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Regional Activity Centre for Cleaner Production

MINISTERIO DE MEDIO AMBIENTE

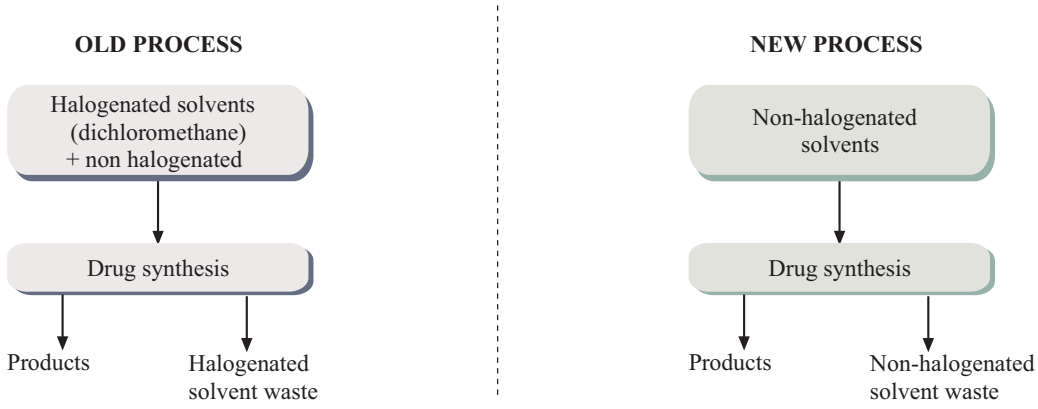
Generalitat de Catalunya
Government of Catalonia
Department of the Environment and Housing

No. 71 Pollution prevention case studies

Green chemistry. The substitution of halogenated solvents

Company	Unión Química Farmacéutica, SA (UQUIFA). Lliçà de Vall (Spain).
Industrial sector	Fine chemistry. The manufacture of basic pharmaceutical products.
Environmental considerations	The use of solvents, including halogenates such as dichloromethane, is still important in the chemical sector due to their physical and chemical properties (such as their boiling point, their low reactivity, low flammability, etc.) as a means for carrying out synthesis reactions and obtaining basic pharmaceutical products. These solvents can, however, have adverse effects on health and the environment due to emissions into the atmosphere and the waste they generate, since the environmental occupational exposure limit values (ELV) and air emission limits are very low. Moreover, the waste generated is classified as hazardous and difficult to manage, and the wastewater compounds contain also needs a specific treatment in order to reduce their impact.
Background	The company UQUIFA, SA used two of these halogenated solvents in the different processes in the manufacture of basic pharmaceutical products and, thus, solvent waste flows were generated among which there were some halogenates that were internally recycled. In 2000, the company started a research programme with the aim of reducing or eliminating the use of these two solvents, which would remove, or at least greatly reduce, the need for their final treatment. Action was directed in accordance with the following premises: • To eliminate or reduce the consumption of halogenated solvents. • To eliminate or reduce the generation of halogenated solvent and non-halogenated waste. • To reduce the emission of volatile organic compounds. • To reduce the pollutant load in wastewater.
Summary of the initiative	Action has consisted in the execution of a research and development project (R&D), following the principles of green chemistry, for the study of the manufacturing process of anti-inflammatory and antiulcerous drugs in which halogenated solvents are involved. The R&D project concentrated on research into non-halogenated solvents and the study of the different stages of synthesis of the active pharmaceutical ingredients which allow their manufacture, obtaining them with the same required standards of quality. The selected solvent has allowed the manufacture of one of the aforementioned drugs giving greater environmental benefits, less occupational danger, fewer manufacturing and purification stages, less work time, lower costs and greater profit. Mention should be made of the internal effort made by the R&D team, as well as the effort to validate the new synthesis system by changing the previously accepted synthesis procedures.

Diagrams



Balances

	Old process	New process
Balance of materials		
Consumption of halogenated solvent	27 l/kg drug	0 l/kg drug
Consumption of non-halogenated solven	43 l/kg drug	14 l/kg drug
Halogenated solvent wast	0 l/kg drug	0 l/kg drug
Non-halogenated solvent waste	57 l/kg drug	34 l/kg drug
Additional benefits		
Chemical yield	65%	75%
Maximum production capacity	3 t/year	7.5 t/year
Economic balance		
Cost of solvents	36.6 €/kg drug	4 €/kg drug
Liquid waste management	9.65 €/kg drug	11.5 €/kg drug
Savings and expenses		
Saving in waste management		–1.85 €/kg drug
Saving in raw materials		32.60 €/kg drug
Saving per kg of drug obtained		30.75 €/kg
Total annual saving (1,500 kg drug)		46.125 €/year
Investment in installations		Negligible
Payback period		Immediate

Conclusions

The execution of the project succeeded in eliminating the use of halogenated solvents and reducing the consumption of non-halogenated solvents by 67%. In addition, the company has managed to reduce the number of manufacturing stages and to reduce the cost of manufacturing the product by 35%, to increase the chemical yield of the synthesis reaction by 10%, which represents a global increase of production capacity by a factor of 2.5, as well as obtaining the intangible benefits of handling less hazardous substances.

In the light of the advantages obtained in this study, the company is carrying out new lines of R&D for the synthesis of other drugs it manufactures.

This action is within the framework of the Twelve Principles of Green Chemistry, a strategy that facilitates the company's compliance with its environmental improvement plans and environmental protection policy. This policy was started with the adhesion of the company to the ISO 14001 environmental management system.

NOTE: This case study seeks only to illustrate a pollution prevention example and should not be taken as a general recommendation.

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