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ChemGenes Corporation

Toxics Use Reduction Case Study

*Cumulative, Decade-long Assistance from OTA and TURI Allow
ChemGenes to Significantly Reduce Toxics and Save Thousands*

Summary

Over the past decade, ChemGenes Corporation, a biotechnology company located in Wilmington, MA, has worked with the Office of Technical Assistance and Technology (OTA) and the Toxics Use Reduction Institute (TURI) to reduce and recycle solvents, improving overall efficiency, and saving thousands of dollars in the process. The first phase of the company's TUR efforts began in 2005 when OTA provided recommendations that led to the company reducing their annual chloroform use by 61% (50,078 pounds/yr) and hexane use by 42% (11,052 pounds) by 2014, and investing in a new chromatography system that significantly improved the efficiency of their manufacturing process and resulted in a net savings of \$215,000 through the end of 2012. ChemGenes started the second phase of their activities in 2012, with TURI at UMass Lowell awarding them an incentive grant to help offset capital costs for a new system to recover and recycle hexane and ethyl acetate. In the long-term, ChemGenes expects to reduce the use of hexane and ethyl acetate by 27,000 pounds over the next three years. Factoring in the TURI grant, ChemGenes realized a return on investment of less than three years for the recycling system.

About ChemGenes

ChemGenes Corporation, a 29-employee company, supplies products related to DNA- and RNA-synthesis for the biotechnology industry. Raw materials for DNA/RNA manufacturing – such as nucleoside phosphoramidites – must be produced to strict standards of purity. The process begins with a set of reactions of biological materials that produce DNA/RNA components. These are then dissolved in a solvent and run through column chromatography to be separated as purified product.

Phase I Activities

In 2005, to address solvent emissions from the process, OTA provided several recommendations on more efficient use of solvents, making clear the benefits and the range of opportunities to examine, including a list of alternatives that have worked for other biotechnology companies. Using a methodology called Design of Experiment, which helps keep track of the many variables key to evaluating trials of changes in process, the company made the following changes to their chromatography process:

1. Improvements to the reaction conditions of a majority of the bulk produced DNA/RNA intermediates were implemented to facilitate ensuing purification steps. In some cases, two column chromatography steps were needed to achieve pure product; the improvements in reaction conditions rendered cleaner crude product at higher yields, eliminating the need for

the second chromatography step and thereby reducing the overall solvent and silica gel consumption per gram of final pure product.

2. Redesign of the separation process so that a hexane/ethyl acetate solvent system could be used instead of a chloroform solvent system. These chemicals are less hazardous than chloroform.
3. Substituting a medium pressure liquid chromatography (MPLC) system for the column chromatography separation process for those products produced in large quantities, reducing the amount of solvent and silica gel used. The MPLC system, with a higher throughput rate, accomplished this reduction with less time and less waste.

Results: Reducing Solvent Use, Increasing Efficiency

Solvent Use Reduction

Before making the changes in 2007, ChemGenes used 82,706 pounds of chloroform and 26,517 pounds of hexane. By 2014, as a result of the changes implemented, they decreased chloroform use to 32,628 lb/year and hexane use to 15,302 lb/year (see Chart 1), reductions of 61% and 42%, respectively. The use of chloroform per gram of product decreased from 0.59 lb/gm to 0.25 lb/gm in 2014, a reduction of almost 58%.

Toxic Solids Reduction

In conjunction with the reduction in solvents, silica gel use was decreased significantly. In 2007, ChemGenes used approximately 11,800 kg and substantially reduced the consumption to 3,802 kg in 2104, a savings of 68% (see Chart 1). Silica gel use per gram of product decreased from 0.084 kg/gm to 0.029 kg/gm over this period, a reduction of 65%.

Chart 1

	Production (Grams)	Chloroform (Pounds)	Chloroform/ Gram of Product	Hexane (Pounds)	Silica Gel (kg)	Silica/Gram of Product
2007	140,451	82,706	0.59	26,354	11,800	0.084
2008	167,314	75,698	0.45	25,696	10,700	0.064
2009	143,832	40,374	0.28	15,879	7,444	0.052
2010	129,864	37,106	0.29	17,034	5,670	0.044
2011	152,022	38,501	0.25	23,675	5,551	0.037
2012	158,992	25,450	0.16	17,612	4,250	0.027
2013	129,028	35,239	0.27	17,612	5,250	0.041
2014	132,293	32,628	0.25	15,302	3,802	0.029

Hazardous Waste Reduction

Reduced use of chloroform and hexane also means that ChemGenes has experienced reductions in hazardous waste disposal costs, and associated regulatory compliance expenses. Also hazardous waste savings resulted from the reduction in spent silica gel from the chromatography process.

Economics

The costs to make the operational changes were approximately \$20,000 for research and development and quality testing, and \$65,000 for the medium pressure liquid chromatography (MPLC) equipment. After successfully incorporating the changes, the company achieved significant cost savings from improved efficiencies and reductions in chemical purchases and waste disposal. After accounting for development and equipment costs, the company's net savings from productivity improvements, reduced purchase costs, reduced disposal costs, and other related costs (such as regulatory compliance) exceeded \$215,000 by the end of 2012. The payback period on the investments in making the changes during Phase I was just about one year. According to Chief Operating Officer Anuj Mohan, "ChemGenes is very appreciative of OTA for planting the seeds of thought for this successful project. Toxics Use Reduction is part of our continuous effort to improve operations, product quality, and reduce environmental impact."

Phase II Activities

Continuing on the success of past solvent reduction projects, ChemGenes next focused on recycling blends of hexane and ethyl acetate generated by the production process. The first attempt involved the use of a 100 L distillation unit designed to separate spent solvent to allow its reuse. However, the instrument operation was labor intensive, resulting in the determination that it was not cost effective compared to buying fresh solvent. OTA recommended that ChemGenes consider a fully automated fractional distillation solvent recycling system manufactured by CBG Biotech (Columbus, OH). The TechnoClean F-2500 was determined to be the right fit based on the current batch size for the mid to large scale manufacturing process. It has a 25-gallon auto fill tank and is a fully automated programmable system with easy drain capabilities. ChemGenes worked with CBG to qualify the system by testing the recovered solvent produced by the process, and found the quality of the recovered solvent to exceed required specifications for reuse in the process. However, the upfront capital cost of equipment and training was high enough that the project did not receive management approval to move forward.



TechnoClean F-2500 Solvent Recycler

ChemGenes needed a financial boost to help them justify investing the upfront capital of approximately \$26,000 to cover equipment costs associated with this solvent recovery project. The Toxic Use Reduction Institute (TURI) industry incentive grant of \$15,000 was a perfect opportunity to move the project forward, and in 2012, ChemGenes was awarded the grant.

Results: Reducing Toxics Use, Saving Money

Solvent Use Reduction

In the spring of 2013, the CBG fractional distillation system was installed. It has been in full operation since May of 2013 with no interruption in the processing line. As a result of implementing this process change, ChemGenes recycled 3,817 liters of solvent (blend of hexane and ethyl acetate)

between May 2013 and April 2015. This corresponds to a savings of approximately \$10,050 in avoided solvent purchases.

Hazardous Waste Reduction

ChemGenes was previously disposing of all solvent as hazardous waste after a single use. Through the April 2015, 3,255 liters of solvent have been reused and therefore not been disposed of as liquid hazardous waste, which translates to approximately \$2,850 in disposal cost savings including fees.

Economics

Based on data collected through April 2015, the overall yield of the solvent recycling system is approximately 85%. The operational costs associated with the new process, including labor, quality control, equipment maintenance, utilities (electricity), and hazardous waste disposal, have been calculated to be approximately 50% of the total cost of the solvent that has been recycled. ChemGenes projected the payback on the solvent recovery system to be approximately 2 to 3 years, factoring in the TURI grant offset. Based on the data collected, ChemGenes is on track to reach this goal (see Chart 2).

Chart 2

Instrument Purchase Price:	\$(25,500.00)
TURI Grant:	\$ 15,000.00
Savings as of 3/31/2015:	\$ 7,498.00
	\$ (3,002.00)

Conclusions

The toxics use reduction experience of ChemGenes illustrates the ability of small companies to improve their environmental footprint while significantly cutting costs. ChemGenes has benefited over the past decade from their relationship with both OTA and TURI – reducing their use of solvents in processes as well as finding ways to reuse materials. ChemGenes is a growing company, and with the resources that the Commonwealth of Massachusetts offers, they are able to continue to grow stronger and compete in an extremely competitive global market.

This case study was prepared by the Office of Technical Assistance and Technology (OTA), a branch of the Massachusetts Executive Office of Energy and Environmental Affairs. The OTA helps businesses and other organizations improve their environmental performance by helping them comply with relevant regulations, reduce toxics use, and conserve energy, water, and other resources.

OTA's **non-regulatory** services are available at **no charge** to Massachusetts businesses and institutions.

For additional information contact OTA at **(617) 626-1060** or at www.mass.gov/eea/ota

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