

# Use of Life Cycle Assessment in Evaluating Solvent Recovery Alternatives in Pharmaceutical Manufacture

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## ABSTRACT

A retrofit case study is presented in this paper to compare various treatment options of pharmaceutical wastes generated in the manufacturing of celecoxib. Celecoxib is the active pharmaceutical ingredient in Celebrex<sup>®</sup>, an arthritis pain medicine produced by Pfizer, Inc.. Each proposed treatment method was evaluated based on its ability to efficiently separate and purify isopropyl alcohol (IPA) from an aqueous waste stream. A pervaporation-distillation hybrid process was identified technically feasible to treat the wastes and to recycle IPA back into the process. The recovery of the spent IPA avoids its incineration and also reduces the inventory of fresh IPA required to operate the celecoxib process. Life cycle inventories have been generated to quantify the environmental performance of each treatment option. A life cycle assessment was then conducted to determine the percent reduction of emissions for each alternative as compared to the base case. It was found that the treatment of all the waste by a combination of pervaporation-distillation and conventional methods can reduce emissions by 92%.

## OBJECTIVE

A case study was developed to measure the environmental performance of several green solvent recovery alternatives to minimize the wastes produced in the celecoxib process [1]. Each recovery alternative was evaluated to determine their ability to efficiently separate and recover IPA from an aqueous waste stream. This can prove to be a difficult separation as IPA forms an azeotrope with water at 12 wt. % which is not pressure sensitive. A life cycle inventory was generated for the recovery methods which were able to effectively separate and purify IPA from the process waste streams. A life cycle assessment was later conducted to measure the environmental performance of each recovery technique as compared to the base case, incineration.

## INTRODUCTION

Celebrex<sup>®</sup> is an arthritis pain medicine which is produced by Pfizer, Inc.. The process used to produce the active pharmaceutical ingredient, celecoxib, was found to be very mass efficient with an E-factor of only 9. Typical E-factors for pharmaceutical processes have been estimated to range from 25 to more than 100 kg waste / kg API [2]. The basic process used to manufacture celecoxib at the Pfizer plant in Barceloneta, Puerto Rico is shown in Fig.1 [2].

Since the production of celecoxib is relatively large, the recovery of the waste streams was thought to provide substantial economic and environmental benefits. In a cooperative effort between Pfizer, Inc. and Rowan

University, several green solvent recovery methods were proposed as alternatives to waste incineration. This project is supported by the U.S. Environmental Protection Agency and Pfizer Green Chemistry Program. The addition of a solvent recovery system would reduce the amount of fresh IPA required for the celecoxib process. This would lower the environmental footprint for the production of celecoxib by avoiding the manufacturing of fresh IPA and reducing the amount of waste to be incinerated.

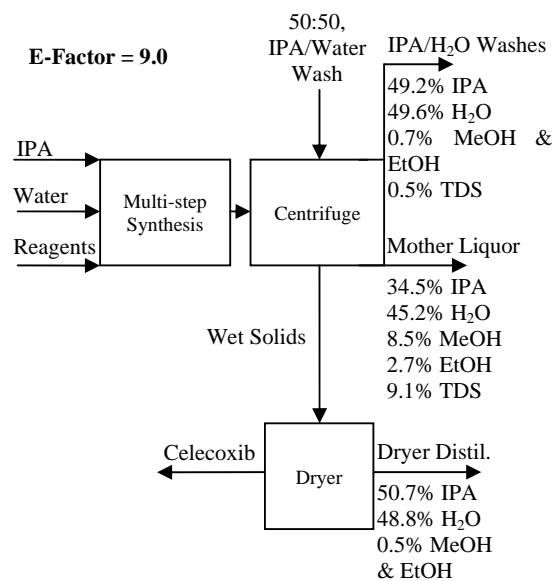


Fig. 1 General celecoxib process flow diagram [3]

## CASE STUDY

Initially, each recovery alternative was modeled to determine if it could be used to efficiently separate a combined IPA/water waste stream. A pressure-swing distillation recovery system was the first proposed alternative to waste incineration. When treating a combined waste stream from the celecoxib process, an IPA purity of only 75% was obtained using this method. If the dryer distillate and centrifuge washes are treated without the mother liquor, the IPA purity increases to 86%. Additional studies showed that the IPA/water azeotrope was not pressure sensitive. Therefore the pressure-swing distillation system was unable to further increase the IPA purity in the distillate to acceptable levels for it to be recycled back into the celecoxib process. [1,3]

An extractive distillation solvent recovery process was also modeled. Extractive distillation involves the addition of an entrainer to extract IPA from water at its azeotropic concentration. Diisopropyl ether, ethylene glycol, and dimethyl sulfoxide were identified as possible entrainers to recover IPA. The use of diisopropyl ether was able to produce a 99% pure IPA product but required that the column operate at 30 atm. Ethylene glycol and dimethyl sulfoxide produced 94% and 99% pure IPA product streams, respectively; however, multiple columns were needed. The extreme operating conditions that extractive distillation would require were found to surpass the equipment limitations at the Barceloneta site and were not considered for further review. [1,3]

Both molecular sieves (MS) and pervaporation (PV) systems were considered as possible solvent recovery alternatives. In both cases distillation is used to bring the waste stream composition to the azeotropic concentration and then followed by either MS or PV systems. When modeling a distillation-MS process, an IPA product stream of 99.5% purity was obtained. This was achieved through the use of a dual MS system to allow for regeneration cycles. The high IPA purity would allow it to be directly recycled back into the celecoxib process making a distillation-MS recovery system a feasible alternative to incineration. However, it was estimated that a \$1.5 MM capital investment would be required to purchase and install the MS units at the Barceloneta site as they are not currently available [1,3].

A common distillation-pervaporation hybrid process was also considered. It was determined that by sending the vapor distillates from a distillation column through a PV system, a 98.4% pure IPA product could be produced based on the capacity of the existing PV units at the Barceloneta site. The addition of a second distillation column following the PV unit further purified the IPA to 99.1%. These results were achieved by treating the dryer distillates and centrifuge washes, leaving the mother liquor to be incinerated or concentrated and sold as a generic

solvent. The main advantage to this solvent recovery system is that the equipment necessary to operate it is available at the production site. Therefore, the use of a hybrid distillation-PV system was also considered to be a feasible alternative to the incineration of the process wastes. [1,3]

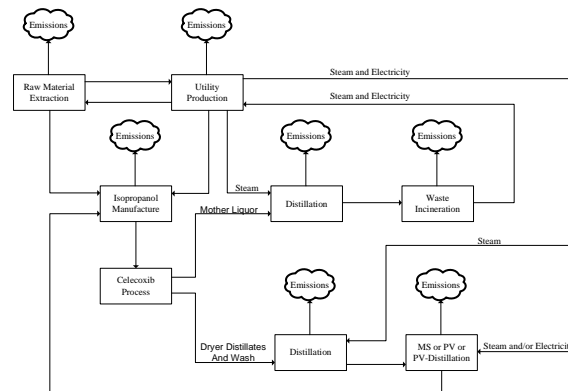
## ENVIRONMENTAL ANALYSIS

Since the distillation-MS, distillation-PV, and distillation-PV-distillation processes proved to be highly efficient at separating the IPA/water waste streams, a LCI/A was performed on each. SimaPro 7.1 (PRé Consultants) and Ecosolvent 1.0.1 were used to determine the LCI for each process step and various waste treatment methods, respectively. As IPA was the main solvent to be recovered, the LCI was generated on that, neglecting the manufacture or disposal of water and other feed stocks.

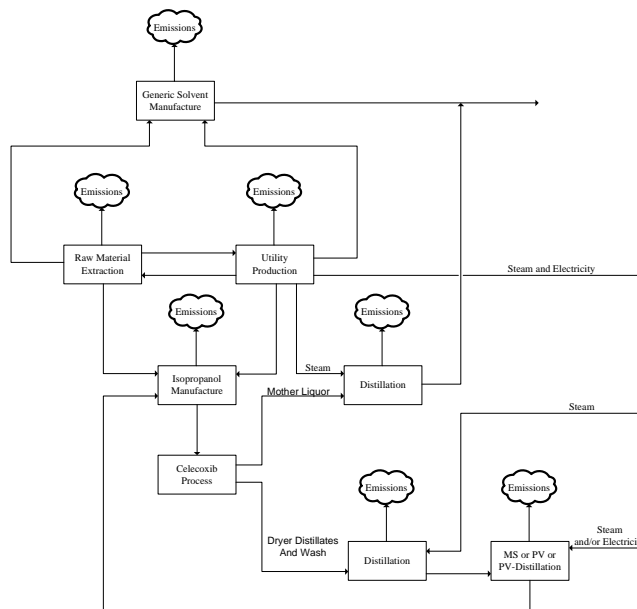
For each recovery method, only the dryer distillates and centrifuge washes were treated. The mother liquor was either incinerated or concentrated and sold as a generic solvent. If the mother liquor is sold as a generic solvent, then it is assumed that its manufacture is avoided when generating the LCI's. Depending on whether the mother liquor is incinerated or sold, the life cycle block flow diagram (BFD) differs slightly, as shown in Fig.2 and Fig.3, respectively.

Using SimaPro 7.1, the total emissions, energy and mass utilization for each solvent recovery alternative was quantified. Fig.4 displays the percent reduction in both total emissions and CO<sub>2</sub> emissions from the use of either membrane-based recovery system when compared to the base case. [1,3]

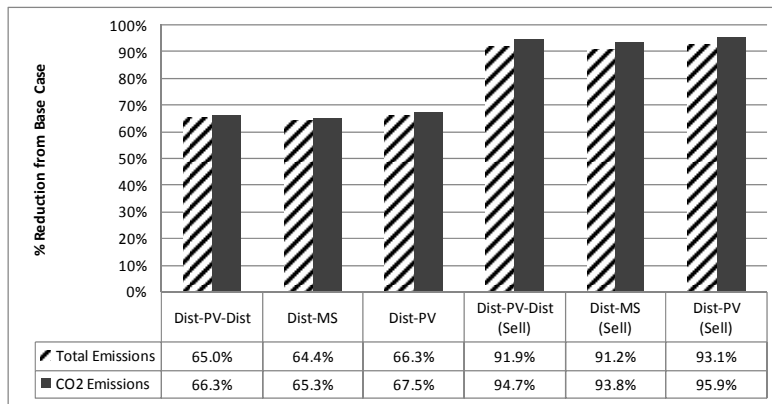
According to Fig.4, the total process emissions are lowered by 64 – 96% depending on the recovery method chosen. It was also determined that selling the mother liquor instead of incinerating it reduced the total emissions by an additional 75 – 80%. The large reduction



**Fig.2 Life Cycle Block Flow Diagram – Solvent Recovery Process with Mother Liquor Incinerated [1]**



**Fig.3 Life Cycle Block Flow Diagram – Solvent Recovery Process with Mother Liquor Sold**



**Fig.4 LCI Percent Reductions from the Base Case [1]**

in LCI emissions was primarily due to the recovery and reuse of spent IPA in the celecoxib process. This avoided the manufacture and disposal of fresh IPA which was no longer required and reduced the environmental footprint of the process. Also, since the mother liquor is considered a generic solvent, its sale avoids the manufacture of other generic solvents which further reduces the LCI emissions. [3]

From the life cycle assessment, the use of a distillation-PV system where the mother liquor is sold was found to have the largest reduction in LCI emissions. However, the distillation-PV-distillation configuration was able to produce IPA at a higher purity with a minimal increase in process emissions, and was therefore

recommended as the best recovery method. The addition of the distillation-PV-distillation recovery method to the current celecoxib process required an additional 10,700 kg steam/batch, 59 kWh electricity/batch, and 345,230 kg cooling water/batch but reduced the total LCI emissions by 12.6 MM kg per year (91.9% reduction from the base case) and the total CO<sub>2</sub> emissions by 11.6 MM kg per year (94.7% reduction from the base case). The cumulative energy demand (CED) was also reduced by 202,706 MJ-Eq for a 111% reduction when compared to the base case. The use of a distillation-PV-distillation solvent recovery system as an alternative to waste incineration therefore increased the overall greenness of the celecoxib process. [1,3]

### ECONOMIC ANALYSIS

The base case annual cost for the celecoxib process was \$5.28 MM. Approximately 45% of this cost resulted from purchasing fresh IPA and the remaining 55% was due to waste disposal costs. Through the implementation of a distillation-PV-distillation recovery process in place of incineration, the total annual operation costs reduced to \$1.46 MM for a 72% savings. The additional polishing column increased the total operating costs by 0.5% when compared to the single distillation-PV recovery system. However, the additional column was required to obtain the desired IPA purity. Since the majority of the spent IPA recovered in the celecoxib process is now available to be recycled, the costs associated with purchasing fresh IPA were reduced by 43%. [3] If the distillation-MS recovery system was used, the total annual savings would only increase by less than 1% but require a \$1.5 MM capital investment [3]. The equipment needed to operate the distillation-PV-distillation system is already available on-site therefore only new membranes would need to be purchased which are incorporated into the operating costs.

### CONCLUSION

A life cycle assessment was performed for several distillation-membrane based recovery methods to separate and purify IPA from a pharmaceutical waste stream. A distillation-PV-distillation recovery system was found to produce 99.1% pure IPA which can be recovered and directly recycled back into the celecoxib process. The addition of this recovery system to treat the dryer distillates and centrifuge washes reduced the total LCI emissions by 91.9% and the total CO<sub>2</sub> emissions by 94.7% assuming the mother liquor was sold as a generic solvent. The CED was also observed to decrease by 202,706 MJ-Eq (111% reduction from base case). Thus the proposed IPA recovery system led to a much greener process.

An economic analysis showed that a distillation-PV-distillation solvent recovery system reduced the annual celecoxib manufacturing costs by \$3.8 MM for a 72% savings when compared to the base case. This resulted from a 43% decrease in the cost to purchase fresh IPA and reduced waste disposal costs in the celecoxib process as none of the wastes are incinerated. Since the equipment necessary to operate the distillation-PV-distillation recovery system is available on-site, no capital investments would be required. Therefore the distillation-PV-distillation recovery method is recommended as the best engineering alternative to waste incineration and provides significant environmental and economic benefits.

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