



Process Change in the Pharmaceutical Industry

COMPANY	Merck & Company, Inc. - Cherokee Plant
PRODUCT/INDUSTRY	Manufacturer of pharmaceutical intermediates (SIC 28)
WASTE STREAM/CHEMICAL	Methylene Chloride
PROCESS	Synthesis of a component of the antibiotic PRIMAXIN
COST	\$34 million
SAVINGS/OTHER BENEFITS	Cost savings for one year period is about \$14 million
SOURCE REDUCTION METHOD	Process Modification Raw material substitution

BACKGROUND

Merck & Company, Inc. established a pharmaceutical manufacturing facility in Riverside, Pa, Northumberland County in 1950. Since 1984, this facility used methylene chloride, a volatile organic solvent, to synthesize imipenem a component of the broad spectrum antibiotic drug PRIMAXIN. Methylene chloride is an animal carcinogen and is listed as a priority pollutant by the federal EPA. Changes in the use of these chemicals revolve around reducing environmental emissions of suspected carcinogens.

In April, 1989, Merck voluntarily established environmental policy goals to reduce air emissions of carcinogens or suspect carcinogens by the end of 1991, then eliminate or reduce air emissions by the end of 1993. Another goal was to reduce all environmental releases of toxic (SARA) chemicals, including transfers of materials off-site for treat-

ment or disposal, by the end of 1995. Although manufacturing operations have grown, Merck has met it's 1991 goal and expects to meet its future goals to reduce or eliminate releases to the environment.

The federal EPA Clean Air Act Amendments address methylene chloride emissions in the pharmaceutical industry through the Hazardous Organic National Emission Standards for Hazardous Air Pollutants (HON) regulations which were released as proposed rules on 12/31/92. Further regulations will be due from US EPA 11/15/97.



Commonwealth of Pennsylvania
Robert P. Casey, Governor

Department of Environmental Resources
Arthur A. Davis, Secretary

PROCESS CHANGE

Methylene chloride was the major solvent used in the synthesis of imipenem. In order to meet their air emissions goals, Merck & Company, Inc. chemists and engineers developed a new manufacturing chemistry process which eliminated the use of methylene chloride in the synthesis of imipenem at a cost of \$34 million. As part of this change, Merck substituted smaller amounts of solvents which are viewed to have fewer environmental effects than methylene chloride. This new process was implemented at the Cherokee plant in 1992.

Some of the other chemistry process modifications are as follows:

1. Computer controlled ultrafiltration technique to filter extremely small particles. This method increases product yield and improved quality of imipenem.
2. In process solvent recovery to reuse solvent which reduces solvent consumption and disposal.

EQUIPMENT CHANGE

When the new process was installed, the factory area was upgraded with a computerized distributed control system (DCS) and equipment modularity. The number of imipenem processing operations were reduced by almost 50 percent with the DCS automated and sequenced chemical reaction steps. Key measurements are continuously monitored by the computer which operates valves, pumps and motors on the equipment to provide control of the chemical process. The DCS reduces the potential for human error.

ENVIRONMENTAL RESULTS

Reduced VOC Management

With the new process Merck & Company eliminated not only purchase of significant quantities of methylene chloride, but also storage and disposal of hazardous waste. According to Merck, the new chemistry process has also resulted in a 75 percent reduction of biological oxygen demand (BOD) load to the on-site waste water treatment plant.

BOD is the amount of oxygen used by microorganisms in the breakdown process of pollutants in polluted water and waste water.

Although another upgrade does not meet the definition of source reduction, best available technology end-of-pipe controls were added with the installation of a fume incinerator. Toxic (SARA) air emissions were decreased more than 300,000 pounds a year in the antibiotic production area by this incinerator.

Bonuses from the new process were decreased risk of accidental spills of hazardous materials, increased employee protection, and ease of achieving compliance with more stringent environmental regulations. Additionally, Merck reduced its environmental liability by implementing source reduction into its manufacturing process.

COST SAVINGS

The improved process lowered production costs of imipenem. At an estimated savings of more than \$14 million per year, Merck & Company expects a short-term payback of their \$34 million investment for the new process.

SOURCE REDUCTION GOAL

The goal of source reduction is to reduce the quantity or toxicity of waste generated within the production process. To achieve this goal and protect the environment, Merck & Company, Inc. Cherokee Plant personnel developed an innovative manufacturing process which eliminated the use of methylene chloride, increased product yield and added manufacturing flexibility for future process changes.

These efforts were recognized when Merck won the Governor's Waste Minimization Award in 1990 and 1992.

This case study illustrates how industry can use innovation to protect the environment by preventing pollution before it is created, contain costs and boost productivity.

For more information about source reduction/pollution prevention approaches contact:

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