CAR 000017277
SIC: 2835

Site information

Gen-Probe is located in San Diego. This facility manufactures In Vitro nucleic acid tests (NATs) used to diagnose human diseases and screen donated human blood. The company markets a broad portfolio of products that use the Company's patented technologies to detect infectious microorganisms, including those causing sexually transmitted diseases (STDs), tuberculosis, strep throat, pneumonia and fungal infections. In blood screening, Gen-Probe developed and manufactures a test for the simultaneous detection of HIV-1, HBV and the hepatitis C virus (HCV) in donated human blood. This site has been in business since 1997 and has about 700 employees.

Major Waste Streams in 2002

Waste Stream	CWC	Pounds	Description/Waste-Generating Processes
Flam liquids, toxic, acetonitrile/dichloromethane	214	11,182	DNA synthesis waste
Water/acetonitrile	343	19,144	HPLC waste
Waste sodium hydroxide solution	122	4,066	Off-spec and solution waste

These waste streams are recycled by the licensed disposal facility vendor and CWC 122 can be recycled or treated off-site or neutralized to non-hazardous waste on site.

Accomplishments

N/A. Since 2002 was the first year that Gen-Probe was subject to SB-14, the facility used that year as the baseline and reporting years.

Projections

Gen-Probe has projected the following measures to be implemented:

For all the streams:

- Operational improvements: New software designs for overall manufacturing process may reduce production scrap overages and improve just in time manufacturing.
- Production Changes: Changes would include reduction in scale production, resulting in less over all waste production. Under consideration are changes to the operational process allowing recycling within the process of some of the acetonitrile components thus reducing overall waste production.
- Administrative steps: Training with employees on the proper waste segregation. Spill prevention. Training presentations, incentives, dissemination of information will be improved.

For CWC 343 (Water/acetonitrile):

Gen-Probe will be researching the feasibility of changing from an organic solvent to salt based purification process. FDA approval or validation would be required after feasibility and equivalency is determined.

Profile #17
Gilead Sciences
San Dimas
CAD982320772
CAD983649930
SIC: 2834

Site Information

Gilead Sciences researches and manufactures drugs, mainly AmBisome™ and Daunoxome™. Manufacturing operations include a spray dry process and vacuum extraction system. Gilead’s wastes are generated from spray drying operations, vapor condenser and carbon bed control, product manufacturing and pilot filling, and laboratory and manufacturing clean-up.

Gilead has been operating under this name since January 2000, and employs about 200 people.

Major Waste Streams

Waste Stream	CWC	Pounds 1998	Pounds 2002	Description
Organic liquids	211	20,132	35,205	Organic solvents, methanol, isopropanol, chloroform
Liquid drug substances	311	0	8,680	RCRA aqueous drugs and off-specification pharmaceuticals
Liquid drug substances	331	4,815	25,465	Non-RCRA waste

Accomplishments

Although Gilead did not report any hazardous waste source reduction accomplishments in their 1998 to 2002 reporting period, they did note the elimination of process waste bottles. Formerly, a production process generated 12 one-gallon bottles per batch, resulting in the disposal of approximately 2,000 bottles annually. Gilead replaced these one-gallon disposable bottles with reusable stainless steel containers, thereby eliminating 2,000 bottles from landfill disposal.

Projections

CWC 211 (Organic liquids)

Gilead estimates a 5% waste reduction per year from a proposed carbon bed system redesign.

Remarks

Since 1998, a major waste stream stemming from product and lab processes was reclassified as non-hazardous waste. The major factor affecting waste generation has been variation in production rates occurring since 1998. Hazardous waste management practices include offsite recycling and incineration.

Profile #18
Grifols Biologicals Inc.
Los Angeles
CAD092694538
SIC Code: 2836

Site Information

Grifols Biologicals Inc. purchased the Los Angeles operating assets of Alpha Therapeutic Corporation and is primarily engaged in the manufacturing of human blood plasma fractions. These include albumin, alpha one proteinase inhibitor (A1PI), and coagulation products, which are produced through chemical and physical extraction processes.

Human plasma is used as the raw manufacturing feedstock. Plasma is the liquid portion of the blood. Plasma, which is 90 percent water, contains many dissolved components, primarily proteins, which are important to the human immune system and coagulation system.

At Grifols, plasma is separated into different protein “fractions” using various chemical and physical methods to allow the concentration of the desired product and the removal of unwanted contaminants. The main separation mechanisms employed are precipitation and solvent extraction (i.e. alcohol fractionation and chromatography).

Grifols has operated at this site since July 2003 and currently employs 392 people.

Major Waste Streams

The facility used 2002 as its baseline and reporting years and provided 2005 data for comparison.

Waste Stream	CWC	Pounds 2002	Pounds 2005	Description of waste generating processes
Water/Acetone Waste	134	0	1,688,220	Cleaning rinse waters. (Previous CWC 135 and 212 water/acetone waste streams)
Water/Acetone Waste	135	603,911	0	Cleaning rinse waters. (Note: CWC changed to 134 in August 2003 to better match waste description.)
Aqueous Acetone /Water Waste	212	818,794	0	Equipment cleaning wastes.(Note: CWC changed to 134.)
Spent Acetone Waste	212	2,289,324	1,633,460	95% acetone waste from suspension and separation of proteins.
Spent Ethanol Waste	212	5,403,202	0	Over 75% ethanol waste from fractionation. Off-site recycling started in October 2003.

Accomplishments

Grifols acquired the operating assets of Alpha Therapeutic Corporation in July 2003, and therefore did not own the facility during the 1998 to 2002 reporting period. Off-site recycling of ethanol started in October 2003 and will continue.

Projections

CWC 134 (Water/Acetone Waste) and CWC 212 (Spent Acetone)

Bulk acetone use will be discontinued within 3 years. A significant reduction will be made within the next 18 months. These two waste streams currently account for over three million pounds of hazardous waste annually.

CWC 212 (Spent Ethanol)

Bulk ethanol will continue to be recycled off-site. The potential for on-site recycling is being evaluated.

Remarks

The increased volumes of Water/Acetone Waste and Spent Acetone are proportionately less than the increased plasma input (activity index) for the facility.

Product waste streams that could contain active product ingredients or possible endocrine disruptors are shipped off-site to permitted facilities for proper treatment and disposal.

Grifols acquired the operating assets of Alpha Therapeutic in July 2003, and therefore did not own the facility during the 1998 to 2002 reporting period.

Profile #19
International Medication Systems, Ltd (IMS)
South El Monte
EPA ID: CAD981434723
SIC: 2834

Site Information

International Medication Systems Ltd. (IMS) produces various parental pharmaceutical products for both domestic and international markets. IMS also manufactures and markets approximately 70 products including Critical Care Drugs (CCDs), pain management and anesthetic drugs. It also has on-site microbiology, chemistry and R&D laboratories that monitor and conduct testing for quality control. The manufacturing facilities include four aseptic filling suites equipped with high-speed filling machines for vials and profiled syringes. This facility is located in South El Monte, California and operates under the Standard Industrial Classification Code (SIC) 2834. IMS has been operating at this facility since 1968. In 2002 it employed 354 employees.

Major Waste Streams in 1998-2002

Waste Stream	CWC	Pounds (1998)	Pounds (2002)	Description/Waste Generating Processes
Unspecified organic liquid mixture	343	8,167	19,794	Cleaning operations (regular and FDA approved)
Off-Specification, aged, or surplus organics	141	0	9,591	Expired or obsolete silicone not meeting FDA approval
Unspecified aqueous solution	135	0	8,632	Inks and excess cleaning products from labeling process
Aqueous soln. with total organic residues <10%	133	0	4,675	
Laboratory waste chemicals	551	2,503	4,169	

Accomplishments

IMS mentioned in its Performance Report that they were not subject to SB 14 in 1998. However they mentioned that the production level was substantially increased from 1998 to 2002, therefore, company experienced 370 percent increase in their total hazardous waste in 2002. The company managed their two wastes (1) unspecified organic liquid mixture (CWC 343) and (2) laboratory waste chemicals (CWC 551) by sending them off-site and conducted recycling.

Projections

IMS had five major waste streams during 2002. The company considered 5 source reduction and recycling measures for all of their five major waste streams. One of the five measures identified as off-site recycling of CWC 343 was selected. Other four measures were rejected.

CWC 343 (Unspecified organic liquid mixture)

This waste stream, a mixture of spent isopropanol, methanol, and dimethylformamide (DMF), is generated through cleaning operations. One of the cleaning operations is conducted in accordance to FDA approved procedures and monitored by the microbiology laboratory for quality control. The cleaning operations are conducted at various levels. The aseptic filling suites are sanitized on a daily basis. The fill lines are sanitized both prior to and after shift is over. The generator was not able to select any source reduction measure for this waste. However, it is considering off-site recycling of waste and expired/obsolete chemicals.

IMS is researching methods to do off-site recycling of waste generated and expired ingredients and reuse in other applications such as in the production of vinyl resins, butadiene, wood adhesives and in organic synthesis. Alternative uses of reclaim methanol include solvent for cleaning purposes, and manufacture of formaldehyde.

If the off-site recycling is implemented for these waste solvents, IMS expects that the waste disposed would decrease by 80%. The savings in the disposal cost would be approximately \$240,000.

CWC 141 (Off-specification, aged, or surplus inorganics)

This waste is the expired or obsolete silicone that does not meet FDA standards for use in product manufacturing. Basically, silicone is used to coat inside tube of the syringe to decrease the viscosity of medication. The generator was not able

to select any source reduction measure for this waste; therefore it cannot project any reduction for 2003-2006 cycle.

CWC 135 (Unspecified aqueous solution)

This waste is comprised of inks and excess cleaning products. The ink is used for product box labeling. In the manufacturing area, the final products are placed into boxes that are labeled and transported from one department to other. The generator was not able to select any source reduction measure for this waste; therefore it cannot project any reduction for 2003-2006 cycle.

CWC 133 (Aqueous solution with total organic residues <10%)

This waste is generated from various cleaning processes. Different manufacturing areas of the plant are sanitized with isopropanol and phosphoric acid. The spent cleaning solutions and spent acid are collected in the drum which eventually incinerated off-site. The generator was not able to select any source reduction measure for this waste; therefore it cannot project any reduction for 2003-2006 cycle.

CWC 551 (Laboratory waste chemicals)

This waste stream is comprised of expired or obsolete chemicals and raw materials used for IMS products. The generator was not able to select any source reduction measure for this waste; therefore it cannot project any reduction for 2003-2006 cycle.

Remarks

IMS reported that it did not generate any SB 14 applicable Category A waste during 1998 and 2002 reporting years. SB 14 applicable Category B waste generation for 1998 and 2002 years were 10,669 lbs. and 50,046 lbs. respectively—an increase of 370 percent. This large increase in their hazardous waste quantities is attributed to increase in their production.

Profile #20
Nektar Therapeutics
San Carlos
EPA ID: CAR 000118133
SIC: 2834

Site information

Nektar Therapeutics is located at San Carlos in San Mateo county. The primary business activities conducted at this site include research and development and the manufacture of drug and associate drug delivery systems for biotechnology and pharmaceutical products. Operations at this site began in 1997. This facility employs about 400 people. Nektar Therapeutics produces these pharmaceutical preparations using spray drying technology. Delivery systems are manually assembled on a batch basis, packaged and shipped.

Major Waste Streams in 2002

Waste Stream	CWC	Pounds	Description/Waste-Generating Processes
Off-spec and waste solids- Non-RCRA hazardous waste solids	352 and 331	26,495	Cleaning activities in the manufacturing area and pharmaceutical byproducts
Lab waste- RCRA hazardous waste solids	352	12,564	Lab debris, e.g. broken pipettes, vials, solvent contaminated wipes
Liquids with halogenated compounds	741	5,496	Waste from HPLC, titration and other lab bench processes

Accomplishments

N/A. The year 2002 was chosen as the reporting and baseline year, since 2002 was the first year Nektar became subject to SB-14.

Projections

Nektar Therapeutics sets a numerical source reduction goal of 10% for all three major waste streams generated for the period January 2004-December, 2007.

CWC 352/331 (Non-RCRA hazardous waste solids)

The facility projected the following source reduction measures for these waste streams:

- Improve the waste profiling process by testing the pH and identifying the hazardous waste characteristics and concentrations so that the waste is managed appropriately.

This assessment would also result in a significant reduction in hazardous waste solids disposed with costs estimated at \$30,000 annually.

- Mop-heads contaminated during cleaning should be triple rinsed. This approach would prevent the need to dispose of contaminated mop heads as hazardous waste. The resulting contaminated water should be neutralized on site. This measure has the potential to reduce the total amount of waste for all the major waste streams by 47 %.
- Improve training and documentation related to the amount of waste generated. Waste logs should include a better description of the waste.
- Assess the schedule for High Efficiency Particulate Air (HEPA) filter replacement and reduce change outs where feasible. Reducing HEPA filter waste by 20% would result in an estimated savings of \$870 in waste collection costs plus additional savings and reduced environmental impact achieved by fewer new HEPA filters as well as avoiding the labor costs associated with change outs and disposal.

CWC 352 (RCRA hazardous waste solids)

Listed below are the source reduction measures identified for implementation on this stream:

- Replace aerosol spray products with bulk solvents or spray pump products that can be emptied or rinsed out.
- Use the smallest possible container size for hazardous liquids to reduce the weight of contaminated debris. A reduction of just 5% by weight would result in a savings of at least \$750 annually in waste collection costs.
- Include empty container disposal protocol and rinse steps for glassware, vials and bottles in written lab protocols to prevent these items from being inappropriately disposed of as hazardous waste; thoroughly empty and triple rinse with minimal water; return empty containers to supplier or recycle. A reduction of solid lab debris by just 20% would result in an estimated annual savings of approximately \$3,000 in hazardous collection costs.
- puncture and drain aerosol cans (as allowed under California Universal Waste regulations, Health and Safety Code 25201.16(h)) on site or recycle non-empty aerosol cans as Universal waste.

- Increase the frequency of waste pick-ups to avoid collection containers from becoming completely full.
- Improve training and documentation regarding waste segregation.
- Better waste segregation of lab packs and contents and more efficient packing of lab packs.
- Better inventory control will avoid unnecessary orders and will therefore avoid unnecessary disposal of unused lab expired products as hazardous wastes.

CWC 741 (RCRA Waste Flammable Liquids)

- -Improved containers labeling training will avoid improper disposal of materials as hazardous waste (e.g. water bottles).

Remarks

This facility reported that FDA regulatory requirement and the need to get FDA approval for process changes were barriers to the implementation of the above proposed measures.

Profile #21
NeoMPS
San Diego
CAR000119040
SIC: 2836

Site Information

NeoMPS, based in San Diego, is a large producer of custom peptides, specializing in the solid phase synthesis of custom research and pharmaceutical grade peptides. NeoMPS develops its own manufacturing processes, buys and stores the raw materials, and performs production and analytical testing required to meet customer requirements. The solid phase organic synthesis used in the manufacturing of peptides consists of three distinct steps: synthesis (the assembly of an amino acid chain on solid support resin); cleavage (the separation of peptides from the support resin); and purification and analysis (the removal of undesired impurities from peptides and characterization of the final product).

While Multiple Peptide Systems was established in 1986 and is part of Groupe SNPE, this facility has operated since September 2002 and employs approximately 45 people. The company supplies the scientific and pharmaceutical community with peptides for research, development, and clinical trials.

Major Waste Streams in 2002

Waste Stream	CWC	Pounds 2002*	Description/Waste-Generating Processes
HPLC (High Performance Liquid Chromatography) liquids	343	25,000	Acetonitrile/methanol/water from HPLC
DCM (dichloromethane) / DMF (dimethylformamide)	211	14,500	Dichloromethane / dimethylformamide from washing of resin, neutralization of trifluoroacetic acid salt, removal of diisopropylethylamine, coupling of amino acid, removal of non-reacted amino acid solution
TFA (trifluoroacetic acid) / IPA (isopropyl alcohol)	741,791	5,000	Trifluoroacetic acid / isopropyl alcohol from Boc protecting group removal or resin swelling, washing of resin

* The baseline and reporting years were the same (2002) for this facility.

Accomplishments

N/A (Baseline and reporting years are the same.)

Projections

CWC 343 (Flammable, Organic Liquid from HPLC)

Reduce this waste stream by about 16% by decreasing solvent flow rate from 70 ml/minute to 60 ml/minute.

Remarks

For some waste streams, the facility reports it has already taken source reduction measures, such as reducing solvent volumes, as far as possible. The company states that one of the main barriers to source reduction is the need to adhere to customer specifications.

Profile #22
Norac, Inc.
Azusa
EPA ID: CAD008352957
SIC: 2834

Site Information

Norac manufactures benzoyl peroxide and tetrahydrocannabinol (THC), in addition to pursuing an active research and development program. Norac also manufactures olivetol and PMD (p-mentha-2, 8-dien-1-ol) which are used in the production of THC. The benzoyl peroxide is used as an ingredient in prescription acne cream. The tetrahydrocannabinol is approved as an anti-nausea agent for cancer patients and to increase the appetite of AIDS patients

Norac was established in 1953 as an organic peroxide manufacturer and started producing pharmaceuticals at the Azusa site in the early 1980s. Since 1999, this facility's main focus has been on pharmaceutical production and pharmaceutical research and development. Norac employs 72 people at this site.

Major Waste Streams in 2002

Waste Stream	CWC	Pounds 2002*	Description/How Generated
Acetone and water	212	15,012	From nonenone synthesis and purification
Hexane, isopropyl alcohol, and methylene chloride	214	9,591	From olivetol carboxylate synthesis
Hydrochloric acid and methylene chloride	791	8,757	From dronabinol synthesis
Cyclohexane	212	8,340	From dronabinol synthesis
Toluene and acetic acid	134	7,177	From olivetol synthesis
Toluene and metabisulfite	134	5,838	From olivetol synthesis

*The facility identified 2002 for both the reporting year and the baseline year.

Accomplishments

N/A (Reporting year and baseline year are the same.)

Projections

None

Remarks

The facility reports that currently the processes are optimized for maximum yield, and that potentially waste-minimizing changes would most likely affect the yield. Additionally, any changes would have to undergo process validation as per current good manufacturing procedures (cGMPs), which can be time-consuming, costly, and could potentially generate excess hazardous waste. Following cGMPs is a requirement of the U.S. Food and Drug Administration.

Current hazardous waste management practices include the following:

Offsite fuels blending for:

- Acetone and water (CWC 212)
- Waste cyclohexane (CWC 212)
- Hexane, isopropyl alcohol, and methylene chloride (CWC 214)

Offsite aqueous treatment for:

- Toluene and metabisulfite (CWC 134)
- Toluene and acetic acid (CWC 134)

Offsite incineration for:

- Hydrochloric acid and methylene chloride (CWC 791)

Profile #23**Pharmavite, LLC****EPA IDs: CAD 982518110****CAR 000064444****CAR 000057190****CAL 00116502****SIC: 2834*****Site information***

Pharmavite consists of four operating areas designated as the San Fernando Manufacturing (SF), Pharmavite Packaging and R&D (Valencia bldg A), Pharmavite Warehouse (Valencia bldg B) and Pharmavite Valencia Distribution Center, all located in Los Angeles County. Since these areas are geographically separate and have different EPA numbers, they are reported as separate sites in Pharmavite's multi-site Source Reduction Evaluation Review and Plan (Plan). Pharmavite LLC manufactures, packages, and distributes vitamins, herbs, and other nutritional supplements. These products are in the form of tablets, two-piece hard shell gelatin capsules or soft elastic gelatin capsules.

Pharmavite SF has been at the current site for approximately 14 years; Valencia Bldg A and Bldg B for 4 years and the Valencia Distribution for 7 years. In 2003, Pharmavite employed 255 employees at San Fernando and Valencia Bldg A, 28 employees in Valencia Bldg B and 80 employees in Valencia Distribution.

The operations at the San Fernando manufacturing area include the manufacturing of: vitamin tablets (Tableting), two-piece hard shell gelatin capsules (2-piece), soft elastic gelatin capsules (Soft Gel), as well as its quality control and quality assurance laboratories. In the Tableting operation, raw materials (mostly powders), are inspected, weighed and then sent to the blending department, for mixing following the appropriate procedures for each formula. After blending, the mixture is discharged into plastic bags and staged for compressing. The material is gravity fed from the bags into the tablet presses. Once formed, the tablets are placed into bags and staged for coating if needed. In the coating department, the tablets are coated, spraying with an aqueous coating solution. This 2-piece hard shell operation is very similar to Tableting, except that hard shell gelatin capsules are filled with blended ingredients instead of being compressed without the coating step. In the Soft Gel operation, most of the ingredients are liquids. They are weighed, blended and then encapsulated into the gelatin capsules. The gelatin capsules are then dried in air tunnels.

Major Waste Streams in 1998-2002

The largest quantity of hazardous waste produced is waste vitamin dust and tablets. Other wastes include mineral oil, machine oil, flammable solvents and other minor wastes.

Dust is generated at various stages of the Tableting operations. This dust is removed using dust collectors and vacuum systems. Also, collected hazardous waste streams can include rejected tablets, test samples and floor droppings. Certain metals, notably copper, zinc and selenium present in the tablet formulation usually cause the dust and vitamin wastes to be classified as hazardous.

Waste Stream	CWC	Pounds 1998	Pounds 2002	Description/Waste-Generating Processes
Aqueous sludge	134*	54,978	123,120	Routine washdown and manufacturing equipment cleaning
Baghouse waste	591*	415,580	462,941	Tableting manufacturing
Spent mineral oil	221	44,150	12,660	Soft Gel manufacturing
Spent machine oil	343	4,206	2,580	Machinery oil changes
Spent flammable organic liquids	214	9,330	6,700	QC Laboratory analyses

*Only two major waste streams identified in 2002.

Accomplishments

CWC 591 (Waste vitamin dust and tablets)

There was an increase in CWC 591 generation from 1998 to 2002 (see Table). The sources for this waste stream include vitamin dust from the manufacturing processes; vitamin tablets from quality control; as well as, returned products and expired and outdated materials. The largest increase in this waste quantity comes from the manufacturing processes. There was actually a decrease in the amount of returns, expired or outdated materials. The approaches of segregation and inventory control had positive waste reduction effects.

CWC 221 (Waste mineral oil)

There was a 71% decrease in this waste stream from 1998-2002. Ingredient changes (using lower viscosity mineral oil) and process changes (removal of excess mineral oil from the gelatin ribbons) have resulted in this decrease.

CWC 134 (Waste aqueous sludge)

CWC 134 increased a little over two times from 1998 to 2002. This increase was due to the frequency of the clarifier cleaning. The amount of waste disposed is a function of the frequency of the clarifier cleaning. No measure was implemented for this stream.

CWC 214 (Waste flammable organics)

A 28 % reduction in CWC 214 was achieved from 1998-2002. The source reduction approach included making material and process changes. This approach involved mainly switching from using organic solvents to manually clean equipment parts to using aqueous base solvents in an automated parts washing cycle.

CWC 343 (Waste machine oil)

A 38% reduction in CWC 343 was achieved from 1998-2002 due to the substitution of longer lasting synthetic machine oils.

Projections

The facility has identified the following measures to be implemented:

CWC 134 (Waste aqueous solution with total organic residues 10 percent or more)

- Reduce mineral oil from the industrial waste stream by testing clarifier waste to determine if it is non-hazardous prior to disposal.

CWC 591 (Waste vitamin dust and tablets)

- Implement a testing program to determine which collected waste vitamins and dust are hazardous prior to disposal.

Previous tests have shown that vitamin dust waste hazard depends upon the formulas in use that produce the waste. When a lot of multi-mineral vitamins are

produced the dust collected is usually high in copper and zinc, thus making the waste hazardous.

Remarks

The main factor responsible for increasing the two major streams produced in 2002 was increased production activity. Production increased by about 8% between 1998 and 2002. New production equipment and process were added to accommodate this production increase. Another factor increased the aqueous sludge waste generation was the frequency of clarifier cleaning. Clarifier cleaning increased from once a quarter to monthly. The Good Manufacturing Practices (GMP) may also impact on these waste streams. GMP requires more thorough cleaning of equipment, not reusing materials, etc. which can reduce the amount of both of the two major waste streams.

Profile #24
Polypeptide Laboratories
Torrance
CAR000030080
SIC: 2833

Site Information

Since 1997, Polypeptide, Torrance, has been manufacturing complex biologically active peptides in bulk quantities for use as the active ingredients in pharmaceutical products. The majority of these products are manufactured on a contract basis for other pharmaceutical companies, initially as “investigational new drugs,” although some are manufactured as bulk, generic drugs. As the company’s business is focused mainly on contract manufacturing for major pharmaceutical companies, most of the products are manufactured on an “as needed” basis, as orders are received.

Polypeptide’s Torrance facility employs approximately 45 people and includes production laboratories for synthesis, cleavage, and purification/lyophilization, a research and development laboratory, a quality control laboratory, a solvent delivery system room, a purified water system room, receiving, storage, and packaging areas, as well as administration offices.

Major Waste Streams

Waste Stream	CWC	Pounds 2000	Pounds 2002	Description/Waste-Generating Process
Unspecified solvent mixture	214	102,629	147,856	Methylene chloride, dimethylformamide, isopropyl alcohol, acetonitrile, trifluoroacetic acid, triethylamine – from multiple washings of solid-phase matrix during peptide synthesis. Also, ether from washing during cleavage and deprotection step.
Unspecified organic liquid mixture	343	338,240	477,784	Acetonitrile, trifluoroacetic acid, acetic acid, and triethylamine – from purification of product in HPLC column.

Accomplishments

None reported.

Projections

Polypeptide plans to use a different peptide synthesis process for new products; more specifically, the facility will be using Fmoc-based peptide synthesis instead of Boc-based peptide synthesis for their new products. Fmoc- and Boc-groups block, or protect, a part of the amino acid molecule while the amino acid is being chemically coupled to another amino acid to form a peptide. Once the peptide is formed, the Fmoc-or Boc-group is removed. Fmoc-based synthesis uses greatly reduced quantities of dichloromethane, and does not use hydrogen fluoride, a highly toxic chemical. The facility decided to adopt the Fmoc-based synthesis for several reasons, including: the reduced cost of the Fmoc-protected amino acids to levels comparable to the Boc-protected amino acids; and its interest in avoiding the hydrogen fluoride cleavage process, which is more time-consuming and potentially more hazardous than the cleavage process used with the Fmoc-based synthesis. Use of Fmoc-technology instead of Boc-technology may reduce the dichloromethane waste stream by 25% to 50%. The Fmoc-technology will be used on new products, with customer approval.

Remarks

Polypeptide reported that factors affecting waste generation include client specifications and process development and improvements.

More specifically, barriers to source reduction include the following. Customers' specifications, which are tied to FDA validation, restrict source reduction. For example, the company cannot change raw materials without authorization from the customer. The customer, in turn, must repeat clinical trials and resubmit their data to the FDA, to prove that the raw material change will not alter the drug quality, strength, safety and efficacy. Production is not regular. Polypeptide is a contract manufacturer; most customers order the same peptide only one or two times, as the ordered product often is of no use after pre-clinical or early clinical trials are completed. Thus it is not economically feasible to optimize a process for a product that will only be manufactured for a limited duration or frequency.

Currently, hazardous waste management practices consist of offsite recycling of CWC 214 and CWC 343 as fuels.

Profile #25
Promega Biosciences, Inc.
San Luis Obispo
CAD982501983
SIC: 2835

Site Information

Promega Biosciences performs research on, develops, and manufactures specialty organic compounds, many with bioluminescent or fluorescent properties, used as components by Promega Corporation in products for the life sciences market. The company has been in existence for about 32 years and has operated at the present site for 20 years. Currently with 55 employees including part-time and temporary positions.

Major Waste Streams in 2002

Waste Stream	CWC	Pounds 1998	Pounds 2002	Description / Waste-Generating Processes
Chlorinated solvents	741	18,574	16,230	Organic synthesis, extractions, separations, and chromatography.
Wastewater – Aqueous Grade 2.3	135	134,449	77,520	Organic synthesis, extractions, separations, and chromatography.
Solvent mixture – fuel grades 1, 2, 3	214	101,266	44,945	Organic synthesis, extractions, separations, and chromatography.

Accomplishments

Promega Biosciences, Inc. has reduced hazardous waste manifested by half since the 1998 reporting year. The major reduction in the waste streams in the 1998 to 2002 time frame was due to the change in the product mix that occurred as Promega Corporation purchased our company in 1999. With that purchase a number of the older larger volume diagnostic reagents and pharmaceutical intermediates were eliminated from the product line resulting in a reduction in our waste streams.

Projections

Based on our current year-to-date hazardous waste generation, we do not anticipate a significant increase or decrease in hazardous waste generation from 2002 to 2006. There have been no changed measures projected to be implemented.

Remarks

Although Promega Biosciences, Inc. continues to look for ways to reduce waste such as re-evaluating the chemistry involved in certain processes, a barrier is Promega's ISO 9000 registry which makes the ability to implement changes and re-qualify approved processes more complex. Hazardous waste currently generated at Promega Biosciences, Inc. is shipped off-site to Romic Environmental (Palo Alto, CA) for recycling.

Profile #26

Sicor Pharmaceuticals (TEVA Pharmaceuticals)

Irvine

EPA IDs: CAR 000009498

SIC: 2834

Site information

Sicor (TEVA) is a multi source injectable drug manufacturer. This facility is located in Irvine. This facility develops, manufactures and markets multi source injectable drugs with a primary focus on the production of anesthesiology, oncology and cardiology products. The manufacturing process steps include compounding (formulation), filling of sterile vials and labeling and packaging of vials. This site has been in business since 1987 and employs 950 people.

Major Waste Streams in 1998-2002

Waste Stream	CWC	Pounds (1998)	Pounds (2002)	Description/Waste-Generating Processes
Oncolytic solutions	135	2,813	13,679	Tank Tailing/Equipment flushing/cleaning
Empty Containers	513	0	16,392	Consolution of waste/Empty Reagent Bottles
HPLC solvents	214/741	8,698	20,332	Lab Chemical Analysis Procedures
Drugs in vials	343	6,284	35,056	Rejected Drug Vials /HPLC Vials
Lab Pack*	551	2,303	1,623	Laboratory operations
Waste oil*	221	2,097	2,931	Maintenance

*only major waste streams in 1998

Accomplishments

In 1998, the development of a new product line resulted in an increase in the amount of hazardous waste generated not only from production, but also from the laboratories. Waste generation increased from 39,362 pounds in 1998 to 97,981 pounds in 2002. During this time, production increased 170 %. The normalized data from 1998 to 2002 shows a small drop (7 %) in waste generation relative to production. The facility also reported in its Summary Progress Report (SPR), generating 768 pounds of Category C (extremely hazardous waste) in 1998 with reduction to 689 pounds in 2002.

The major waste streams were managed offsite by either treatment or incineration.

CWC 221 (Waste oil)

Source reduction measures implemented included employee education and training and a program to identify leaks, thus reducing the amount of waste generated. This stream was sent offsite for recycling.

CWC 551 (Lab Packs)

CWC 551 was reduced by 37 % for the period 1998-2002. This was accomplished by implementing a laboratory inventory management system, which helped to reduce the expiration of chemicals. Waste segregation was another measure. This stream was sent offsite for incineration.

CWC 214/741 (HPLC solvents)

CWC 214/741 was reduced by 6% for the period 1998-2002. Measures implemented for this waste stream included employee education and training, implementing an inventory management tracking system and controlling the amount of GC and HPLC column rinse water discharged into the collection container. This waste stream was sent offsite for use as fuel.

Projections

Sicor (TEVA) has projected the following source reduction measures to continue to be implemented:

For all of the major waste streams:

Employee source reduction education and training.

CWC 741 (HPLC Solvent Waste)

- Inventory control- Sicor will fine tune its computerized inventory management system. An inventory management system is being used in all the laboratories in the facilities. Employees have been assigned to track hazardous chemicals in the laboratories.

CWC 343 (Drugs in vials)

- Pharmaceuticals drug containers will be separated from HPLC solvent vials. The segregation of this waste would avoid non-hazardous pharmaceutical drugs from becoming hazardous by being mixed with HPLC vials. Consequently, separate disposal methods would be used for each segregated waste stream.

CWC 513 (Empty Containers)

The facility would:

- Check the classification of waste previously present in each lot of vials. Not all of these vials would be hazardous
- Research and determine if glass which once contained hazardous waste can be sent to a glass recycler.

This stream is currently sent offsite for incineration.

Remarks

Sicor (TEVA) mentioned having a production increase from 1998 to 2002. During these four years, the production increased 170 %. This production increase significantly increased the amount of waste generated in the laboratories as the result of the increase in required testing of raw materials and finished drug products. The startup of the oncology manufacturing facility added a new waste stream to the facility's inventory.

The major SB-14 waste quantities increased from 22,195 pounds in 1998 to 90,013 pounds in 2002. Total SB-14 hazardous waste generation increased from 39,362 pounds in 1998 to 97,981 pounds in 2002. The normalized data from 1998 to 2002 shows a small drop (7 %) in waste generation relative to production.

Profile #27
3M Pharmaceuticals
Northridge
CAD050807122
SIC: 2834

Site Information

3M Northridge manufactures medicinal drugs in the form of tablets, transdermal patches, and bronchial dilator aerosol inhalers, in three major manufacturing departments: Solid Dose, Aerosol, and Transdermal Drug Manufacturing. The 3M Northridge facility has been operating for approximately 45 years, and currently employs 450 people.

Major Waste Streams

Waste Stream	CWC	Pounds 1998	Pounds 2002	Description/Waste-Generating Processes
Transdermal Drug Delivery (TDD) solids	311	347,220	298,153	Pharmaceutical patches, liner and roll stock: from cutting coated roll stock into single dose patches; packaging; quality control testing.
Conventional drug delivery (CDD) solids*	311	58,146	23,178	Pharmaceutical tablets, powders and packaging: from powder handling, mixing, and packaging.
Inhalation Drug Delivery (IDD) CFC solids	211	132,817	122,651	Compressed gas aerosols, bulk, batch tailing: from batch mixing and filling; batch tailings from production operations.
IDD CFCs	211	49,783	62,675	Liquid Freon (aerosol): from cleaning operations, batch mixing, and filling.
TDD Flammable liquid	212	83,006	66,696	Ethyl acetate from tank and equipment cleaning.
IDD Flammable, liquid	212	67,825	165,053	Isopropyl alcohol rinse from tank and equipment cleaning.

* Not a major waste stream, but included in Plan.

Accomplishments

CWC 311 (Conventional Drug Delivery Solids)

The facility reported a 14% reduction in its patches, liner, and roll stock solid waste, due to the following factors:

- Reduced production volume by 25%;
- Replaced old vision system with newer technology to increase accuracy of tracking defects;
- Replaced reject gate with newer design, which reduced false rejected patches;
- Improved heat seal station to reduce waste generated by poor seal;
- Improved converting line setup training to reduce startup rejects;
- Changed liner from 5 mil to 3 mil for all Minitran products, which reduced overall weight of liner waste;
- Implemented a Six Sigma converting and packaging waste reduction project.

CWC 211 (IDD CFCs)

Facility reported a 5% reduction in its compressed gas aerosols and batch tailings by installing state-of-the-art formulation tanks on IDD line 2, and a 2.2% waste reduction by installing batch tailing and bulk propellant collection cylinders. Again, the facility reported a greater than 25% production volume decrease.

Projections

CWC 311 (TDD waste solid, patches, liners, roll stock and packaging)

3M proposes to implement a Six Sigma TDD Line 5 Converting and Packaging waste reduction project. Six Sigma is a management system that strives to limit the number of defects or mistakes per specified units of production, through a process to define, measure, analyze, improve and control (DMAIC). The facility estimates a decrease of 10,000 pounds per year of this waste stream.

CWC 211 (IDD waste CFC compressed gas aerosols, bulk & batch tailings)

Production process change: install clean-in-place (CIP) devices for tank cleaning; install state-of-the-art formulation tanks; implement bulk and batch tailing recovery cylinders. Estimate decrease of 5,000 pounds/year.

CWC 211 (IDD waste CFC liquid Freon (aerosol))

Production process change: install state-of-the art formulation tanks and implement bulk and batch tailing recovery cylinders. Estimate decrease of 3,000 pounds/year.

CWC 212 (IDD waste flammable liquid, IPA)

Production process change: install CIP tank cleaning system. Estimate decrease of 5,000 pounds/year.

CWC 212 (TDD waste flammable liquid, ethyl acetate)

Production process change: install CIP tank cleaning system on mixing tank. Estimate decrease of 3,000 pounds/year.

Remarks

Factors affecting waste generation include production volume changes. The main barrier to source reduction appears to be the validation process for new formulation tanks and new cleaning-in-place (CIP) devices. Hazardous waste management practices include source reduction and offsite recycling approaches.

Profile #28
Watson Laboratories
Corona
EPA ID: CAD 106931488
SIC: 2834

Site Information

Watson Laboratories, Inc. is a wholly owned subsidiary of Watson Pharmaceuticals, Inc. The Watson Laboratories Corona site produces tablets and capsules of hormonal and non-hormonal products as well as controlled and non-controlled drug substances. The business activities of this facility include pharmaceuticals manufacturing, quality control laboratory operations, and research and development. The major products produced include solid dosage pharmaceuticals, including analgesics and oral contraceptives.

This facility has been in business since 1985 and employs 1,481 people.

Major Waste Streams in 1998-2002

Waste Stream	CWC	1998	2002	Description/How Generated
Ignitable solvents	343	57,820	121,690	QC lab-HPLC wastes
Ignitable solvents	212	29,480	31,766	Process cleaning wastes

Accomplishments

None reported.

Projections

None reported.

Remarks

The major barrier to considering additional source reduction measures, according to this facility, is the requirement for FDA approval (a time-consuming and costly process) for new materials, changes in production processes, and product reformulations. However, the facility currently implements just-in-time (JIT) management for inventory control, based on ordering the minimal amount of inventory necessary to complete requested job orders. Watson Labs plans to

investigate maintenance operations of the HPLC and GC/MS equipment, to determine if modifications could reduce hazardous waste generation in the quality control lab, and will also examine overall site management practices (including housekeeping) for avoiding waste generation.

IV. CONCLUSIONS

The 28 facilities included in our study generated a total of approximately 39 million pounds of hazardous waste in major waste streams, in 2002. (See Table 4) This represents an approximately 20 million pound increase since 1998, the previous SB 14 reporting year (due to production increases and other factors – see item 3 below for a more detailed explanation). The 28 facilities in our study projected a 2.9 million pound reduction in the next four years of the SB 14 reporting cycle.

- 1) Most of the wastes generated and noted in Figure 2 are CWC 212, oxygenated solvents.
- 2) Table 2 shows manifested (category B) total hazardous waste quantities generated by the 28 facilities subject to SB-14. This includes a total of 19 million pounds in 1998 and about 39 million pounds in 2002. Note that we do not present category A waste quantities as most of the reporting facilities (85%) do not report Category A waste. This is because :
 - a. The facility does not use an onsite waste treatment unit and the waste stream is disposed offsite and listed as category B and/or
 - b. The facility claims an exemption due to the biotechnology elementary neutralization activities provision (H&SC 25201.15)²

Some of the facilities that reported category A wastes did not use the same accounting method in 2002 as compared to 1998; and, therefore, the data reported for those two years is not comparable. Another facility did not claim exemption in 1998, but did so in 2002. This gives the initial appearance that the facility reduced waste due to source reduction.

- 3) Manifested hazardous waste generation for 2002 was double that manifested in 1998. The reasons for this increase were due to:
 - a. Twelve more facilities becoming subject to SB 14 in 2002, explaining the large increase in waste generation. If one compares only the facilities that were subject to SB 14 in both years, a 35 % waste generation increase is evident.
 - b. A production increase by most of the facilities
 - c. Some waste streams were generated in 2002, but not in 1998.
- 4) The amount of industry-wide waste projected for reduction for the 2002-2006 period is 2.9 million pounds/year (see Table 3a). This projection is only based on the reported major waste streams (Table 2 from SPR).

² Note that while a limited number of facilities claimed an exemption under Health and Safety Code section 25201.15, the department has not verified the legality of this claim as an SB 14 exemption at the time of report preparation.

This represents 8 % of the total amount of major hazardous waste streams generated in 2002.

- 5) Table 3b shows that 3.1 million pounds per year of waste was avoided through source reduction from 1998-2002.
- 6) Considering the general pharmaceutical industry, one can see from both Table 4 and Figure 2 that the greatest hazardous waste quantities were generated by Pharmaceutical Preparations (SIC 2834) producing 28.3 million pounds of major waste streams in 2002, followed by Biological Products (SIC 2836) generating 9.4 million pounds, Medicinals and Botanicals (SIC 2833) producing 620 thousand pounds, followed by In Vivo and In Vitro Diagnostic Substances (SIC 2835) generating 340 thousand pounds.
- 7) The most common SB 14 source reduction measures include waste segregation, inventory control and employee training. Although there are some operational improvements and some facilities presented some process change measures e.g., Genentech San Francisco, switched from using a deionization resin bed in their wastewater process by installing a reverse osmosis unit with some standby deionization resin beds, thus reducing the generation of corrosive wastewater. See Table 5 for a summary of source reduction measures.
- 8) Product-specific production techniques and cleaning/maintenance approaches take years to develop and receive final FDA approval. Changing these processes and procedures, requires supplemental FDA approval. This barrier can add a significant delay to time necessary to implement source reduction practices. Some source reduction opportunities do exist when developing new products.

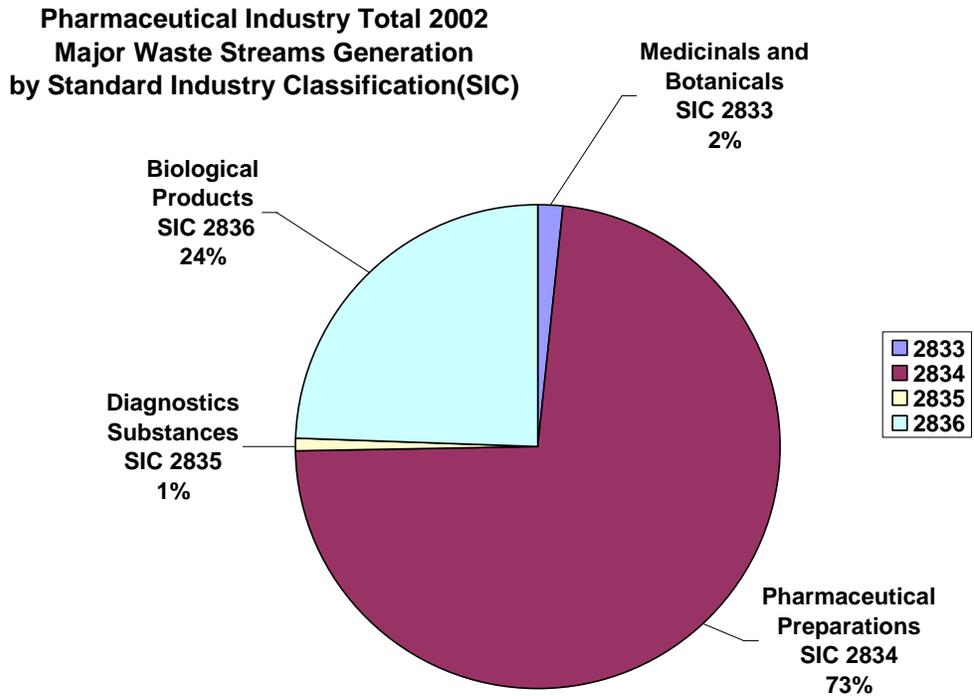


Figure 2. Hazardous Waste Generation by SIC.

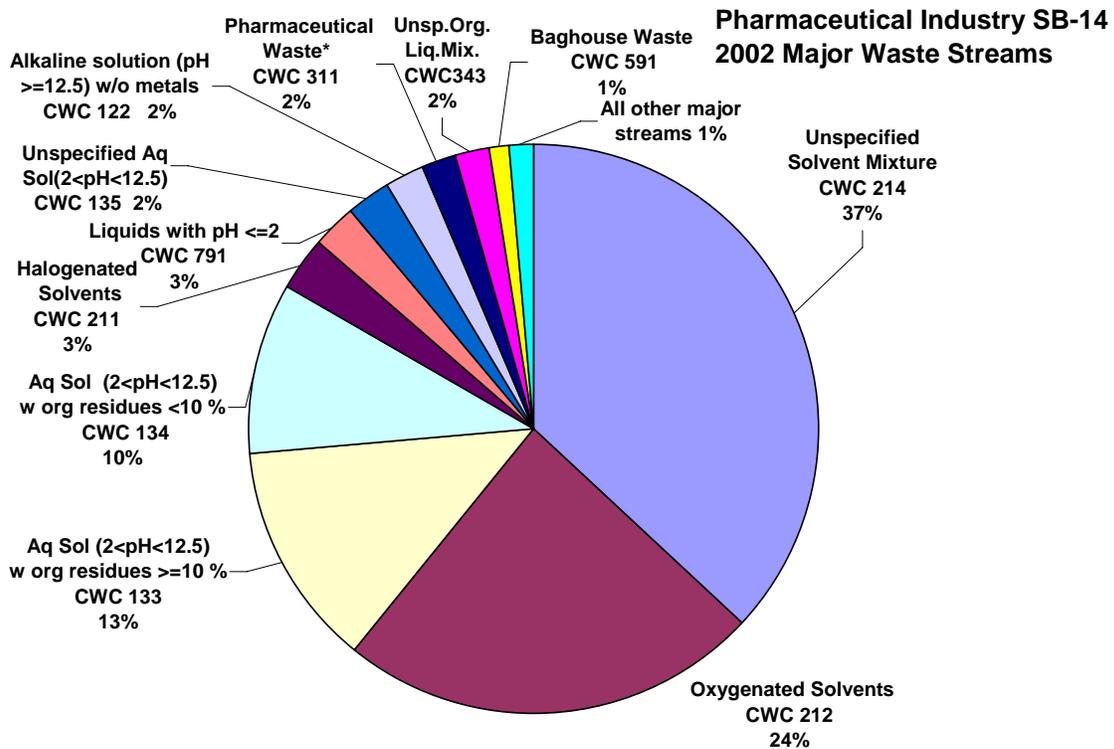


Figure 3. Pharmaceutical Industry (SICs 2833,2834,2835 and 2836)SB-14 Major Waste Streams (by California Waste Code).

Profile order	Table 2	Pharmaceutical Industry Category B Hazardous Waste Generation Data for 1998 and 2002			
	EPA ID	Facility Name	City	1998(pounds)	2002(pounds)
1	CAR000069153	AEROJET FINE CHEMICALS (AMPAC)	Rancho Cordova	14,135,000	19,760,000
2-A	CAD061622783	ALZA CORPORATION	Palo Alto	20,292	43,631
2-B	CAD981973712	ALZA CORPORATION	Menlo Park	45,769	33,536
2-C	CAD982475964	ALZA CORPORATION	Vacaville	1,324,833	1,668,408
2-D	CAD982503534	ALZA CORPORATION	Mountain View	158,429	83,998
2-E	CAR000016782	ALZA CORPORATION	Mountain View	24,200	34,704
2-F	CAD981694961	ORTHO MCNEIL (ALZA CORPORATION)	Redwood city	0	167,723
3	CAD981450893	AMGEN INC	Thousand Oaks	102,582	391,975
4	CAL000137397	ANASPEC INC	San Jose	37,937	112,908
5	CAD042236844	BAXTER BIOSCIENCE	Los Angeles	39,111	21,204
6	CAR000010207	BAXTER BIOSCIENCE	Thousand Oaks	0	30,488
7	CAD009126418	BAYER CORPORATION	Berkeley	0	31,000
8	CAD072518517	BECKMAN COULTER INC	Carlsbad	39,510	111,675
9	CAD046866463	CHIRON CORPORATION (NOVARTIS)	Emeryville	27,568	45,301
10	CAD000099259	DADE BEHRING INC.	Cupertino	46,615	53,065
11	CAR000096040	DEPOMED INC	Menlo Park	0	26,794
12	CA0000921544	DEY L_P	Napa	0	52,739
13	CAD983660689	EMD BIOSCIENCES INC	San Diego	41,680	35,778
14	CAD080129000	GENENTECH INC	So. San Francisco	1,120,818	1,516,923
15	CAR000017004	GENENTECH INC	Vacaville	0	2,204,185
16	CAR000017277	GEN-PROBE INCORPORATED	San Diego	0	32,216
17	CAD982320772	GILEAD SCIENCES	San Dimas	40,908	69,350
18	CAD092694538	GRIFOLS BIOLOGICALS INC. ³	Los Angeles	0	9,530,425
19	CAD981434723	IMS LTD	So. El Monte	10,669	50,046
20	CAR000118133	NEKTAR	San Carlos	0	49,338
21	CAR000119040	NEO MPS	San Diego	0	50,200
22	CAD008352957	NORAC INC	Azusa	0	77,022
23	CAD982518110	PHARMAVITE LLC SFI	San Fernando	531,171	579,787
24	CAR000030080	POLYPEPTIDE LABS INC	Torrance	0	625,640
25	CAD982501983	PROMEGA BIOSCIENCES INC	San Luis O'Bispo	273,434	148,615
26	CAR000009498	SICOR PHARMACEUTICALS INC (TEVA)	Irvine	35,960	98,700
27	CAD050807122	3M PHARMACEUTICALS	Northridge	883,419	798,785
28	CAD106931488	WATSON LABORATORIES, INC	Corona	111,207	168,901
	Total			19,051,112	38,705,060

³ Grifols (profile #18) acquired the operating assets of Alpha Therapeutic Corporation in July, 2003, and, therefore, did not own the facility during the 1998 to 2002 reporting period.

Table 3a Hazardous Waste Reduction Projection by Waste Stream for 2002-2006

Pharmaceutical Industry's Hazardous Waste Reduction Projection by Waste Stream for 2002-2006		
CWC	Waste Description	Projection (pounds/year) 2002-2006
122	Alkaline solution without metals pH ≥ 12.5	216
123	Unspecified alkaline solution	36,617
132	Aqueous solutions with metals	100
134	Aqueous solutions with total organic residues less than 10 percent	201,742
135	Unspecified aqueous solution	635,512
141	Off-specification, aged or surplus inorganics	90
181	Other inorganic solid waste	2,330
211	Halogenated solvents	28,436
212	Oxygenated solvents	1,890,718
221	Waste oil and mixed oil	7,549
311	Pharmaceutical waste	41,407
331	Off-specification, aged or surplus organics	11,278
343	Unspecified organic liquid mixture	9,000
352	Other organic solids	5,189
512	Empty containers 30 gallons or more	20,009
513	Empty containers less than 30 gallons	550
551	Laboratory waste chemicals	5,969
591	Baghouse waste	46,300
725	Liquids with mercury ≥ 20 Mg/L	15,000
741	Liquids with halogenated organic compounds ≥ 1000 Mg/L	1,500
791	Liquids with pH ≤ 2	36,749
	total	2,996,261

**Table 3b Annual Hazardous Waste SourceReduction by the Pharmaceutical Industry
-as reported in 2002**

CWC	Waste Description	Pounds
134	Aqueous solutions with total organic residues less than 10 percent	2,765,156
135	Unspecified aqueous solution	2,813
141	Off-specification, aged or surplus inorganics	320
211	Halogenated solvents	45,053
212	Oxygenated solvents	8,319
214	Unspecified solvent mixture	2,600
221	Waste oil and mixed oil	31,500
311	Pharmaceutical waste	237,300
331	Off-specification, aged or surplus organics	13,240
343	Unspecified organic liquid mixture	1,600
512	Empty containers 30 gallons or more	19,000
513	Empty containers less than 30 gallons	1,895
551	Laboratory waste chemicals	6,392
591	Baghouse waste	35,000
791	Liquids with pH \leq 2	2,160
	total	3,172,345

Table 4-Major Waste Streams by SIC

Pharmaceutical Industry in assessment report 2002-SB-14 Major Wastes (28 facilities)					
CWC/SIC	2834	2833	2835	2836	Total (lbs)
122 ALKALINE SOLUTION (PH>=12.5) W/O METALS	866,630		14,400		881,030
123 UNSPECIFIED ALKALINE SOLUTION				36,617	36,617
131 AQ SOL 2 < PH < 12.5" CONTG REACTIVE ANIONS			1,600		1,600
132 AQ SOL WITH METALS(SMALLER THAN RESTRICTED LEVELS AND SEE 121)			1,200		1,200
133 AQ SOL (2 < PH < 12.5) W ORG RESIDUES >= 10%	4,974,675				4,974,675
134 AQ SOL (2 < PH< 12.5) W ORG RESIDUES < 10%	3,799,625		1,800		3,801,425
135 UNSPECIFIED AQUEOUS SOLUTION (2 < PH < 12.5)	81,902		77,520	785,565	944,987
141 OFF-SPEC, AGED, OR SURPLUS INORGANICS	9,591		6,000		15,591
181 OTHER INORGANIC SOLID WASTE	8,254		22,550	5,175	35,979
211 HALOGENATED SOLVENTS	1,159,982			20,025	1,180,007
212 OXYGENATED SOLVENTS	973,716			8,317,820	9,291,536
214 UNSPECIFIED SOLVENT MIXTURE	13,926,291	147,856	44,945	180,990	14,300,082
221 WASTE OIL AND MIXED OIL	22,614			13,660	36,274
311 PHARMACEUTICAL WASTE	720,545				720,545
331 OFF-SPEC, AGED, OR SURPLUS ORGANICS	38,723		60,057	19,000	117,780
343 UNSPECIFIED ORGANIC LIQUID MIXTURE	179,120	477,784	31,060	31,030	718,994
352 OTHER ORGANIC SOLIDS	60,811		6,470	20,365	87,646
512 OTHER EMPTY CONTAINERS >= 30 GALLONS	61,455				61,455
513 EMPTY CONTAINERS < 30 GALLONS	8,693			1,395	10,088
551 LABORATORY WASTE CHEMICALS	7,868		28,595	16,622	53,085
591 BAGHOUSE WASTE	462,941				462,941
725 LIQUIDS WITH MERCURY >= 20 MG/L			30,440		30,440
741 LIQ W/ HALOG ORGANIC COMP > = 1000 MG/L	35,056		16,510	5,000	56,566
791 LIQUIDS W PH<=2	964,198		13,840		978,038
Totals (lbs)	28,362,690	625,640	356,987	9,453,264	38,798,581

Table 5 Pharmaceutical Industry Accomplished Source Reduction Measures

CWC	Measure	Facility	Profile#
122 ALKALINE SOLUTION (PH>=12.5) W/O METALS 791	Switched from resin bed system requiring periodic regeneration to a reverse osmosis system, whose maintenance does not generate corrosive wastewater	Genentech San Francisco	14
132 AQ SOL WITH METALS(LESS THAN RESTRICTED LEVELS AND SEE 121)	Statistical analysis to determine if the number of quality control analyses can be reduced	Dade Behring, Inc.	10
134 AQ SOL (2 < PH< 12.5) W ORG RESIDUES < 10%	Substitute column regenerator, eliminate column rinse and change column resin;	Genentech Vacaville	15
	Optimization initiative to increase resource use efficiency	Dade Behring	10
	New products that do not generate hazardous product recovery solutions	Genentech San Francisco	14
211 HALOGENATED SOLVENTS	Reduction of chlorinated solvents in purification process	EMD Biosciences	13
	Installation of state-of-the-art formulation tanks on one of the Inhalation Drug Delivery lines. This measure contributed to 5% yield improvement and 5 % waste reduction.	3M Pharmaceuticals	27
	Installation of batch tailing and bulk propellant collection cylinders to collect all batch tailings and scrap formulation. This contributed to 2.2 % waste reduction.		
212 OXYGENATED SOLVENTS	Inventory control	Alza, Inc., Chiron Corporation	2, 9
	Decrease flow rates in HPLC equipment runs if feasible to minimize waste generation	Dey, L.P.	12
	Recycle oxygenated solvents in analytical systems. Installed Alltech recycler	Alza	2
214 UNSPECIFIED SOLVENT MIXTURE	Inventory control and employee education and training	Sicor Pharmaceuticals	26
	Switching from using organic solvents to manually clean equipment parts to using aqueous base solvents in an automated parts washing cycle	Pharmavite	23
	Extend solution life time Switching from using organic solvents to aqueous base solvents in an automated parts washing cycle.	Dey, L.P.	12

Table 5 (continued)

CWC	Measure	Facility	Profile #
221 WASTE OIL AND MIXED OIL	Employee education and training	Sicor Pharmaceuticals	26
	Removal of excess mineral oil from the gelatin ribbons	Pharmavite	23
	Ingredient changes (lower viscosity mineral oil),		
	Less frequent oil changeouts	Dey, L.P.	12
	Replace pumps with "oil less" vacuum pumps	Baxter Biosciences, LA	5
	Maintenance operations to identify leaks		
311 PHARMACEUTICAL WASTE	Replacement of the old vision system with newer technology to increase accuracy of tracking defects	3M Pharmaceuticals	27
	Replacement of reject gate with newer design, which reduced false rejected patches		
	Improved heat seal station to reduce waste generated by poor seal		
	Changed liners from 5 to 3 mil to reduce overall weight of liner waste Implemented a Six Sigma converting and packaging waste reduction project		
331 OFF-SPEC, AGED, OR SURPLUS ORGANICS	Inventory control and employee education and training	Bayer, Dade Behring, Alza	7, 10
	Chemical exchange programs (avoiding excess materials from going to landfill)	3M Pharmaceuticals, Amgen	27, 3
343 UNSPECIFIED ORGANIC LIQUID MIXTURE	Substitution of longer lasting synthetic machine oils	Pharmavite	23
	Replace thimerosal by a less toxic chemical	Baxter Biosciences TO	6
352 OTHER ORGANIC SOLIDS	Waste segregation	Dey,L.P.	12
	Reuse rags by incorporating these rags in the biohazardous bin clean up procedure	Baxter Biosciences, LA and TO	5, 6
513 EMPTY CONTAINERS < 30 GALLONS	Replacement of 1 gallon bottles with reusable stainless steel containers , replacement with reusable plastic containers	Gilead Sciences, Alza	17, 2
551 LABORATORY WASTE CHEMICALS	Waste segregation and inventory control	Sicor Pharmaceuticals	26
	Laboratory inventory management system	Beckman Coulter	8
591 BAGHOUSE WASTE	Waste segregation	Pharmavite	23
	Inventory control		
725 LIQUIDS WITH MERCURY >= 20 MG/L	Reduce use of thimerosal as a preservative	Dade Behring	10
	Change batch mix procedures to match production quantity to final product		

References

- [1] World Bank Group, Pharmaceuticals manufacturing-Pollution Prevention Abatement Handbook-World Bank Group, effective July 1998.
- [2] Air Pollution Engineering Manual- Chapter 16: Pharmaceutical Industry, Michael J. Barboza, Theodore V. Chleboski, Richard Crume and Jeffrey Portzer, 2nd ed. Davis, W.T., 2000, Air and Waste Management Association, Wiley Interscience
- [3] Daughton, Christian G., and Ternes, Thomas A., "Pharmaceuticals and Personal Care Products in the Environment: Agents of Subtle Change?", *Environmental Health Perspectives*, Vol 107, Supplement 6, December 1999
- [4] Boxall, Alistair B. A., Kolpin, Dana W., Halling-Sorensen, Bent, and Tolls, Johannes, "Are Veterinary Medicines Causing Environmental Risks?," *Environmental Science & Technology*, August 1, 2003
- [5] Richard, Williams T., *Human Pharmaceuticals: Assessing the Impacts on Aquatic Ecosystems*, SETAC, 2005

Appendix A

California Waste Codes (CWC)

Inorganics

- 121. Alkaline solution (pH > or = 12.5) with metals (antimony, arsenic, barium, beryllium, cadmium, chromium, cobalt, copper, lead, mercury, molybdenum, nickel, selenium, silver, thallium, vanadium, or zinc)
- 122. Alkaline solution without metals (pH > or = 12.5)
- 123. Unspecified alkaline solution
- 131. Aqueous solution (2 < pH < 12.5) containing reactive anions (azide, bromate, chlorate, cyanide, fluoride, hypochlorite, nitrite, perchlorate, and sulfide anions)
- 132. Aqueous solution with metals (restricted levels and see waste code 121 for a list of metals)
- 133. Aqueous solution with total organic residues 10 percent or more
- 134. Aqueous solution with total organic residues less than 10 percent
- 135. Unspecified aqueous solution
- 141. Off-specification, aged, or surplus inorganics
- 151. Asbestos-containing waste
- 161. Fluid-cracking Catalyst (FCC) waste
- 162. Other spent catalyst
- 171. Metal sludge (see 121)
- 172. Metal dust (see 121) and machining waste
- 181. Other inorganic solid waste

Organics

- 211. Halogenated solvents (chloroform, methyl chloride, perchloroethylene, etc.)
- 212. Oxygenated solvents (acetone, butanol, ethyl acetate, etc.)
- 213. Hydrocarbon solvents (benzene, hexane, Stoddard, etc.)
- 214. Unspecified solvent mixture
- 221. Waste oil and mixed oil
- 222. Oil/water separation sludge
- 223. Unspecified oil-containing waste
- 231. Pesticide rinse water
- 232. Pesticides and other waste associated with pesticide production
- 241. Tank bottom waste
- 251. Still bottoms with halogenated organics
- 252. Other still bottom waste
- 261. Polychlorinated biphenyls and material containing PCBs
- 271. Organic monomer waste (includes unreacted resins)
- 272. Polymeric resin waste
- 281. Adhesives
- 291. Latex waste

- 311. Pharmaceutical waste
- 321. Sewage sludge
- 322. Biological waste other than sewage sludge
- 331. Off-specification, aged, or surplus organics
- 341. Organic liquids (nonsolvents with halogens)
- 342. Organic liquids with metals (see 121)
- 343. Unspecified organic liquid mixture
- 351. Organic solids with halogens
- 352. Other organic solids

Solids

- 411. Alum and gypsum sludge
- 421. Lime sludge
- 431. Phosphate sludge
- 441. Sulfur sludge
- 451. Degreasing sludge
- 461. Paint sludge
- 471. Paper sludge/pulp
- 481. Tetraethyl lead sludge
- 491. Unspecified sludge waste

Miscellaneous

- 511 Empty pesticide containers 30 gallons or more
- 512 Other empty containers 30 gallons or more
- 513 Empty containers less than 30 gallons
- 521 Drilling mud
- 531 Chemical toilet waste
- 541 Photochemicals/photoprocessing waste
- 551 Laboratory waste chemicals
- 561 Detergent and soap
- 571 Fly ash, bottom ash, and retort ash
- 581 Gas scrubber waste
- 591 Baghouse waste
- 611 Contaminated soil from site clean-ups
- 612 Household wastes
- 613 Auto-shredder waste California Restricted Wastes
- 711 Liquids with cyanides > or = 1000 Mg/L
- 721 Liquids with arsenic > or = 500 Mg/L
- 722 Liquids with cadmium > or = 100 Mg/L
- 723 Liquids with chromium(VI) > or = 500 Mg/L
- 724 Liquids with lead > or = 500 Mg/L
- 725 Liquids with mercury > or = 20 Mg/L
- 726 Liquids with nickel > or = 134 Mg/L
- 727 Liquids with selenium > or = 100 Mg/L
- 728 Liquids with thallium > or = 130 Mg/L
- 731 Liquids with polychlorinated biphenyls > or = 50 Mg/L

- 741 Liquids with halogenated organic compounds \geq 1000 Mg/L
- 751 Solids or sludges with halogenated organic compounds \geq 1000 mg/Kg
- 791 Liquids with pH \leq 2
- 792 Liquids with pH \leq 2 with metals
- 801 Waste potentially containing dioxins Source: California Code of Regulations, Title
- 22 Division 4.5, Chapter 11, Appendix XII.

Appendix B

List of Acronyms

AFC	_____	Aerojet Fine Chemicals
API	_____	Active Product Ingredient
BAK	_____	Benzalkonium chloride
CCDs	_____	Critical Core Drugs
CDD	_____	Conventional Drug Delivery
CIP	_____	Cleaning In Place
CFC	_____	Chlorofluorocarbon
CPI	_____	Continual Process Improvement
CWC	_____	California Waste Code
DBI	_____	Dade Behring
DMF	_____	DiMethylFormamide
DTSC	_____	Department of Toxic Substances Control
EDTA	_____	EthyleneDiamine Tetracetic Acid
EHS	_____	Environmental Health and Safety
EMS	_____	Environmental Management Software
FDA	_____	Food and Drug Administration
FFS	_____	Form, Fill and Seal
GMP	_____	Good Manufacturing Practices
HCV	_____	Hepatitis C virus
HIV	_____	Immunodeficiency virus
HPLC	_____	High Performance Liquid Chromatography
IDD	_____	Inhalation Drug Delivery
IMS	_____	International Medication Systems
IPA	_____	Isopropyl Alcohol
JIT	_____	Just in Time
NATs	_____	In Vitro Nucleic Acid Tests
GS/MS	_____	Gas chromatograph/Mass spectrometer
OROS	_____	Oral Osmotic Systems
PMD	_____	p-mentha-2-8-dien-1-ol
POCL	_____	Phosphorous Oxychloride
POTW	_____	Publicly Owned Treatment Works
R&D	_____	Research and Development
SIC	_____	Standard Industrial Classification
SPR	_____	Summary Progress Report
TDD	_____	Transdermal Drug Delivery
THC	_____	TetraHydroCannabinol
TTS	_____	Transdermal Therapeutic System
VIP	_____	Value Improvement Project
VOICE	_____	Visions of Involved Care Employees