



ROCHE COLORADO CORPORATION

ENVIRONMENTAL PROGRAMS STATUS REPORT

September, 2005

Roche Colorado Pollution Prevention Certifications and Memberships:



Introduction

This annual report is part of the voluntary pollution prevention program at Roche Colorado Corporation (RCC). An updated version of RCC's Pollution Prevention Master Plan and Statement of Commitments was submitted to the City of Boulder in August of 1999. This annual report is provided to supplement that Master Plan and to update the current status of our pollution prevention program. This section details the production activities at RCC and the voluntary environmental performance programs in which RCC participates.

The remainder of this annual Environmental Programs Status Report includes the following sections:

- **Environmental Compliance or Regulatory Status Changes**
- **2004 Pollution Prevention Activities**
- **2005-2006 Pollution Prevention Goals and Projects**
- **2004 Summary Tables**

Manufacturing Activities

Roche Colorado Corporation is a subsidiary of Roche Holdings, Inc. and is a manufacturer of bulk pharmaceutical intermediates, active ingredients for prescription and over-the-counter medicines and fine chemicals. The compounds that Roche Colorado produces are sent to other manufacturing sites for formulation into finished pharmaceutical products. Roche Colorado operates as a multi-purpose, large scale and small scale production facility, where the manufactured products change frequently as market demand or new product development requires. The main compounds that Roche Colorado currently produces are intermediates for the following products:

- Enfuvirtide (T-20 or Fuzeon[®])

Enfuvirtide, also known as T-20, is the first of a new class of HIV therapies called "fusion inhibitors." Enfuvirtide provides hope for AIDS patients who have developed resistance to the previously available treatment regimes.

- Ganciclovir (Cytovene[®] or Cymevene[®]) and Valganciclovir (Cymeval[®])

Ganciclovir and Valganciclovir are drugs for the treatment of CMV retinitis in patients with compromised immune systems, including patients with AIDS and organ transplant recipients.

- Tamiflu (oseltamivir phosphate)

Tamiflu is a medicine to treat flu (infection caused by an influenza virus). It belongs to a group of medicines called neuraminidase inhibitors. These medications attack the influenza virus and prevent it from spreading inside the body.

- Saquinavir (Invirase®) and Nelfinavir (Viracept®)

Saquinavir and Nelfinavir are protease inhibitors that act to impede an enzyme that is vital in the later stages of HIV reproduction. These compounds are also key components of HIV drug "cocktail" therapies.

- Highly Active Pharmaceutical Products and Other Manufacturing Activities

Roche Colorado's facilities also include small scale manufacturing laboratories for work in the production of highly active pharmaceutical products. Some of the laboratory scale pharmaceutical compounds currently in production at Roche Colorado include Nafarelin (Synarel®) for the treatment of endometriosis and Calcitriol (Rocaltrol®) for the treatment of osteoporosis. Other products made at the facility are used as catalysts for polyethylene manufacturing.

Boulder Technology Center

Roche Colorado houses the nationally recognized Boulder Technology Center (Tech Center). The Tech Center serves as a center of excellence for the development of pharmaceutical production processes which provide high purity drug products at the lowest possible cost to our customers, and with optimized reliability and safety to our manufacturing operations. The Tech Center's on-going operations also have a significant, and positive, impact on the environment:

- Improving the inherent safety of our manufacturing processes, by the discovery and development of chemical synthesis routes that minimize or eliminate the use of undesirable materials and minimize or eliminate the use of high pressure and high temperature process conditions. These process safety development steps also help to prevent pollution from any accidental release.
- Starting with the simplest materials as building blocks for our products, and improving the efficiency of our manufacturing processes, minimizes the demand of raw materials, which in turn reduces the processing performed by our suppliers. This has an overall effect of reducing the use of natural resources, transportation through city streets, energy consumed, and the wastes and pollution generated from manufacturing activities.
- Maximizing the ability of our existing equipment to manufacture our products minimizes the need for new facilities and the energy and materials needed to construct them.

The Tech Center includes both laboratory areas for development and pilot scale production facilities where drug product is manufactured to supply the clinical trials for new drugs and new processes are demonstrated in quantities necessary for approval by regulatory agencies.

The Tech Center has received a great deal of attention in recent years. In 2000, Roche Colorado received the Presidential Green Chemistry Challenge Award in the Alternative Synthetic Pathways category for the production of Cytovene, a potent antiviral agent. The Tech Center has also been recognized for its work in developing a production process for Enfuvirtide. The string of 36 amino acids that comprise Enfuvirtide makes it one of the most complex pharmaceutical compounds ever produced on a large scale using synthetic chemistry. The final transfer of the Enfuvirtide production process from the Tech Center to Roche Colorado's manufacturing facilities occurred in November of 2001.

Voluntary Environmental Performance Programs

Roche Colorado recognizes that a true commitment to pollution prevention entails the pursuit of goals that exceed applicable regulatory and legal standards. It is with these goals in mind that Roche Colorado participates in a variety of federal, state, local and industry-wide initiatives that set challenging pollution prevention standards. The following are examples of the pollution prevention programs in which Roche Colorado currently participates:

Responsible Care[®] Program

Roche Colorado is a member of the American Chemistry Council's Responsible Care[®] Program. The Responsible Care[®] Program entails performance guidelines, "codes," for every aspect of research, production and distribution in the chemical industry. A specific Pollution Prevention Code consists of management practices that are designed "to achieve ongoing reductions in the amount of all contaminants and pollutants released to the air, water, and land" and "to achieve ongoing reductions in the amount of wastes generated." Roche Colorado has achieved "Practice in Place" certifying that all fourteen management practices under the Pollution Prevention Code are fully developed and in place. In 2005, Roche Colorado received the Roche Corporate Award for Responsible Care[®] achievements.

Partners for A Clean Environment

Roche Colorado is excited about its certification under the City of Boulder's Partners for A Clean Environment (PACE) program. PACE businesses must meet a stringent list of criteria, demonstrating a sincere commitment to a company-wide pollution prevention program and the implementation of projects that have a quantifiable benefit to the environment.

Commuter Choice Leadership Initiative

Roche Colorado is registered as a charter member of the United States Environmental Protection Agency and Department of Transportation Commuter Choice Leadership Initiative (CCLI). The Commuter Choice Leadership Initiative commits companies to providing their employees with a menu of benefits as incentives for using alternative transportation modes in their commutes to work. The Commuter Choice Leadership Initiative also sets a specific alternative transportation goal for each participating company, mandating that at least 14 percent of each company's employees commute to work through some form of alternative to the single occupant vehicle.

Roche Colorado offers a range of alternative transportation incentives to its employees, including free Eco-Passes, on-site shower facilities, and protected lockers for bikes and personal belongings. A 2005 employee survey found that 30 percent of Roche Colorado employees are using alternative transportation modes in their daily work commute. Roche Colorado has recently been designated one of the Best Workplaces for Commuters through the CCLI. The designation recognizes companies that promote alternatives to single-occupant vehicle travel amongst their employees, providing them with benefits and services that facilitate the use of more environmentally sound commute options. According to the program website, the Best Workplace for Commuters designation is "a mark of excellence for environmentally and employee-friendly companies." It is also worth noting that RCC is an annual participant and financial sponsor of the City of Boulder's Bike-to-Work Week activities.

City of Boulder Pollution Prevention Program

Roche Colorado has been a voluntary participant in the City of Boulder's Pollution Prevention Program since its inception. Participation in the Pollution Prevention Program began with the development of a "Pollution Prevention Master Plan and Statement of Commitments." This document maps Roche Colorado's comprehensive commitment to pollution prevention in all of its pharmaceutical research, development, and manufacturing activities. In particular, the "Pollution Prevention Master Plan and Statement of Commitments" sets specific emissions reduction targets and the strategies for realizing these and other pollution reduction goals. Roche Colorado tracks its success in abiding by the terms of the "Pollution Prevention Master Plan and Statement of Commitments" through an annual update report (now titled "Environmental Programs Status Report") that it provides to the City of Boulder Office of Environmental Affairs.

Environmental Leadership Recognition

In 2003, Roche Colorado received the highest environmental honor that the State of Colorado bestows, the title of Environmental Leader. Environmental Leadership certification recognizes companies that voluntarily perform above and beyond the existing mandated environmental regulations. Environmental Leaders, like Roche Colorado, must have a comprehensive and operational environmental management system and a pollution prevention plan that commits the company to a program of continuous environmental improvement. In its letter announcing the Environmental Leader certification, the Colorado Department of Public Health and Environment thanked Roche Colorado for the "effort and dedication" it brings to environmental issues.

EPA Climate Leaders Program

In 2004, the Roche Group affiliates in the US became an EPA Climate Leaders Partner. Climate Leaders is a voluntary industry-government partnership that encourages companies to develop long-term comprehensive climate change strategies and to set greenhouse gas emissions reduction goals. Roche Group affiliates in the US set an aggressive goal to reduce greenhouse gas emissions by 10 percent by the end of 2008, against a base year of 2001. In 2005, Roche Colorado modified a site position, Facilities Engineer, to include the responsibility of developing and implementing an energy conservation and management program.

Environmental Compliance or Regulatory Status Changes

None in 2004.

2004 Pollution Prevention Activities

This section highlights some of the pollution prevention activities that occurred at Roche Colorado over the last year. These pollution prevention activities include both production-related projects with an impact on waste generation as well as more general company activities and systems that affect the tracking and implementation of pollution prevention opportunities. Some of these activities responded to specific pollution prevention goals that Roche Colorado set in its 2004 Environmental Programs Status Report.

Quantitative Pollution Prevention Goals

1. *Goal:* Reduce annual methylene chloride cleaning requirements by approximately 3,600 L.
Achievement: The target process and equipment were modified, requiring additional assessment.
2. *Goal:* Implement measures to increase onsite Ethyl Acetate recovery by an estimated 9,600 L annually.
Achievement: Complete. Recovery has increased by 2,800 L in 2005 to date. Projected annual savings is 8,500 L.
3. *Goal:* Install a heat recovery system in the HVAC system for the expansion of one plant. Heat will be recovered from the exhaust air stream before it is discharged outside. An estimated 2.6 million pounds of steam will be saved annually.
Achievement: Complete. An estimated 30,000 therms is being saved annually. Based on this success, RCC is considering its application in other areas of the plant site.

Other Pollution Prevention Goals and Projects

4. *Goal:* Evaluate several aqueous waste streams for the possibility of treating them in the onsite wastewater treatment plant instead of sending them offsite as hazardous waste for incineration.
Achievement: Evaluation complete. Determined feasible for future implementation, but these aqueous waste streams do not currently exist onsite.
5. *Goal:* Evaluate the option of performing onsite methylene chloride recovery for Enfuvirtide production in 2005.
Achievement: Initial evaluation complete. Further focused evaluation planned for 2005-2006.
6. *Goal:* Evaluate different uses for the low endotoxin purified water (LEPW) reject stream, which is currently discharged. Ideas include returning it as feed to the LEPW system, using it for irrigation, and using it as makeup water in the thermal oxidizer scrubbers.
Achievement: Evaluation complete. Decision was made not to proceed with implementation because it was not financially feasible.
7. *Goal:* Use recovered NMP to replace virgin material in more steps of Enfuvirtide. This will require an evaluation to ensure that recovered NMP is consistent with GMP requirements for raw materials.
Achievement: Implementation scheduled for fall of 2005.

8. *Goal:* Team with EPA Region 8 to implement a school laboratory clean-up program. This program will help schools to have safe and environmentally sound disposal of unwanted laboratory chemicals.
Achievement: Complete. Roche Colorado partnered with the EPA to develop guidance materials. An initial pilot program targeted Native American schools in the Denver area. Following successful implementation of one pilot school laboratory survey, the EPA and Roche Colorado team is refining the procedures and plans to offer the program to other schools.
9. *Goal:* Change locker room shower heads to high pressure, low volume heads. Annual water savings are estimated at 216,000 gallons.
Achievement: High pressure, low volume heads did not get installed; rather low flow shower heads have been installed.

Other Pollution Prevention Activities

The following activities represent additional efforts to prevent pollution in 2004 and early 2005:

- A team has been formed to perform a comprehensive evaluation of potential solvent recovery projects.
- Roche Colorado issued the Energy Conservation & Management Program procedure in 2005. This program will aid in the implementation and tracking of energy conservation opportunities. Also, Roche Colorado began collecting real-time energy usage data. The data will be evaluated to determine if it could potentially assist in identifying future energy reductions.
- In 2005, as part of its effort to encourage alternative modes use, Roche Colorado initiated an Eco-Pass promotion program. The promotion program first entailed ensuring that every employee received their free Eco-Pass. The company then offered incentives, such as raffle prizes, associated with use of the Eco-Pass and the completion of educational quizzes concerning Regional Transportation District services. In addition, Roche Colorado initiated a Bike Pool program. The Bike Pool program offers employees access to on-site bikes for use on errands and for exercise during the working hours.
- RCC helped sponsor Boulder County schools' "I Care About Clean Air" classes for 5th to 7th grade students. The class is taught by an air quality expert from the local recycling center. The program includes interactive classroom demonstrations, followed by several experiments from the "Clean Air Trunk." The class ends with a challenge to students and their families to take a pledge to do three or more activities to help clean up our air. This program could not be offered without the help of sponsors, such as Roche Colorado.
- All employees received the Colorado Air Pollution Control Division's electronic notices of Winter High Pollution "Red" Advisory Notices and Summer Ozone Action Alerts and are encouraged to avoid pollution-causing activities on those days.
- A new company brochure was created to communicate information about Roche Colorado to the public. A special insert for the new company brochure, titled "Commitment to Sustainability" (attachment), summarizes RCC's environmental programs.

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- Roche Colorado began purchasing 20% bio-diesel for vehicles.

2005-2006 Pollution Prevention Goals and Projects

Roche Colorado is committed to pursuing the following pollution prevention goals and projects for 2005 and 2006:

Quantitative Pollution Prevention Goals

1. Implement measures to decrease drummed waste weight by 10 metric tons per year from two intermediate products.
2. Conduct a lighting retrofit to replace T-12 lamps and electromagnetic ballasts with T-8 lamps and ballasts. The project could save 800,000 kwh of electricity per year.
3. Recycle over 50% of the hexane used in the production of one Tamiflu intermediate.
4. Increase onsite recycling of acetic acid by approximately 16,000 L per year.
5. Increase onsite recycling of HMDS by approximately 1,200 L per year.

Other Pollution Prevention Goals and Projects

6. Create a long term phase out plan for all ozone depleting compounds.
7. Evaluate the possibility of increasing onsite hexane recovery in the production of one Tamiflu intermediate.
8. Evaluate the possibility of onsite methylene chloride recovery in the production of one Fuzeon intermediate.
9. Evaluate the possibility of onsite methylene chloride recovery in the production of one Tamiflu intermediate.
10. Evaluate potential lighting modifications in the plants to improve lighting efficiency.
11. Work with Xcel Energy to conduct a recommissioning study that identifies no- and low-cost measures to reduce electricity demand and consumption.
12. Phase out canned air (used to clean electronic office equipment) that contains halogenated hydrocarbons as propellants. A replacement product has been identified.
13. Increase bottle, can, and paper recycling by increasing the availability of recycling containers around the plant site and by better educating employees about recycling procedures.
14. Evaluate the option to generate nitrogen onsite. This change would reduce nitrogen tanker visits (and associated truck pollution) by up to 80%.

Other Pollution Prevention Activities

In addition to those projects and plans mentioned above, all Roche Colorado process teams will continue to identify and evaluate pollution prevention opportunities in their areas of expertise. As the pressure to increase the production of the life-saving AIDS drug, Fuzeon, continues, the Pollution Prevention Team will continue to support and track pollution prevention efforts, with a focus on reducing solvent usage and increasing solvent recovery in that production process.

2004 Summary Tables

2004 Production at Roche Colorado

In 2004, Roche Colorado produced approximately the same amount of bulk pharmaceuticals, pharmaceutical intermediates, and fine chemicals as in the previous year. **RCC obtained an overall decrease in TRI emissions of 52% and VOC emissions of 18% from the prior year.** MACT controls were brought on-line in the fourth quarter of 2003. The emission reductions in 2004 were primarily due to a full year of MACT implementation. In 2004, Roche Colorado began production of a pharmaceutical intermediate for Tamiflu, a treatment for the flu virus. Production of other pharmaceutical products and intermediates, such as Enfuvirtide, saquinavir, nelfinavir, ganciclovir, and other fine chemicals and small production scale compounds, continued.

Onsite Recycling of Raw Materials

The list below compares consumption and recycling for chemicals that were recycled onsite. A raw material is "consumed" in a process when it has been chemically converted into another chemical or has become part of an unrecoverable waste stream. The "amount recycled" reflects the reuse of a compound in a process, when possible, rather than disposing of it.

Chemical ¹	Amount consumed (lbs)	Amount recycled (lbs)
Acetic Acid	153,490	243,584
Acetonitrile	1,316,659	1,152,326
Ethyl Acetate	791,042	55,503
Hexane	1,243,353	301,217
HMDS	41,575	12,416
Tetrahydrofuran	110,399	98,345

¹ Offsite recycling is not included in this list

Water Usage

The following table details where water was used at RCC in 2004:

Type of Usage	Amount used in 2003 (gallons)	Amount used in 2004 (gallons)
Process	18,750,948	19,053,851
Commercial	3,919,777	3,847,666
Cooling	11,978,475	11,142,777
Irrigation	2,912,800	2,939,706
Total	37,562,000	36,984,000

Wastewater Pretreatment Plant Discharge

Aqueous wastes from production pass through Roche Colorado's on-site pretreatment facility. The wastewater leaving that system is discharged to the City of Boulder treatment facility. The following table lists the major components of the wastewater that Roche Colorado discharges to the City of Boulder treatment facility:

	Discharge (in Pounds unless otherwise indicated)					
	1995 (Baseline)	2000	2001	2002	2003	2004
Volume, gal	21,035,000	19,444,939	13,885,540	10,890,001	11,922,735	11,929,650
Total Organic Content (TOC)	115,000	33,128	13,428	15,170	27,788	34,152
Chromium	31	22.1	3	5.2	25.8	13.0
Copper	4.3	14	1.0	1.5	8.5	16.6
Lead	2.8	2.4	ND	0.6	ND	0.5
Nickel	4.1	6.8	2.8	2.4	6.4	4.4
Zinc	73	21.1	18.1	14.8	54.5	36.0

ND = Not detected

Bulk Liquid Sent Offsite

The following values represent the amount of material sent offsite for energy recovery, incineration, and recycling:

Description	2001	2002	2003	2004
Total bulk liquid sent offsite (kg)	775,500	9,680,000	18,822,000	7,798,000
% Change from previous year	-20%	+238%	+94%	-59%
% Sent offsite to recycling or heat recovery	68%	70%	67%	72%

Energy Consumption

Energy Type	2000	2001	2002	2003	2004
Natural Gas (therms)	1,284,641	1,298,255	1,393,836	1,424,601	1,271,630
Electricity (KWH)	23,218,191	23,198,798	25,914,856	26,899,267	27,259,168

Air Emissions

The following table displays Roche Colorado's air emissions, divided into Toxic Release Inventory (TRI) compounds, Hazardous Air Pollutants (HAPs), and Volatile Organic Compounds (VOCs). MACT controls were brought on-line in the fourth quarter of 2003. The emission reductions in 2004 were primarily due to an entire year of MACT controls. Additionally, the 2003 construction of a secondary thermal oxidizer caused some thermal oxidizer collection system downtime, which resulted in higher emissions that year.

	1989 (Baseline)	2000	2001	2002	2003	2004
Reported under SARA Title III, Toxic Inventory Report (TRI) [values in pounds]						
Acetonitrile ^{1,2}	--	900	4,000	10,200	12,600	2,396
Dimethylformamide ^{1,2}	--	1,400	1,200	9,400	1,880	330
Hexane ^{1,2}	36,600	12,000	4,900	3,900	7,100	11,100
Methanol ^{1,2}	109,600	27,000	25,000	24,000	9,500	7,800
Methyl chloride ^{1,2}	6,700	--	--	--	--	--
n-Methyl-2-pyrrolidinone ²	--	20,000	7,100	22,100	240	78
Methylene chloride ¹	103,300	5,700	15,000	22,200	27,200	6,200
Toluene ^{1,2}	284,400	10,100	2,800	22,200	9,300	7,800
Triethylamine ^{1,2}	--	--	--	--	--	83
Acetone ³	242,500	1,200	790	7,213	2,606	2,075
Hydrochloric acid ¹	4,000	1,400	5,900	30,200	15,072	4,557
Methyl Tert-Butyl Ether ²	--	400	750	12,900	13,500	6,100
Pyridine ²	--	--	--	--	70	31
Total TRI air emissions (tons)	375	39	30	79	48	23
% change from previous year	--	-42%	-23%	+163%	-39%	-52%
% change from 1989	--	-90%	-92%	-79%	-87%	-94%

Total HAP emissions (tons)	293	29	29	68	47	24
% change from previous year	--	-59%	0%	134%	-31%	-49%
% change from 1989	--	-90%	-90%	-77%	-84%	-92%

Total VOC emissions (tons)	490	41	29	89	39	32
% change from previous year	--	-61%	-29%	207%	-56%	-18%
% change from 1989	--	-92%	-94%	-82%	-92%	-93%

¹ These chemicals are also classified as HAPs and are included in the HAP total above.

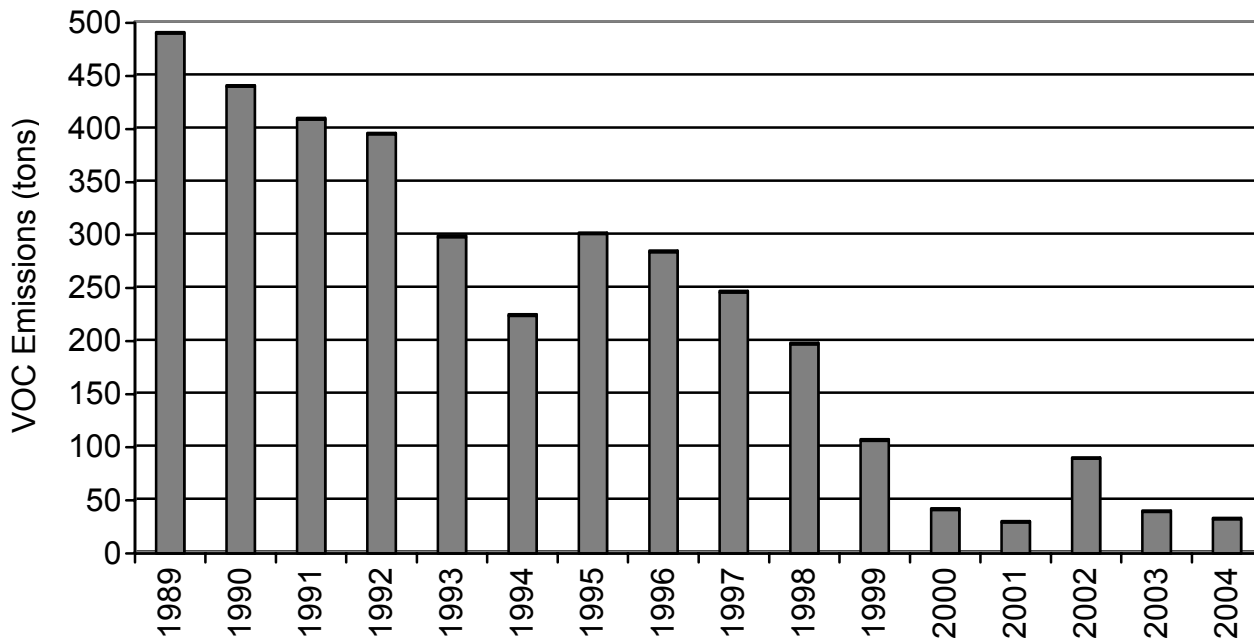
² These chemicals are also classified as VOCs and are included in the VOC total above.

³ Acetone is no longer included in TRI. It is also no longer classified as a VOC. After 1996, it is not included in the VOC total. Shaded blocks indicate that TRI reporting for that chemical was not required during that year. They are not included in the TRI emission total.

HAP = Hazardous Air Pollutant

VOC = Volatile Organic Compound

VOC Emissions Trend



General Waste Recycling

In 2004, Roche Colorado recycled a considerable amount of general waste:

- Recycled paper: 65 metric tons (31% of total waste paper)
- Recycled cardboard: 6 metric tons (23% of total waste cardboard)
- Metals: 133 metric tons (97% of total waste metal)
- Wood: 98 metric tons
- Carbon: 6.0 metric tons
- Lamps: 0.7 metric tons
- Batteries: 0.8 metric tons

In 2004, Roche Colorado recycled approximately 158,000 pounds of office paper, shredded documentation, newspaper, cardboard, magazines, and phone books. These efforts helped to save an estimated 650 trees from destruction.

Pollution Control Investments and Expenditures

This section summarizes the costs associated with pollution control and waste prevention measures in 2004. It is important to note that the amount of money spent can not be an indicator of a successful pollution prevention program. The best forms of pollution prevention, primarily source reduction, do not always involve significant investments in equipment or other capital expenditures, but rather necessitate mostly employee time and resources for research, development, and implementation of process changes.

Investments	Expenses
\$4,914,000	\$6,301,000