

ABSTRACT

JIMÉNEZ-GONZÁLEZ, CONCEPCIÓN. Life Cycle Assessment in Pharmaceutical Applications. (Under the direction of Michael R. Overcash).

In the present work, life cycle information is developed to provide environmental input into process development and chemical selection within the pharmaceutical industry. The evaluation at various stages of the development process for Sertraline Hydrochloride, an effective chiral antidepressant, was conducted. This evaluation included the Life Cycle Inventory (LCI) and further Life Cycle Assessment (LCA) to compare several synthetic routes and production processes of this pharmaceutical product.

To complete the Sertraline analysis, a methodology to generate gate-to-gate life cycle information of chemical substances was developed based on a transparent methodology of chemical engineering process design (an ab initio approach). In the broader concept of an LCI, the information of each gate-to-gate module can be linked accordingly in a production chain, including the extraction of raw materials, transportation, disposal, reuse, etc. to provide a full cradle-to-gate evaluation.

Furthermore, the refinery, energy and treatment sub-modules were developed to assess the environmental burdens related to energy requirements and waste treatment.

Finally, the concept of a 'Clean/Green Technology Guide' was also proposed as an expert system that would provide the scientists with comparative environmental and safety performance information on available technologies for commonly performed unit operations in the pharmaceutical industry.

With the expected future application of computer-aid techniques for combinatorial synthesis, an increase of the number of parallel routes to be evaluated in the laboratory scale might be predicted. Life cycle information might also be added to this combinatorial synthesis approach for R&D. This input could be introduced in the earlier stages of process design in order to select cleaner materials or processes using a holistic perspective. This life cycle approach in pharmaceutical synthesis is intended to facilitate the evaluation, comparison, and selection of alternative synthesis routes, by incorporating the overall environmental impact of routes.

LIFE CYCLE ASSESSMENT IN PHARMACEUTICAL APPLICATIONS

By

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North Carolina State University
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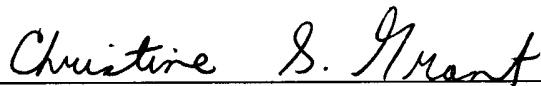
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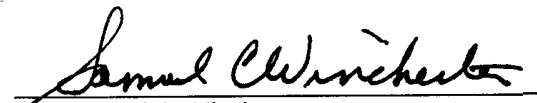
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To my family
to the one I love,
to my friends,
and to my God.

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- LCI of refinery products: review and comparison of commercially available databases. C. Jimenez-Gonzalez and M. Overcash. AIChE Annual Conference, Dallas TX, 1999, ASAP Article 10.1021/es991140f S0013-936X(99)01140-2. Web Release Date: October 11, 2000.
- Methodology of Developing Gate-to-Gate Life Cycle Analysis Information. C. Jimenez-Gonzalez, S. Kim and M. Overcash. International Journal of Life Cycle Assessment, 5 LCA (3) 153-159, 2000.
- Energy sub-modules applied in life cycle inventory of processes. C. Jimenez-Gonzalez and M. Overcash. J. of Clean Products and Processes, 1, 57-66; 2, 2000.
- Cárdenas, J.C., Husted, B., Jiménez-González, C. “Janssen Pharmaceutical: Case Study”, Spanish version by C. Jiménez-González. Sustainable Enterprise in Latin America. World Resources Institute, 99-116, 1997.
- Jiménez-González, C., I. Jarquín-Arellanes. “Manual de Prevención y Control de la Contaminación para la Industria”. Ed. FOMCEC, 1996.
- Jiménez-González, C., Cázares-Rivera, E., “Remoción de Cromo Hexavalente Utilizando Columnas Empacadas con Zeolitas Modificadas Químicamente”. XXV Research Exchange Meeting of ITESM System Proceedings, 285-294, Jan. 1995.
- Jiménez-González, C. “Biological Treatment: an Alternate Solution for Detergent Removal from Water”. Calidad Ambiental, Vol II, Num 1, 11-14 pp, Dec. 1994.

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1. LIFE CYCLE IN FINE CHEMICAL AND PHARMACEUTICAL PROCESSES: LITERATURE REVIEW

The use of life cycle assessment for process selection and development in pharmaceuticals is a novel area of research. This area has been encouraged in part by the need of improving process development in pharmaceuticals (Pisano, 1997; Thayer, 1998) and by the increasing use of techniques such as combinatorial chemistry (Studt, 1997; Studt, 1997a), which allows the discovery chemist to develop several chemical routes for the synthesis of a particular drug.

Although pharmaceutical companies recognize the importance of including the environmental aspects from the beginning of process design, and some pharmaceutical companies have looked at concepts like green chemistry and atom economy (Freitas dos Santos, 1999; Anastas and Warner, 1998), the application of life cycle for the process design of drugs has been limited.

Almost all the research in environmental issues for the pharmaceutical industry, including the ones based on pollution prevention, deal mainly with specific issues outside the life cycle perspective, like solvent recovery or the minimization of a specific waste (Ahmad and Barton, 1994; Forman et. al., 1994).

Nevertheless, it was found that Curzons et. al. have developed a methodology for evaluating synthetic organic reaction in pharmaceutical processes through the lens of sustainable practices, including the life cycle viewpoint. This methodology consists in the development of a series of heuristics and metrics. The heuristics permit derivation of data for each of the environmental metrics, since the metrics provide a measurement of environmental characteristics for the evaluation and comparison of synthetic reactions.

Finally, Koller et. al. (1998), and Heinzle et. al. (1998) have also proposed a general procedure for ecological and economic assessment during process design in fine chemical and pharmaceutical production that includes the life-cycle viewpoint. This procedure proposes three type of indices: mass, cost and environmental. All three indices are based on mass balances and can be calculated only with literature data, or including early process knowledge.

References

- Pisano, G. P., The Development Factory. Harvard Business School Press, Boston, MA, 1997.
- Thayer, A. M., Pharmaceuticals: Redesigning R&D. C&EN, February 23, 25-41, 1998
- Studt, T., Maturing Combinatorial Chemistry Creates New Technology Base, R&D Magazine, August, 32-34, 1997
- Studt, T., Combinatorial Chemistry Successes Create New Process Demands, R&D Magazine, November, 38-42, 1997a
- Freitas Dos Santos, L., Green Chemistry: Practical Considerations, Version 1., SmithKline Beecham, ERL, Harlow, UK, March 1999
- Anastas, P. T., Green Chemistry: Theory and Practice, Oxford, New York, oxford University Press, 1998
- Curzons, A. D.; Constable, D. J.; Mortimer, D. N. and Cunningham, V. L., So you think your process is green, how do you know? Using Principles of Sustainability to determine what is green, a Corporate Perspective of SmithKline Beecham. SmithKline Beecham report. Worthing, UK, 2000.

Ahmad, B. S., and Barton, P. I., Solvent Recovery: Targeting for Pollution Prevention in Pharmaceutical and Specialty Chemical Manufacturing. Pollution Prevention via Process and Product Modifications. AIChE Symposium Series. Volume 90, No. 303, 59-73, 1994

Forman, A. L.; Venkataramani, E. S.; McKenzie, P. F.; Magliette, R. J.; Quick, G. B.; McKinney, D.; Vaughn, W.; and Boyle, R. Environmentally Proactive Pharmaceutical Process Development. . Pollution Prevention via Process and Product Modifications. AIChE Symposium Series. Volume 90, No. 303, 36-45, 1994

Koller, G; Weirich, D.; Brogli, F.; Heinzle, E.; Hoffmann, V. H.; Verduyn, M. A. and Hungerbuhler, K. Ecological and Economic Objective Functions for Screening in Integrated Development of Fine Chemical Processes. 2. Stream Allocation and Case Studies. Ind. Eng. Chem. Res. 37, 3408-3413, 1998.

Heinzle, E.; Weirich, D.; Brogli, F.; Hoffmann, V. H.; Koller, G; Verduyn, M. A. and Hungerbuhler, K. Ecological and Economic Objective Functions for Screening in Integrated Development of Fine Chemical Processes. 1. Flexible and Expandable Framework Using Indices. Ind. Eng. Chem. Res. 37, 3395-3407, 1998.

2. LIFE CYCLE ASSESSMENT IN PHARMACEUTICAL APPLICATIONS.

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2. LIFE CYCLE ASSESSMENT IN PHARMACEUTICAL APPLICATIONS.

Abstract

Source reduction of wastes can be achieved in industry through changes in products, raw materials, process technologies or procedural practices. There is also a need to introduce environmental factors as an integral part of the decision-making process at the Research and Development (R&D) stages of design for drug manufacturing. This may improve efficiency, lower costs, and avoid environmental consequences in the production stage.

In the present work, life cycle information is developed to provide environmental input into process development and chemical selection within the pharmaceutical industry. The evaluation at various stages of the development process for Sertraline Hydrochloride, an effective chiral antidepressant, was conducted at Pfizer Pharmaceuticals.

With the expected future application of computer-aid techniques for combinatorial synthesis, an increase of the number of parallel routes to be evaluated in the laboratory scale might be predicted. Life cycle information might also be added to this combinatorial synthesis approach for R&D. This input is expected to be introduced in the earlier stages of process design in order to select cleaner materials or processes using a holistic perspective. This life cycle approach in pharmaceutical synthesis is intended to facilitate the evaluation, comparison, and selection of alternative synthesis routes, by incorporating the overall environmental impact of routes.

Keywords: Pharmaceutical industry, pharmaceutical process development, life cycle analysis, chiral synthesis.

2.1. Introduction: Process Development in the Pharmaceutical Industry

What organizations learn during the initial drug development phase clearly has an effect on production, as each process development project not only creates new production capabilities, but also adds to the company's know-how. Thus, a successful initial process development project can be visualized as improving the starting point on the process development curve (Pisano, 1997 and Overcash, 1988). Better initial conditions lead to shorter time to achieve a determined level of efficiency with a new drug

Process development for bulk pharmaceuticals is oriented to several key objectives. The first priority is to design a process that can reproducibly synthesize an extremely high quality final product. Another priority is to improve process efficiency in order to reduce the capital expense required to achieve the first priority (Forman, 1994). Each stage of compound development has different characteristics, and as far as the preclinical stage is concerned, the efforts are traditionally focused on synthesizing high quality material as fast as possible. This leads to priorities for the availability of raw materials, while the cost is only a secondary consideration. As many as a third of the route candidates fail at this stage, making it advisable to use the initial discovery route or a close modification.

As a consequence, development objectives are addressed only after extensive screening of unsuitable compounds and routes. For instance, of the 5,000 compounds evaluated in preclinical testing, only about 5 progress far enough to enter clinical trials and on average only 1 might actually gain approval by the US FDA for marketing (Pisano, 1997). Thus, given the average 12 years required to get approval for a new drug candidate, time allocated for process development must be optimized.

Synthetic routes represent the basic process technology concept for pharmaceuticals. In theory, problems with synthetic routes can be detected long before a process reaches the factory. Therefore, learning about route selection and how it affects development performance and quality offers broader conceptual lessons.

Changes to a synthetic route late in the development cycle can require a great deal of rework, as optimization conditions and new solutions are developed. The same concept applies to changes due to environmental factors. Including overall environmental criteria as inherent factors of process development and optimization is an essential part of anticipating and attempting to solve problems that might arise in actual production, as well as an intrinsic characteristic of environmentally conscious manufacturing (USEPA, 1991).

Furthermore, there is an emphasis on evaluating multiple routes at various phases of R & D. With the expected future application of computer-aid techniques for combinatorial synthesis, an increase in the number of parallel routes to be evaluated at the laboratory scale might be predicted (Studt, 1997). The life cycle inventory analysis approach thus represents an integrated part of the synthesis and route selection processes, allowing the prediction of potential environmental problems that might arise and offer global environmental criteria for route selection.

It has been formerly discussed that quality in the route selection process, expressed as early selection of the most attractive route, can influence overall process design quality, including cost and complexity reduction. Introducing environmental life cycle information at this stage would represent a powerful tool to face the potential global environmental problems before the manufacturing phase. This allows the company to rapidly cycle through multiple

routes early in the development process, while leaving sufficient time to optimize and refine the process.

As a case study, a life cycle was conducted at Pfizer Pharmaceuticals Inc. on a chiral product, Sertraline Hydrochloride, an effective antidepressant, which has been evaluated at various stages of the development process. The present work is focused in the results obtained in this case study.

2.2. Sertraline: A Case Study

In recent years, interest in the synthesis of pure enantiomers has received new impetus, largely as a result of the increasing awareness of the importance of optical purity in the context of biological activity. Although chirality is not a prerequisite for biological activity, when bioactive molecules contain a chiral center, differences are usually observed in the activities of the individual enantiomers. In reality, a chiral drug administered as a racemic mixture amounts to two separate drugs, each with different pharmacodynamics and pharmacokinetics (Sheldon, 1990).

The number of new pharmaceutical agents being developed and marketed as single stereoisomers continues unabated. Pure enantiomers now constitute over half of the drugs undergoing clinical evaluations (Quallich and Woodall, 1992). The commercial importance of this trend in pharmaceuticals is that the combined sales of the 'chiral top ten' in 1994 amounted to more than 16 billion dollars. Eight of these top ten drugs are marketed as single enantiomers (Table 2.1; Sheldon, 1996).

The evaluation of a development process for a drug is being conducted to analyze the effects in the environment that are produced by chemical, technological and process changes

throughout various R&D stages of design for drug manufacturing. The product chosen as a model was Sertraline Hydrochloride (Sertraline) of Pfizer Pharmaceuticals.

Sertraline, which has demonstrated excellent efficacy as an antidepressant (Quallich et al., 1990), is another member of the drug class marketed as pure enantiomers (Williams and Quallich, 1990; Welch et al., 1994; Sheldon, 1990). From all four possible isomers tested for activity (Figure 2.1a) the required high selectivity resided in the cis(+) isomer (cis-1S,4S), Sertraline.

At an industrial level, the main raw material in the synthesis of Sertraline is tetralone in the form of a racemate (Figure 2.1b). The process currently performed at Pfizer is the conversion from racemic tetralone to Sertraline. Racemic tetralone manufacture is outsourced, then racemic Sertraline is produced, followed by a resolution with D-mandelic acid to isolate the desired enantiomer. This synthesis is processed as batches in 4 steps.

For Sertraline there are three alternate processes reported (Welch, 1984; Pfizer, 1985; Pfizer 1999) which use different solvents in the first three steps of the conversion. These variations were labeled as THF, EtOH and Tol process after the solvent used in the first step in each alternative (Fig. 2.2). The process development of these alternatives has occurred at three stages: laboratory, pilot and full scale.

Figure 2.3 shows routes under study for making tetralone (Pfizer 1989; Pfizer, 1988; Pfizer 1991; Quallich and Woodall, 1992). Tetralone was originally prepared in five steps at 8% overall yield (Route 1), with the possibility to employ a different starting material (Route 2). Later, another preparation of tetralone was conceived, which employed Friedel-Crafts reactions to construct all of the carbon-carbon bonds, Route 3 (37% yield). This route was further consolidated with one less step via double Friedel-Crafts reaction with isolation of the

intermediate compound, Route 7 (49% yield) or without isolation, Route 8 (47% yield). Afterwards, the current commercial route for tetralone production was developed with reported laboratory yields as high as 79.6%, Route 4.

An asymmetric synthesis of tetralone was also sought to eliminate processing the undesired enantiomer of Sertraline through the resolution stage. The synthesis of the chiral tetralone was successfully performed at a laboratory level with yields of 12 and 55% (Routes 5 and 6), followed by a direct synthesis of chiral Sertraline at the laboratory level. Chiral tetralone has been produced at laboratory level with an optical purity of 84% ee for route 5 (Or a 92:8 ratio of enantiomers. Enantiomer excess is the difference between the percentages of the two enantiomers) and 88.6% ee for route 6.

In addition to the asymmetric synthesis, Simulated Moving Bed (SMB), a chromatographic-based separation method has been studied for isolating the desired enantiomer from racemic tetralone. Recoveries up to 75% in laboratory scale and 82% in pilot scale were reported (Guham, 1997). The refinement of this technology would be to re-racemize the unwanted enantiomer and recirculate it again into the separation process. There is laboratory scale evidence of the possibility of re-racemizing the unwanted enantiomer under strong basic conditions, but the racemization has not been fully developed or considered yet in any of the routes.

2.3. Goal, Scope and Functional Unit of the Life Cycle Assessment of Sertraline

Goal

To provide life cycle insight into process selection and development of complex drugs within the pharmaceutical industry was the main goal of this study. Therefore, it aims to

facilitate the evaluation, comparison and selection of alternative Sertraline synthesis routes, incorporating the overall environmental impact of the routes.

The findings of this research are expected to be utilized in early stages of Pfizer process design in order to select cleaner materials or processes using a life cycle perspective.

Besides the general goal, there are some specific interest areas to which the findings of this LCA are intended to provide some understanding. Those interest areas are:

- 1) Influence of number of steps (complexity) and at what step to introduce chirality on total chemical losses.
- 2) Influence of similar chemical structure in starting raw materials with the same final product on the overall energy use and chemical losses.
- 3) Influence of solvent recovery and non-isolation techniques on environmental factors.
- 4) External (supply chain) versus Internal (pharmaceutical facility) environmental impacts
- 5) Relationship between yield (overall efficiency) and total waste.
- 6) General understanding of inclusion of environmental factors in early stages of route selection and the relationships to process performance.
- 7) Influence of scale of manufacturing.
- 8) Unit process life cycle description.

Scope

This study is a comparative assessment of different synthetic routes (production processes) for manufacturing of Sertraline, using LCA as a tool in a cradle-to-gate approach.

The analysis of packaging and distribution of the drug once manufactured are not considered (Figure 2.4).

The research examined both the Sertraline processes and Tetralone Routes. In total, four variations of the process for Sertraline, and eight development routes for tetralone have been identified. The Tetralone routes include two that involved the synthesis of chiral tetralone.

Such a system involves different scale production, different chemicals used, and different process principles (e.g. separation-synthesis, racemic synthesis-separation, and asymmetric synthesis).

For the assessment phase, neither land use, biotic resource depletion, terrestrial ecotoxicity, nor landfill volume are being considered in the analysis. Landfill volume is not included since at the time of the analysis no assessment factors were available for this category, besides most of the data obtained express the solid waste in mass units instead of volume. Terrestrial ecotoxicity is not included because the data for landfilling is expressed as total metals to soil, instead of the individual metals which have assessment factors for this category.

Functional unit

The functional unit has to be defined in order to make a reliable comparison of different processes. For this research, the functional unit was defined as 1000 kg of Sertraline produced.

This functional unit was chosen since the exact amount of Sertraline dosages that would fulfill the function of the drug will vary depending on the patient and the severity of the

ailment. Besides, since this research has been conducted using the cradle-to-gate approach, a mass-based functional unit makes the comparison between routes and processes easier.

2.4. Methodology

The general methodology for this life cycle study is represented in Figure 2.5. A description of the methodology is given in the following paragraphs, and more detail explanations of methods are described in subsequent chapters.

2.4.1. Identification of the Routes under Study.

The research was divided into Sertraline processes and Tetralone Routes. In total, four variations of the process for Sertraline and eight development routes for tetralone have been identified. The Tetralone routes include two that involved the synthesis of chiral tetralone. The routes involve different scale production, different chemicals used, and different process principles (e.g. separation-synthesis, racemic synthesis-separation, and asymmetric synthesis). Figure 2.6 summarizes the routes to be analyzed.

2.4.2. Definition of the system boundaries

In this study, a cradle-to-gate approach of life cycle assessment was used. In a cradle-to-gate approach the boundaries of the life cycle assessment are set to analyze the activity from the extraction of raw materials until the end of the manufacturing process. The packaging, distribution, use and disposal of the drug are assumed to not vary among the production processes, and therefore, the analysis and selection of synthetic routes and production process is independent of the downstream system (post-manufacturing). As a

result, this research does not include the life cycle issues related to packaging, distribution, use and disposal of Sertraline.

The 'cradle' part of the boundaries was set back into raw materials extracted from earth (petroleum, metals) or produced in agriculture (corn). All the production data included in this research consider post-treatment emissions, although the emissions from treatment are presented separately in order to compare pre versus post treatment data.

2.4.3. Data Collection for Sertraline processes and Tetralone routes.

The information for the tetralone routes was mainly obtained in literature articles that described the processes for tetralone synthesis.

For the Sertraline processes the information at a laboratory level was gathered from literature articles and laboratory notebooks. At pilot scale it was obtained from pilot plant archives, and at full scale from production records inside of the company.

The data found included the complete description of the process with the typical quantities of each chemical incorporated to the route, as well as the description of the unit operations and temperatures. For the tetralone routes, block flow diagrams were developed to better illustrate the lengthy routes. The data found in those articles were thoroughly reviewed by scientists in Pfizer. In general, much of the actual data had been previously published.

2.4.4. Estimation of chemical losses inside the pharmaceutical manufacturing boundary.

To estimate the chemical losses generated in the different tetralone routes and sertraline processes, mass balances were performed using the information from the process description. All the information about amounts of materials entering the system was provided in the literature or directly from records from the company at the different scales of production. The output of the mass balances was sent to the company for review.

2.4.5. Estimation of Energy Requirements for tetralone and sertraline processes.

For calculating the energy requirements for tetralone routes and sertraline processes, typical thermodynamic equations were used. The heat capacities and unknown heat of reactions were estimated using the group contribution theory. The procedure for estimating the energy requirements for tetralone routes and sertraline processes is described in detail in Chapter 7.

2.4.6. Energy-Related Emissions: Development of Energy sub-modules.

To include the energy-related emissions in this life cycle assessment, energy sub-modules were developed for steam production, cooling using refrigeration, and cooling using a cooling tower. A detailed explanation of the methodology for the energy sub-modules and the life cycle information of the sub-modules, including electricity production, is presented in chapter 4.

For the emissions related to the primary energy carriers (e.g. natural gas, fuel oil, etc.), the averages of the reported data in several commercial databases were used. The detailed

comparison of several commercial databases is presented in chapter 5, and a summary of the data employed for the energy-related emissions is presented in Table 2.2.

2.4.7. Development of Waste Treatment sub-modules.

To obtain the input of the emissions generated in treatment and disposal, waste treatment sub-modules were generated. Models for the waste water treatment plant, solvent incinerator and solvent recovery were developed. Models for landfill disposal were taken from the literature. The detailed description of the treatment modules is given in chapter 6.

2.4.8. Development of a Life Cycle Inventory (LCI) Database.

A substance tree was generated for the Sertraline processes and tetralone routes. A substance tree is a graphic tool that shows all the precursor raw materials required in the production of a specific product or compound, extended back to the materials extracted from nature. The substance tree documents all the materials involved in each one of the synthetic routes and production processes. Figure 2.7 illustrates the substance tree of route 3.

After the substance was generated and all the cradle-to-gate raw materials identified, all the information regarding the raw material production for tetralone and sertraline was estimated using a pre-treatment gate-to-gate approach, according to the methodology presented in chapter 3. This approach was chosen because initially insufficient information was found for the rather large number of substances involved in the system.

2.4.9. Modeling

To expand the boundaries of the analysis beyond the pharmaceutical manufacturing plant limits, the life cycle study was performed in a modular manner, incorporating the energy sub-modules, the waste treatment modules and the gate-to-gate information for the raw materials to the in-plant processes.

After comparing several life-cycle software packages (e.g. PEMS, SIMAPRO, ECOPRO, LCAIT), ECOPRO 1.5 was the software selected for the modeling, mainly for the capability of this software to work in a modular manner, and to export the results for further analysis and interpretation. The mechanics of the modeling are described in Figure 2.8.

2.4.9.1. Transportation-related Emissions.

Since the gate-to-gate estimation approach was used no specific suppliers were considered. To include the transportation of raw materials to the production centers, the average distances for transportation of goods and contributions related to the mode of transportation were used as reported by the US Department of Commerce, Economics and Statistics Administration, US Census Bureau (US Department of Commerce, 1999).

For the present research, the transportation of basic chemicals, metallic ores and concentrates, non-metallic minerals, cereals and grains, coal and fuels were included. The transportation modes included in the analysis were truck, rail and boat.

The transportation-related emissions factors were taken directly from the database in ECOPRO 1.5 for diesel trains, 40 ton trucks (50% capacity) and river-size diesel boat (70% capacity). The values for distances and mode of transportation distribution are shown in Table 2.3.

2.4.9.2. Allocation factor

When a specific process produces more than one product of commercial value, the waste treatment option, raw material requirements, energy consumption, and emissions need to be allotted or allocated. In this research the allocation factor used in the modeling was product mass ratio. That is, if a given process produces 25 kg of product A and 75 kg of product B, then the emissions, raw materials, energy, etc., will be distributed in a proportion of 25% for product A and 75% for product B.

2.4.9.3. Life Cycle Inventory

The inventories (chemical emissions and energy requirements) for the tetralone routes and Sertraline processes were generated using the modular system described above. The material requirements for the tetralone routes and Sertraline processes were determined by linking the gate-to-gate life cycle information over the substance tree back to the raw material database. The energy requirements were linked to the energy sub-modules, the waste generated were linked to the treatment modules, and the transportation modules were added to each substance system. A final inventory was developed, containing the information on material consumption, energy requirements, and chemical emissions obtained.

2.4.9.4. Solvent Recovery Scenarios

For the life cycle inventory and assessment modeling, two scenarios were considered: with and without solvent recovery in the pharmaceutical processes and routes.

The average solvent recovery percentage used was 75%. The details of the solvent recovery module are described in detail in Chapter 6.

For the solvent recovery module, the avoided emissions from solvent recovery are considered. To account for these avoided emissions, the corresponding amounts of solvent that are 'saved' through recovering the solvent are entered in the modeling as credits ('negative requirements'). If the recovery of solvent brings large benefits regarding solvent savings, it might translate into negative assessment values if they are larger than the energy and/or solvent required for a process.

2.4.9.5. Life Cycle Impact Assessment Models

To analyze the results of the inventories, a life cycle assessment was made with three different methodologies:

- a) BUWAL 132. Critical volumes method (BUWAL, 1991). Includes factors for air, water, energy, soil, and landfill. Since in this research land use and landfill volume are not being considered, these factors were not included in the assessment with BUWAL 132
- b) CML (Centrum voor Milieukunde in Leiden, NL, Heijungs, 1992). Problem oriented method based on environmental effects. Includes Greenhouse effect, Nutrification, ozone layer depletion, photochemical oxidation, eco-toxicity, human toxicity and abiotic depletion. As stated in the methodology, terrestrial eco-toxicity is not included in this research.
- c) Eco-indicator 95 (Goedkoop, 1995)
 - Characterization. Problem oriented method based on environmental effects. Includes global warming, ozone depletion, acidification, nutrification, heavy metals, carcinogenic, winter smog and summer smog.

- Eco-Indicator 95, Valuation. Transforms the output of the characterization step into a single-indicator output (Ecopoints)

All the factors used for these methodologies were taken directly from the database of ECOPRO.

2.5. Results and Discussion

2.5.1. Tetralone Routes

2.5.1.1. Total Emissions inside of the pharmaceutical manufacturing plant boundaries

In order to study the relationship between material wastes and system complexity, the generation of material wastes in Sertraline synthesis using different tetralone routes were compared. Basically, the information available of the tetralone routes was found at laboratory level. Routes 7 and 4 (Fig 2.3) have been used for commercial purposes, route 4 being the one used currently, because it proved more economical in the past.

Figure 2.9 shows the material wastes directly generated at the laboratory level in Sertraline synthesis via different Tetralone routes. At the laboratory level there is no recycling of materials whatsoever. For the racemic Tetralone the total waste of a route follows a fairly good correlation with the number of steps or isolations of the same route. Route 8 is an exception, which is explainable by the fact that in this route a much higher amount of solvent is used in the non-isolation step equivalent to two steps of route 7.

Meanwhile, the chiral Tetralone routes had different behavior in comparison with the non-chiral routes. Routes 5 and 6 have both a total of 9 isolation steps, but different amount

of waste produced. This is explained by the fact that Route 6 has a better overall chemical yield.

Route 4 is the one that produces the least amount of wastes, according with the results from laboratory level. This same route was demonstrated to be also the most economical route, with the highest yield and with the lowest level of complexity, carrying out the synthesis in only one isolation step to tetralone. This route also has a starting raw material that is more similar in chemical structure to the final product.

2.5.1.2. Life Cycle Inventory: Mass Intensity and Total Carbon Dioxide production

The life cycle inventory was performed as described in the methodology section. Once the raw materials, chemical losses and energy requirements were calculated for each of the tetralone routes, the gate-to-gate information of all the substances of the chemical tree was incorporated, as well as the energy, treatment, and transportation sub-modules.

A comparison of the mass intensity and total carbon dioxide emissions is shown in Figures 2.10 and 2.11. Mass intensity is defined as the total amount of the raw materials taken directly from nature per mass unit of product (including treatment and transportation). As an example, for aluminum chloride production, bauxite, chlorine and air are required; for chlorine production water and sodium chloride are needed and, finally, sodium chloride is extracted from salt rock. The mass intensity for aluminum chloride will be then the summation of the amounts of bauxite, air, water and salt rock needed per unit of aluminum chloride.

In this analysis, routes 5 and 6 (chiral routes) are covered in the sertraline analysis because they are designed for the production of chiral tetralone. Again, the route with lowest

mass intensity and lowest carbon dioxide emissions is route 4. This route, as it has been shown earlier, is simpler, has fewer steps and has raw materials that can be synthesized in mass- and energy-efficient processes (refinery products).

It also can be seen that recovering the solvent has an effect in diminishing the mass intensity and carbon dioxide emissions proportional to the percentage of solvent in the total inputs (Figure 2.12). It is interesting to note that in a life cycle framework the solvent recovery has a big impact on the total mass intensity, but even bigger to the total carbon dioxide emissions. Furthermore, for most of the routes, the effect in mass intensity and carbon dioxide emissions is larger in percentage than the proportion of solvent in the inputs. The exception is the mass intensity for route 4, but this can be explained by the lower proportion of solvents (Table 2.4), and a smaller substance tree.

2.3.1.3. Life Cycle Impact Assessment.

A life cycle assessment was performed using the methods shown in the methodology section. Figure 2.13, 2.14, 2.15, and 2.16 show the results of the life cycle assessment for the tetralone routes using the methods of BUWAL 132 (1996), CML, Ecoindicator 95 (characterization only) and Ecoindicator 95 (valuation).

In all the assessment methods, route 4 is the one that fares the best in all the categories, followed by routes 7 and 8. It is interesting to observe that the routes fared better in proportion of their development time, that is, the routes that developed later fared better in the assessment. Also, when the scenario with solvent recovery is considered, the impact indicators have values between two and three times smaller than when the solvent recovery scenario is not considered.

Regarding the contribution of processes, thermal energy, electricity generation, disposal (treatment) and transport to the different impact categories, the distribution for the ecoindicator 95 (characterization) are shown in Table 2.5. As it can be appreciated in Table 2.5, some routes present negative values for some contributions; this is caused by relatively large amounts of potential energy recovery of these routes (heat to be recovered from hot streams by heat integration, see chapter 3) compared with the heating requirements of the routes, as explained in the methodology section.

As expected, most of the global warming potential contributions come from disposal and energy-related emissions (electricity and thermal). In routes 7 and 8, the contribution of energy-related emissions to the global warming potential is less due mainly to the large amount of potential energy to be recovered from energy integration. As a matter of fact, most contributions to the assessment impacts categories are dominated by the energy-related emissions.

The process-generated emissions are important contributors in the categories of acidification (average 27%), nitrification (average 55%), carcinogens (average 30%), winter smog formation (average 39%) and summer smog formation (average 59%, not including values over 100%). Transport-related emissions have important contributions only in the ozone depletion potential (average 38%).

The importance of these contributions is that these allow to target process design and optimization regarding a specific environmental effect. By example, if the priority of the design is to improve the process conditions regarding global warming, then effort should be directed to optimize energy. These percentages also show the importance of the

environmental credits given to a process by recovering the solvent, either internally or externally.

2.5.2. Sertraline Processes

2.5.2.1. Total Emissions inside of the pharmaceutical manufacturing plant boundaries

In order to study the relationship between material wastes and system complexity, the generation of material wastes in Sertraline processes was assessed. The TOL, THF and EtOH processes (Figs. 2.2 and 2.6), have been used for commercial purposes in that order, and the information was obtained for laboratory, pilot and full scale.

Figure 2.17 shows the material wastes directly generated for all the scales in the Sertraline synthesis from racemic Tetralone. At the full-scale level, although the THF process presents slightly larger amount of waste produced, there is not significant difference between the THF and EtOH processes regarding in-plant material waste production. Nevertheless, for the TOL process, the chemical losses are two-fold in comparison to the THF and EtOH processes, mainly due to the larger use of solvents in said TOL process (Table 2.4)

For the laboratory and pilot scale the trend is the same, with the exception of the TOL process at laboratory scale, which presents a remarkably larger amount of chemical losses per unit of product (6.6 times higher than THF process at laboratory scale). This can be explained by a larger number of solvents used in the laboratory synthesis, and by the fact that the toluene processes was the first one to be developed.

2.5.2.2. Life Cycle Inventory: Mass Intensity and Total Carbon Dioxide production

A life cycle inventory was carried out for the sertraline processes, comparing the chiral and non-chiral processes, that is, including the TOL, THF and EtOH processes and the routes 5 and 6. Even though information was available in all the scales for the TOL, THF and EtOH processes, the comparison was made only at full scale, scaling-up the laboratory information for the chiral routes (routes 5 and 6). For the production of racemic tetralone prior to the sertraline processes, route 4 was employed. The life cycle inventory was performed as described in the methodology section.

Once the raw materials, chemical losses and energy requirements were calculated for each of the sertraline processes, the gate-to-gate information of all the substances of the chemical tree was incorporated, as well as the energy, treatment, and transportation sub-modules.

A comparison of the mass intensity and total carbon dioxide emissions is shown in Figures 2.18 and 2.19. Mass intensity is defined as the total amount of primary raw materials per mass unit of product.

It can be seen that the process with the least mass intensity and carbon dioxide emissions is the EtOH process. This is a non-isolation process that uses the same solvent throughout the first 3 steps of the synthesis, and avoids the formation of a waste cake in the first step. However, it is important to note that for carbon dioxide production the difference between the EtOH and the THF is twice as big as for mass intensity (34% vs 12% difference between the processes), which indicates that with regard to emissions, the EtOH has a better environmental performance in comparison to the other processes analyzed.

It also can be seen that recovering the solvent has an effect in diminishing the mass intensity and carbon dioxide emissions proportional to the percentage of solvent in the total inputs (Figure 2.20). As well as with the tetralone routes, in a life cycle framework the solvent recovery has a big impact on the total mass intensity, but even bigger to the total carbon dioxide emissions. But contrary to what occurred with the tetralone routes, the effect in mass intensity and carbon dioxide emissions is smaller in percentage than the proportion of solvent in the inputs, for most of the processes. This last point is expected, and explained by the fact that the chemical tree of the processes is larger by the Sertraline synthesis, and therefore, the effect of solvent is relatively smaller than for the tetralone routes, although nevertheless important in the contribution to mass intensity and carbon dioxide emissions.

The exception of the above is the chiral route 6, in which the carbon dioxide emissions saved with solvent recovery are in percentage larger than the solvent input, which can mainly be explained by the large absolute amount of solvent input employed in this synthesis (Table 2.4).

2.5.2.3. Life Cycle Impact Assessment.

A life cycle assessment was performed using the methods shown in the methodology section. Figures 2.21, 2.22, 2.23, and 2.24 show the results of the life cycle assessment for the tetralone routes using the methods of BUWAL 132 (1996), CML, Ecoindicator 95 (characterization only) and Ecoindicator 95 (valuation).

In all the assessment methods, the EtOH process is also the one that fares the best in all the categories, followed by the TOL and THF processes. As well as with the tetralone routes, when the scenario with solvent recovery is considered for the racemic tetralone

processes (TOL, THF and EtOH), the impact indicators present values between two and three times smaller than when the solvent recovery scenario is not considered. For the chiral routes, the impact is not as large. The non-chiral processes represent a better option almost in all the impact categories compared with the two chiral routes.

Regarding the contribution of processes, thermal energy, electricity generation, disposal (treatment) and transport to the different impact categories, the distribution for the Ecoindicator 95 (characterization) are shown in Table 2.6.

As expected, most of the global warming potential contributions come from energy-related emissions (electricity and thermal), and disposal in a lower percentage (around 8% average). As a matter of fact, most contributions to the assessment impacts categories are dominated by the energy-related emissions in a very uniform manner.

The process-generated emissions are important contributors in the categories of acidification (11% average), eutrophication (average 33%), carcinogens (average 46%), winter smog formation (10% average) and summer smog formation (average 50%). Transport-related emissions do not represent in general a significant contribution to the impacts (less than 2% in average in all the cases).

2.6 Data Quality

Data quality is the specific characteristic of data as expressed through information about the data. The data quality indicators used were (Weidema and Wesnaes, 1996): reliability (R), completeness (C), geographical correlation (G), temporal correlation (time), and technological correlation (Tech). A 1 to 5 scale for each indicator is used, 1 being the most accurate data and 5 the least accurate. Table 2.7 shows the criteria parameters used in

this research to determine the data quality indicators, and Table 2.8 shows a summary of the data quality indicators for the present research.

2.7.- Conclusions and Recommendations.

When designing a process, a myriad of interrelated factors must be taken into consideration. Environmental aspects are also a complex set of interrelated variables. The inclusion of environmental issues could be facilitated by producing a better understanding of the relations among different factors that contribute to global wastes. Also, it could help to determine a realistic influence of factors such as yield and starting materials on emissions.

A better understanding of the relationship between the stages of scale-up (laboratory, pilot and full scale) can help to anticipate, if not predict, the possible burdens and environmental problems when selecting or designing a route. Chemical usage and wastes follows a fairly linear scale-up, while the main advantage of experimenting at pilot scale before producing commercially seems to be energy optimization.

According to the work done with Sertraline, it seems that there is a strong relationship between the complexity of the system and the environmental aspects in the early stages of synthesis in a pharmaceutical product. The more steps, intermediate isolation, and solvents that are involved in a single route in the synthesis, the more wastes seems to be generated. If this factor is taking into consideration when comparing different routes in the beginning of the selection process (e.g. lab scale) some of the environmental differences can be addressed from the start.

The results also show that two factors seem to have great influence over environmental performance: solvent utilization and energy usage.

Solvent utilization is an important part of the synthesis of pharmaceuticals and plays a very important role in the overall waste generation. Non-isolation of intermediates and the use of the same solvent throughout steps reduce the amount of waste streams, as well as the energy requirements for separating the solvent. Recycling solvents and favoring the use of a single solvent that implies less production waste produce a large effect in the overall life cycle of the system.

Energy usage is a factor that historically has been overlooked in the pharmaceutical industry, but according to the life-cycle assessment, it plays an important role in the environmental performance (especially in the categories of global warming, acidification, ozone layer depletion), and the results justify investing resources in improving the energy usage. These factors are important to take into consideration when designing a new process, when possible.

On the other hand, transportation does not play an important role in the system analyzed. This result might justify, on a preliminary basis, employing non-site-specific methodologies, like the one utilized in this research, to model pharmaceutical systems.

In a future perspective, this research project is intended to coordinate with route selection and design in the pharmaceutical industry. The rapid development of computer-aided synthesis, combined with the stricter environmental regulations and above all, the need for environmentally conscious manufacturing are the driving forces for future utilization of life cycle assessment.

Since solvent usage is a very important factor in pharmaceutical synthesis, analyzing different recycling percentages and methods is another research target to be taken into consideration in the future. The role that the experiments at pilot scale play in optimizing

energy, as well as the role and importance of different energy-related unit operations are other subjects to be evaluated in order to understand and help to improve the design process.

Finally, economics is always a driving force for processes of any kind. Logic seems to point out that the most economical alternative will be the one with less wastes. Future research including economical comparison between routes could provide a way to examine this hypothesis.

The relevance of this kind of research stands by the fact that the progress in cleaner process design is directly proportional to the understanding we have of the system and of the many factor that are interrelated to it.

2.8.- Acknowledgments

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2.9.- References.

BUWAL, Ökobilanzen von Packstoffen; Schriftenreihe Umwelt Nr.132; Bundesamt für Umwelt, Wald und Landschaft (BUWAL); Bern 1991

Forman et al, Environmentally Proactive Pharmaceutical Process Development. Pollution prevention Via Process Modifications., 1994. Halwagi and Petrides, Ed.

Goedkoop M.J.; Demmers M.; Collignon M.X.; The Eco-indicator 95, Manual for designers; NOH report 9524; PRé consultants; Amersfoort (NL); july 1995

Guham, S., Guinn, M., and Charton, R. N., Separation of the Sertraline-Tetralone Enantiomers by Simulated Moving Bed. Submitted for publication. 1997

Heijungs R.; Environmental life cycle assessment of products, Guide and Backgrounds, NOH report 9266 and 9267, commissioned by the National Reuse of Waste Research Programme (NOH), in collaboration with CML, TNO and B&G. Leiden; 1992;

Overcash, M. Hazardous Waste Reduction- Measurement of Progress. Haz. Wastes and Haz. Materials. Vol. 5, No. 3, 1988

Pfizer Inc., US Patent 4,536,518. Aug. 20, (1985).

Pfizer Inc., US Patent 4,777,288. Oct. 11, 1988

Pfizer Inc., US Patent 4,839,104. Jun. 13, 1989

Delalande SA, US Patent, 5,019,655. May 28, 1991

Pfizer Inc., World Patent WO 9936394A1. Jul. 22, (1999).

Pisano, G. P., The Development Factory. Lessons from Pharmaceuticals and Biotechnology. Harvard Business School Press, 1997

Process Monograph Description. Pfizer, Internal Document, 1997

Quallich, G. J. and Woodall, T. M. Synthesis of 4(S)-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone by SN2 Cuprate Displacement of an Activated Chiral Benzylic Alcohol. Tetrahedron, Vol. 48, No. 47, pp. 10239-10248, 1992

Quallich, G. J., and Woodall, T.M., Synthesis of 4(S)-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone by SN2 Cuprate Displacement of an Activated Chiral Benzylic Alcohol. Tetrahedron, Vol. 48, No. 47, pp. 10239-10248, 1992

Sheldon, R. A. The Industrial Synthesis of Pure Enantiomers. Drug Information Journal. Vol. 24, pp. 129-139, 1990

- Sheldon, R. A. The Industrial Synthesis of Pure Enantiomers. Drug Information Journal. Vol. 24, pp. 129-139, 1990
- Studt, T. Maturing Combinatorial Chemistry. R & D Magazine, August, 1997
- U.S. Environmental Protection Agency. Guides to Pollution Prevention in the Pharmaceutical Industry. October, 1991
- US Department of Commerce, Economics and Statistics Administration, US Census Bureau. US Department of Transportation. Bureau of Transportation Statistics. 1997 Economic Census. Transportation. 1997 Commodity Flow Survey (Issued in December 1999). EC97TFC-US
- Weidema, B. P. and Wesnaes, M. S. Data quality management for life cycle inventories-- an example of using data quality indicators. Journal of Cleaner Production, 4 (3-4) 1996
- Welch, W. M., et. al. Nontricyclic Antidepressant Agents Derived from cis- and trans-1-Amino-4-aryltetralins. Journal of Med. Chem., Vol. 27, 1508-1515. 1984
- Williams, M. T, and Quallich, G. J., Sertraline: Development of a Chiral Inhibitor of Serotonin Uptake. Chemistry and Industry, 21 May 1990

Table 2.1. The Chiral Top Ten (1994)

Drug	Therapeutic class	Sales^a (\$ million /year)
Amoxicillin	Antibiotic	2,200
Enalaprin	Antihypertensive	2,100
Ampicillin	Antibiotic	2,000
Captopril	Antihypertensive	1,800
Pravastatin	Antihypercholesteraeic	1,700
Diltiazem	Antihypertensive	1,500
Ibuprofen ^b	Antiinflammatory	1,500
Lovastatin	Antihypercholesteraeic	1,300
Naproxen	Antiinflammatory	1,200
Fluoxetine ^b	Antidepressant	1,200

^a Bulk formulated drug

^b Marketed as racemate

Source: Chirotechnology: Designing Economic Chiral Synthesis. Sheldon, R.A., J. Chem. Tech. Biotechnol., 1996, 67, 1-14.

Table 2.3 Average Transportation Distances and Mode Contribution

Mode	Reported Value						Value to use in modeling					
	Basic Chemicals	Metallic ores and concentrates	Non-metallic minerals	Cereal grains	Coal	Fuel Oils	Basic Chemicals	Metallic ores and concentrates	Non-metallic minerals	Cereal grains	Coal	Fuel Oils
Average distance/shipment (mi)	332	303	174	125	81	28	330	300	175	125	80	30
Average distance/shipment (km)	531	485	278	200	130	45	530	480	280	200	128	48
Contribution of modes (% of ton-mi)												
<i>Truck</i>	26.4	4.6	31.2	9	1.7	50.7	30	5	33	10	2	51
<i>Rail</i>	50.8	76.8	39.3	58	81.2	1.4	50	75	44	60	93	2
<i>Water</i>	19.3	18.6	19.7	29	4.2	11.2	20	20	23	30	5	12
<i>Air</i>	-	-	-	-	-	-	-	-	-	-	-	-
<i>Pipeline</i>	-	-	-	-	-	34.2	-	-	-	-	-	35
<i>Multiple modes</i>	2.2	-	9.8	1.5	12	1.2	-	-	-	-	-	-
<i>Other unknown</i>	1.3	-	-	2.5	0.9	1.3	-	-	-	-	-	-
Total	100	100	100	100	100	100	100	100	100	100	100	100

Table 2.4. Total waste, total solvent input and percentage of solvent in waste for the internal processes for Tetralone and Sertraline

Tetralone routes	Total waste pre-treatment (before solvent recovery), kg/kg tetralone	Solvent input, kg/kg tetralone	% Solvent in total waste
1,2	644.17	370.46	57.5%
3	225.92	80.19	35.5%
4	16.07	5.32	33.1%
7	112.43	4.71	4.2%
8	174.19	43.69	25.1%

Sertraline processes	Total waste pre-treatment (before solvent recovery), kg/kg sertraline	Solvent input, kg/kg sertraline	% Solvent in total waste
5	3,660.99	2,481.56	67.8%
6	1,642.97	471.23	28.7%
EtOH-lab	73.93	68.47	92.6%
EtOH-pilot	134.39	129.09	96.1%
EtOH-full	93.76	89.47	95.4%
THF-lab	104.06	94.66	91.0%
THF-pilot	154.64	143.05	92.5%
THF-full	96.88	88.88	91.8%
TOL-lab	915.97	889.86	97.1%
TOL-pilot	215.58	206.59	95.8%
TOL-full	221.23	213.79	96.6%

Table 2.5. Distribution of the potential effects for the Tetralone routes. Method: Ecoindicator 95, Characterization only. (sr denotes with solvent recovery. The averages were calculated without including values over 100% or negative values).

GWP

	Process	Themic	Electric	Disposal	Transport	Total CO2-eq
route 1, 2	1.26%	93.31%	0.94%	4.07%	0.45%	2.69E+07
route 3	1.52%	90.50%	1.85%	5.60%	0.53%	6.11E+06
route 4	6.23%	-45.64%	21.43%	114.32%	3.65%	1.74E+04
route 7	6.05%	6.10%	28.18%	56.87%	2.80%	9.15E+04
route 8	3.99%	0.89%	23.77%	68.46%	2.88%	2.47E+05
1-2 sr	1.45%	91.92%	1.57%	4.42%	0.64%	7.90E+06
3 sr	1.76%	88.63%	3.14%	5.76%	0.70%	2.79E+06
4 sr	5.37%	13.26%	32.76%	41.08%	7.53%	6.93E+03
7 sr	5.21%	14.09%	30.57%	47.24%	2.89%	8.43E+04
8 sr	4.19%	8.96%	27.78%	55.87%	3.20%	1.55E+05
average	3.70%	45.30%	17.20%	40.37%	2.53%	

ODP

	Process	Themic	Electric	Disposal	Transport	Total CFC11-eq
route 1, 2	0.00%	99.20%	0.05%	0.00%	0.75%	1.87E+01
route 3	0.00%	99.03%	0.24%	0.00%	0.97%	4.14E+00
route 4	0.00%	5.23%	10.25%	0.00%	84.53%	8.53E-04
route 7	0.00%	30.82%	21.15%	0.00%	48.03%	6.10E-03
route 8	0.00%	23.00%	23.60%	0.00%	53.40%	1.00E-02
1-2 sr	0.00%	98.88%	0.19%	0.00%	1.12%	5.34E+00
3 sr	0.00%	98.36%	0.23%	0.00%	1.09%	1.83E+00
4 sr	0.00%	5.14%	3.07%	0.00%	91.67%	6.48E-04
7 sr	0.00%	31.60%	21.68%	0.00%	46.72%	5.95E-03
8 sr	0.00%	22.00%	22.80%	0.00%	55.20%	1.00E-02
average	0.00%	51.33%	10.33%	0.00%	38.35%	

HM

	Process	Themic	Electric	Disposal	Transport	Total Pb-eq
route 1, 2	0.00%	90.51%	8.81%	0.00%	0.68%	22.130
route 3	0.01%	83.11%	15.95%	0.00%	0.75%	5.330
route 4	0.51%	0.90%	90.79%	0.00%	7.81%	0.010
route 7	0.03%	0.98%	95.24%	0.00%	1.50%	0.210
route 8	0.02%	0.66%	97.37%	0.00%	2.63%	0.380
1-2 sr	0.00%	85.10%	14.01%	0.00%	0.89%	6.710
3 sr	0.02%	73.58%	25.66%	0.00%	0.75%	2.650
4 sr	1.45%	2.29%	77.59%	0.00%	18.48%	0.003
7 sr	0.03%	0.98%	95.24%	0.00%	1.43%	0.210
8 sr	0.02%	0.65%	97.30%	0.00%	2.70%	0.370
average	0.21%	33.88%	61.79%	0.00%	3.76%	

Table 2.5. (continued)

AP

	Process	Themic	Electric	Disposal	Transport	Total SO2-eq
route 1, 2	13.02%	84.35%	0.44%	1.62%	0.56%	3.00E+05
route 3	26.15%	69.90%	0.74%	2.66%	0.56%	8.00E+04
route 4	48.59%	-144.27%	73.73%	85.23%	36.72%	2.38E+01
route 7	27.01%	2.39%	14.07%	52.85%	3.69%	9.63E+02
route 8	25.80%	-1.73%	17.02%	53.27%	5.64%	1.74E+03
1-2 sr	22.81%	73.46%	0.66%	2.37%	0.71%	9.87E+04
3 sr	39.90%	54.75%	1.02%	3.74%	0.60%	4.51E+04
4 sr	21.42%	3.33%	34.33%	16.17%	24.75%	2.91E+01
7 sr	25.34%	4.93%	13.92%	52.34%	3.47%	9.72E+02
8 sr	21.88%	2.90%	14.36%	56.56%	4.31%	1.59E+03
average	27.19%	37.00%	17.03%	32.68%	8.10%	

NP

	Process	Themic	Electric	Disposal	Transport	Total Phos-eq
route 1, 2	26.33%	70.17%	0.15%	2.87%	0.49%	5.91E+04
route 3	28.98%	64.95%	0.29%	5.24%	0.54%	1.41E+04
route 4	95.01%	-2.89%	1.02%	5.66%	1.19%	1.25E+02
route 7	66.39%	0.78%	1.57%	30.23%	1.03%	5.86E+02
route 8	53.66%	-0.06%	2.66%	41.58%	2.16%	7.76E+02
1-2 sr	30.26%	64.44%	0.24%	4.42%	0.65%	1.84E+04
3 sr	33.35%	57.24%	0.44%	8.32%	0.65%	7.06E+03
4 sr	96.86%	0.16%	0.62%	1.35%	1.01%	1.22E+02
7 sr	66.04%	1.23%	1.57%	30.18%	0.98%	5.87E+02
8 sr	54.14%	0.98%	2.04%	41.30%	1.54%	7.59E+02
average	55.10%	32.49%	1.06%	17.11%	1.02%	

WS

	Process	Themic	Electric	Disposal	Transport	Total SO2-eq
route 1, 2	1.59%	95.04%	2.70%	0.00%	0.51%	4.51E+04
route 3	2.98%	90.91%	5.23%	0.00%	0.59%	1.04E+04
route 4	92.54%	-109.42%	107.20%	0.00%	7.79%	1.53E+01
route 7	64.09%	-0.17%	32.86%	0.00%	1.27%	3.80E+02
route 8	54.76%	-5.05%	45.81%	0.00%	2.23%	5.98E+02
1-2 sr	2.99%	91.63%	4.42%	0.00%	0.70%	1.35E+04
3 sr	4.46%	85.68%	8.61%	0.00%	0.74%	4.91E+03
4 sr	50.87%	0.00%	44.22%	0.00%	4.62%	2.12E+01
7 sr	61.44%	2.93%	32.51%	0.00%	1.19%	3.84E+02
8 sr	56.27%	1.45%	38.20%	0.00%	1.69%	5.52E+02
average	39.20%	52.52%	32.18%	0.00%	2.13%	

Table 2.5. (continued)

CG

	Process	Themic	Electric	Disposal	Transport	Total PAH-eq
route 1, 2	12.25%	86.03%	1.23%	0.00%	0.74%	4.08E+00
route 3	71.07%	27.86%	0.71%	0.00%	0.36%	2.80E+00
route 4	49.03%	1.08%	35.09%	0.00%	14.70%	9.32E-04
route 7	14.84%	5.14%	72.05%	0.00%	7.98%	6.94E-03
route 8	11.20%	4.35%	69.15%	0.00%	15.30%	1.00E-02
1-2 sr	32.68%	65.36%	1.31%	0.00%	0.65%	1.53E+00
3 sr	53.85%	43.59%	2.56%	0.00%	0.54%	7.80E-01
4 sr	36.18%	2.73%	22.73%	0.00%	38.57%	2.93E-04
7 sr	14.91%	5.17%	72.36%	0.00%	7.63%	6.91E-03
8 sr	11.20%	4.17%	73.93%	0.00%	10.70%	1.00E-02
average	30.72%	24.55%	35.11%	0.00%	9.72%	

SS

	Process	Themic	Electric	Disposal	Transport	Total PCOP-eq
route 1, 2	25.75%	73.62%	0.04%	0.14%	0.45%	6.95E+04
route 3	28.98%	70.17%	0.08%	0.25%	0.52%	1.61E+04
route 4	266.38%	-183.50%	2.75%	4.31%	10.13%	1.60E+01
route 7	95.48%	-2.39%	1.12%	3.35%	2.43%	2.69E+02
route 8	104.42%	-7.55%	0.50%	1.30%	1.33%	1.36E+03
1-2 sr	26.54%	72.55%	0.07%	0.21%	0.63%	2.04E+04
3 sr	30.01%	68.78%	0.14%	0.40%	0.67%	7.36E+03
4 sr	92.15%	-7.49%	2.41%	1.16%	11.86%	1.12E+01
7 sr	86.12%	6.09%	1.30%	3.80%	2.70%	2.31E+02
8 sr	94.25%	-0.61%	0.95%	3.01%	2.40%	5.28E+02
average	59.91%	58.24%	0.76%	1.54%	2.71%	

GWP = Global Warming Potential

AP = Acidification Potential

ODP = Ozone layer Depletion Potential

NP = Nitrification Potential

WS = Winter Smog

SS = Summer Smog

HM = Heavy Metals

CG = Carcinogenics

Table 2.6. Distribution of the potential effects for the Sertraline processes. Method: Ecoindicator 95, Characterization only. (sr denotes with solvent recovery).

GWP

	Process	Themic	Electric	Disposal	Transport	Total, CO2-eq
EtOH	1.33%	87.71%	2.38%	8.06%	0.51%	3.39E+06
EtOH sr	1.47%	82.66%	5.26%	9.74%	0.86%	1.26E+06
THF	1.32%	87.56%	2.68%	7.90%	0.55%	5.16E+06
THF sr	1.51%	81.75%	5.98%	9.92%	0.83%	2.02E+06
TOL	1.41%	89.95%	1.44%	6.68%	0.51%	8.17E+06
TOL sr	1.52%	87.03%	3.24%	7.38%	0.83%	2.14E+06
5	1.57%	87.93%	2.51%	7.32%	0.66%	6.05E+07
5 sr	1.52%	89.62%	3.69%	4.52%	0.68%	5.01E+07
6	2.50%	81.21%	4.79%	10.07%	1.17%	1.49E+07
6 sr	3.38%	76.60%	7.67%	10.62%	1.73%	8.22E+06
average	1.75%	85.20%	3.96%	8.22%	0.83%	

ODP

	Process	Themic	Electric	Disposal	Transport	Total, CFC11eq
EtOH	0.00%	98.68%	0.15%	0.00%	0.88%	2.27
EtOH sr	0.00%	98.70%	0.37%	0.00%	1.30%	0.77
THF	0.00%	98.97%	0.26%	0.00%	0.77%	3.89
THF sr	0.00%	98.48%	0.76%	0.00%	1.52%	1.32
TOL	0.00%	98.99%	0.08%	0.00%	0.84%	5.93
TOL sr	0.00%	97.93%	0.20%	0.00%	1.38%	1.45
5	0.00%	97.99%	0.09%	0.00%	1.93%	23.33
5 sr	0.00%	97.27%	0.31%	0.00%	2.36%	16.11
6	0.00%	97.65%	0.32%	0.00%	2.14%	9.35
6 sr	0.00%	96.30%	0.62%	0.00%	3.29%	4.87
average	0.00%	98.10%	0.31%	0.00%	1.64%	

HM

	Process	Themic	Electric	Disposal	Transport	Total, Pb-eq
EtOH	0.00%	81.27%	18.06%	0.00%	1.00%	2.99
EtOH sr	0.01%	63.57%	34.88%	0.00%	1.55%	1.29
THF	0.00%	80.31%	18.92%	0.00%	0.77%	5.18
THF sr	0.01%	61.14%	37.55%	0.00%	1.31%	2.29
TOL	0.00%	88.69%	10.47%	0.00%	0.84%	7.16
TOL sr	0.01%	76.24%	22.28%	0.00%	1.49%	2.02
5	0.31%	85.99%	12.07%	0.00%	1.70%	28.76
5 sr	0.35%	66.44%	31.60%	0.00%	1.61%	25.51
6	0.00%	68.68%	29.85%	0.00%	1.46%	14.37
6 sr	0.00%	54.99%	43.06%	0.00%	1.95%	9.22
average	0.07%	72.73%	25.87%	0.00%	1.37%	

Table 2.6 (continued)

AP

	Process	Themic	Electric	Disposal	Transport	Total, SO2-eq
EtOH	8.53%	85.90%	1.16%	3.72%	0.68%	3.54E+04
EtOH sr	9.08%	78.81%	2.56%	8.41%	1.14%	1.32E+04
THF	8.89%	85.27%	1.20%	3.98%	0.66%	5.90E+04
THF sr	9.38%	77.33%	2.77%	9.48%	1.04%	2.25E+04
TOL	8.69%	87.96%	0.67%	2.03%	0.65%	8.89E+04
TOL sr	8.97%	83.65%	1.53%	4.79%	1.07%	2.30E+04
5	9.60%	85.84%	1.53%	1.82%	1.21%	4.50E+05
5 sr	8.95%	81.80%	2.47%	5.48%	1.29%	3.59E+05
6	20.02%	70.45%	2.05%	6.12%	1.37%	1.75E+05
6 sr	26.96%	58.99%	2.97%	9.24%	1.84%	1.07E+05
average	11.91%	79.60%	1.89%	5.51%	1.10%	

NP

	Process	Themic	Electric	Disposal	Transport	Total, Phos-eq
EtOH	27.20%	65.85%	0.38%	6.05%	0.53%	7.59E+03
EtOH sr	30.84%	55.10%	0.76%	12.49%	0.80%	3.09E+03
THF	26.57%	66.08%	0.39%	6.45%	0.52%	1.27E+04
THF sr	28.41%	55.62%	0.83%	14.38%	0.76%	5.15E+03
TOL	26.28%	69.59%	0.22%	3.38%	0.53%	1.86E+04
TOL sr	29.74%	61.54%	0.47%	7.45%	0.80%	5.14E+03
5	25.76%	69.23%	0.60%	3.33%	1.08%	8.56E+04
5 sr	24.12%	63.80%	0.93%	9.99%	1.15%	6.86E+04
6	52.61%	38.97%	0.48%	7.15%	0.79%	5.20E+04
6 sr	62.47%	27.10%	0.58%	8.98%	0.87%	3.84E+04
average	33.40%	57.29%	0.56%	7.96%	0.78%	

WS

	Process	Themic	Electric	Disposal	Transport	Total, SO2-eq
EtOH	4.16%	88.26%	6.61%	0.00%	0.65%	5.76E+03
EtOH sr	8.70%	76.03%	13.50%	0.00%	1.07%	2.32E+03
THF	5.39%	86.43%	7.18%	0.00%	0.64%	9.14E+03
THF sr	9.68%	73.66%	14.90%	0.00%	0.96%	3.86E+03
TOL	3.44%	91.77%	3.99%	0.00%	0.61%	1.38E+04
TOL sr	6.24%	83.78%	8.54%	0.00%	1.01%	3.80E+03
5	10.35%	82.66%	6.17%	0.00%	0.71%	1.04E+05
5 sr	9.84%	79.98%	9.16%	0.00%	0.70%	9.03E+04
6	19.14%	68.19%	11.07%	0.00%	1.09%	2.99E+04
6 sr	27.55%	54.88%	15.41%	0.00%	1.40%	1.91E+04
average	10.45%	78.56%	9.65%	0.00%	0.88%	

Table 2.6 (continued)

CG

	Process	Themic	Electric	Disposal	Transport	Total, PAH-eq
EtOH	4.35%	91.30%	2.17%	0.00%	1.06%	0.46
EtOH sr	11.76%	82.35%	5.88%	0.00%	2.03%	0.17
THF	3.80%	92.41%	2.53%	0.00%	1.27%	0.79
THF sr	10.00%	83.33%	6.67%	0.00%	1.64%	0.3
TOL	87.47%	12.20%	0.22%	0.00%	0.11%	9.1
TOL sr	87.82%	11.34%	0.42%	0.00%	0.42%	2.38
5	48.63%	49.43%	1.03%	0.00%	1.03%	8.76
5 sr	56.80%	39.60%	2.67%	0.00%	0.93%	7.5
6	69.59%	28.13%	1.63%	0.00%	0.65%	6.15
6 sr	80.91%	16.82%	1.89%	0.00%	0.57%	5.29
average	46.11%	50.69%	2.51%	0.00%	0.97%	

SS

	Process	Themic	Electric	Disposal	Transport	Total, PCOP-eq
EtOH	36.25%	62.92%	0.10%	0.27%	0.46%	9.59E+03
EtOH sr	50.54%	48.21%	0.18%	0.45%	0.62%	4.39E+03
THF	35.03%	64.10%	0.11%	0.29%	0.47%	1.52E+04
THF sr	52.70%	46.06%	0.19%	0.49%	0.56%	7.59E+03
TOL	29.87%	69.41%	0.06%	0.17%	0.48%	2.21E+04
TOL sr	40.72%	58.17%	0.12%	0.31%	0.68%	6.63E+03
5	82.17%	17.57%	0.03%	0.04%	0.18%	5.47E+05
5 sr	84.11%	15.61%	0.04%	0.07%	0.17%	5.17E+05
6	44.12%	54.22%	0.19%	0.45%	1.01%	4.38E+04
6 sr	49.45%	48.12%	0.29%	0.69%	1.45%	2.52E+04
average	50.50%	48.44%	0.13%	0.32%	0.61%	

GWP = Global Warming Potential

AP = Acidification Potential

ODP = Ozone layer Depletion Potential

NP = Nutrifcation Potential

WS = Winter Smog

SS = Summer Smog

HM = Heavy Metals

CG = Carcinogenics

Table 2.7 Criteria for determining the data Quality Indicators (DQI) for the Sertraline Case Study.

INDICATOR	1	2	3	4	5
Reliability	Verified* data based on measurements**	Verified data partly based on assumptions or non-verified data based on measurements	Non-verified data partly based on assumptions	Qualified estimate (e.g. by industrial expert)	Non-qualified estimate
Completeness	Representative data from a sufficient sample of sites over an adequate period to even out normal fluctuations	Representative data from a smaller number of sites but for adequate periods	Representative data from an adequate number of sites but from shorter periods	Representative data but from a smaller number of sites and shorter periods or incomplete data from an adequate number of sites and periods	Representativeness unknown or incomplete data from a smaller number of sites and/or from shorter periods
Temporal correlation	Less than three years of difference to year of study	Less than six years difference	Less than 10 years difference	Less than 15 years difference	Age of data unknown or more than 15 years of difference
Geographical correlation	Data from area under study	Average data from larger area in which the area under study is included	Data from area with similar production conditions	Data from area with slightly similar production conditions	Data from unknown area or area with very different production conditions
Technological correlation	Data from enterprises, processes and materials under study	Data from processes and materials under study, but from different enterprises	Data from processes and material under study, but from different technology	Data on related processes or materials, but same technology	Data on related processes or materials, but different technology

* Verification may take place in several ways, e.g. by on-site checking, by recalculation, through mass balances or cross-checks with other sources.

** Includes calculated data (e.g. emissions calculated from inputs to a process), when the basis for calculation is measurements (e.g. measured inputs). If the calculation is based partly on assumptions, the score should be two or three.

Table 2.8. Data Quality Indicators for the Sertraline Case Study.

Factor Evaluated	R	C	G	time	Tech
Material wastes of Sertraline Processes at full and pilot scale	1	1	1	1	1
Material wastes of tetralone routes and Sertraline processes at lab scale	2	2	1	1	1
Mechanical Energy Requirements	1	2	1	1	1
Heating and cooling requirements	2	2	1	1	1
Transportation distances and means	2	1	2	1	2
LCI information related to mechanical energy requirements	1	1	2	1	2
LCI information related to heating and cooling requirements	2	1	1	1	2
LCI information related to transportation	1	2	3	1	2
LCI information related to disposal/waste treatment systems	2	2	3	1	2
LCI information related to substances of the substance tree	2	2	4	3	2

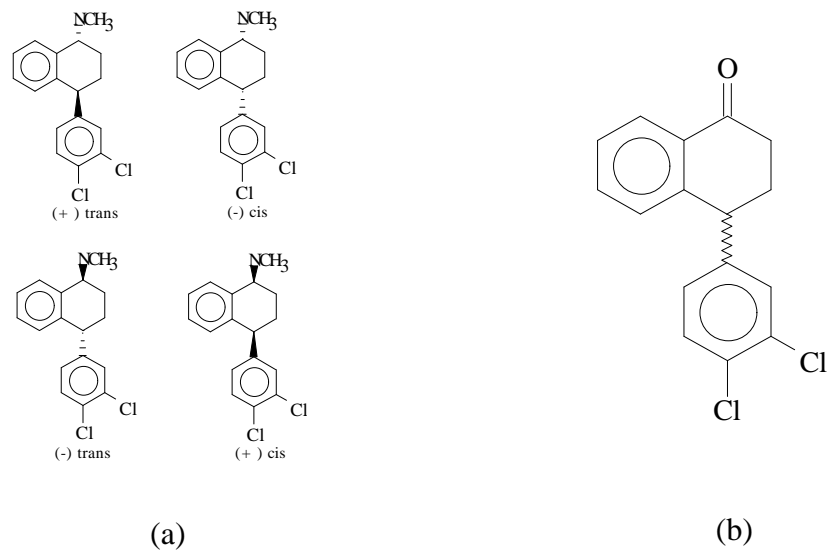


Figure 2.1. (a) Isomers of Sertraline. (b) Tetralone in the Racemic representation

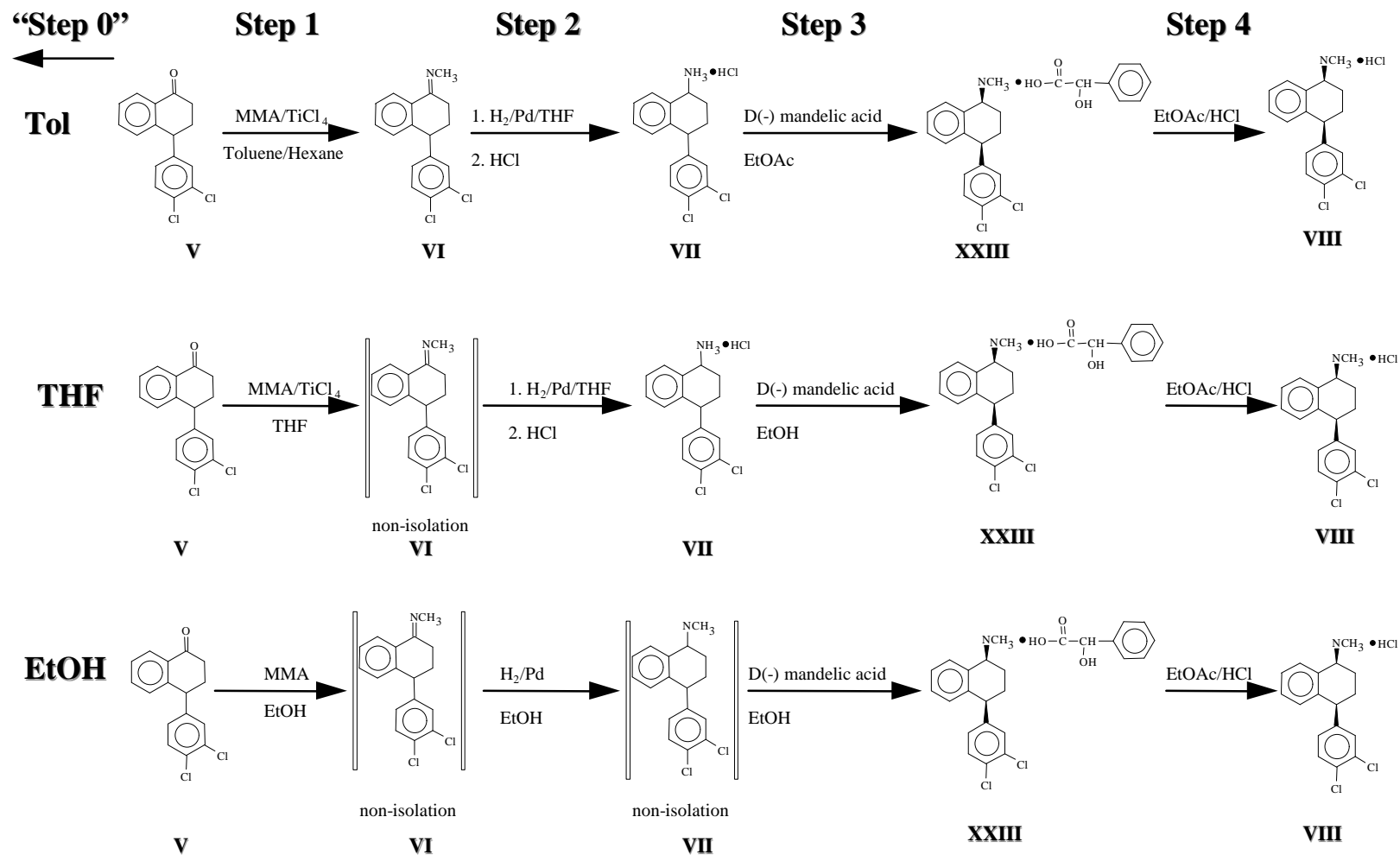


Figure 2.2. Description of the Sertraline processes.

Tol=Toluene, THF=Tetrahydrofuran, EtOH= Ethanol, MMA=Monomethyl amine, EtOAc=Ethyl acetate.

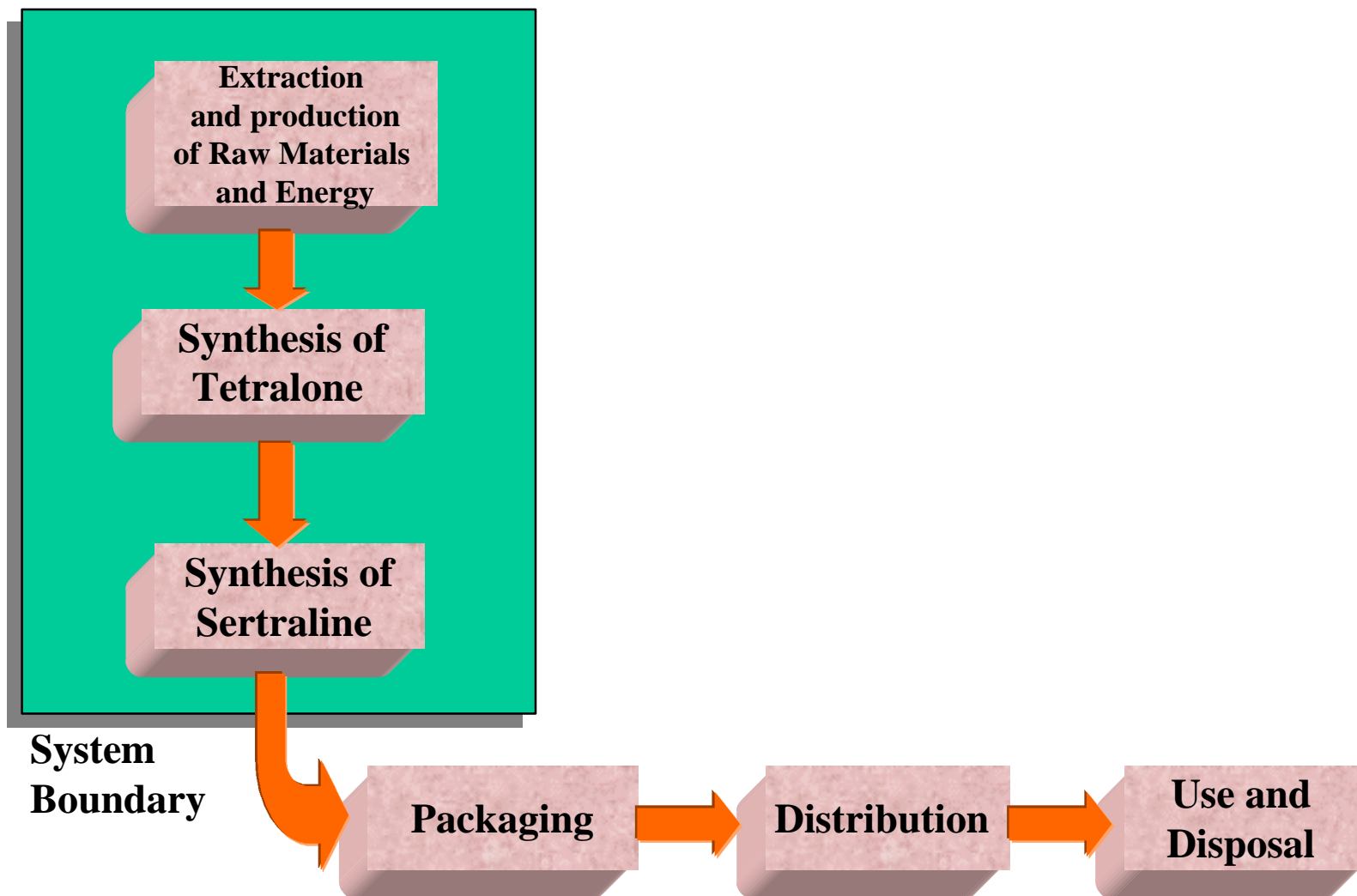


Figure 2.4. Definition of the boundaries for the life cycle of sertraline.

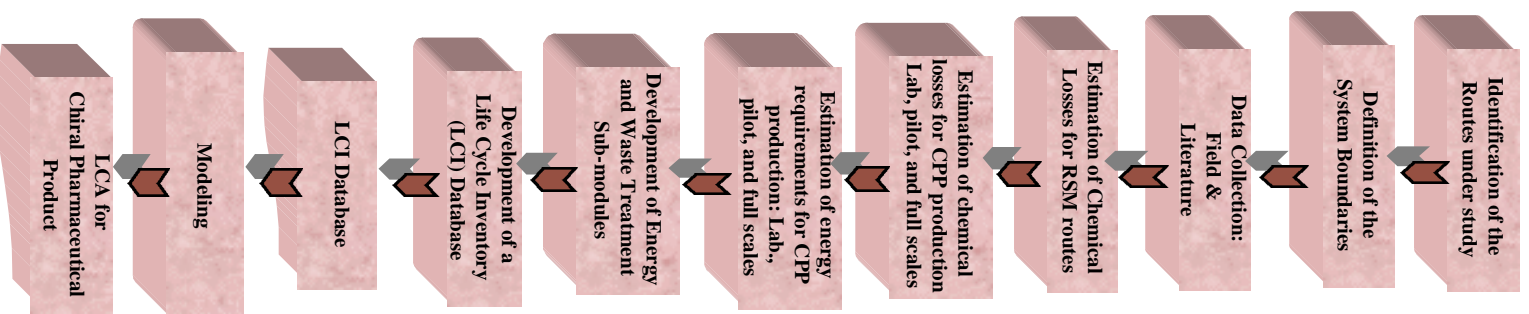


Figure 2.5. Graphic representation of the methodology for the life cycle of serrtraline.
RSM= Regulatory Starting Material (Tetralone), CPP= Chiral Pharmaceutical Product (Serrtraline)

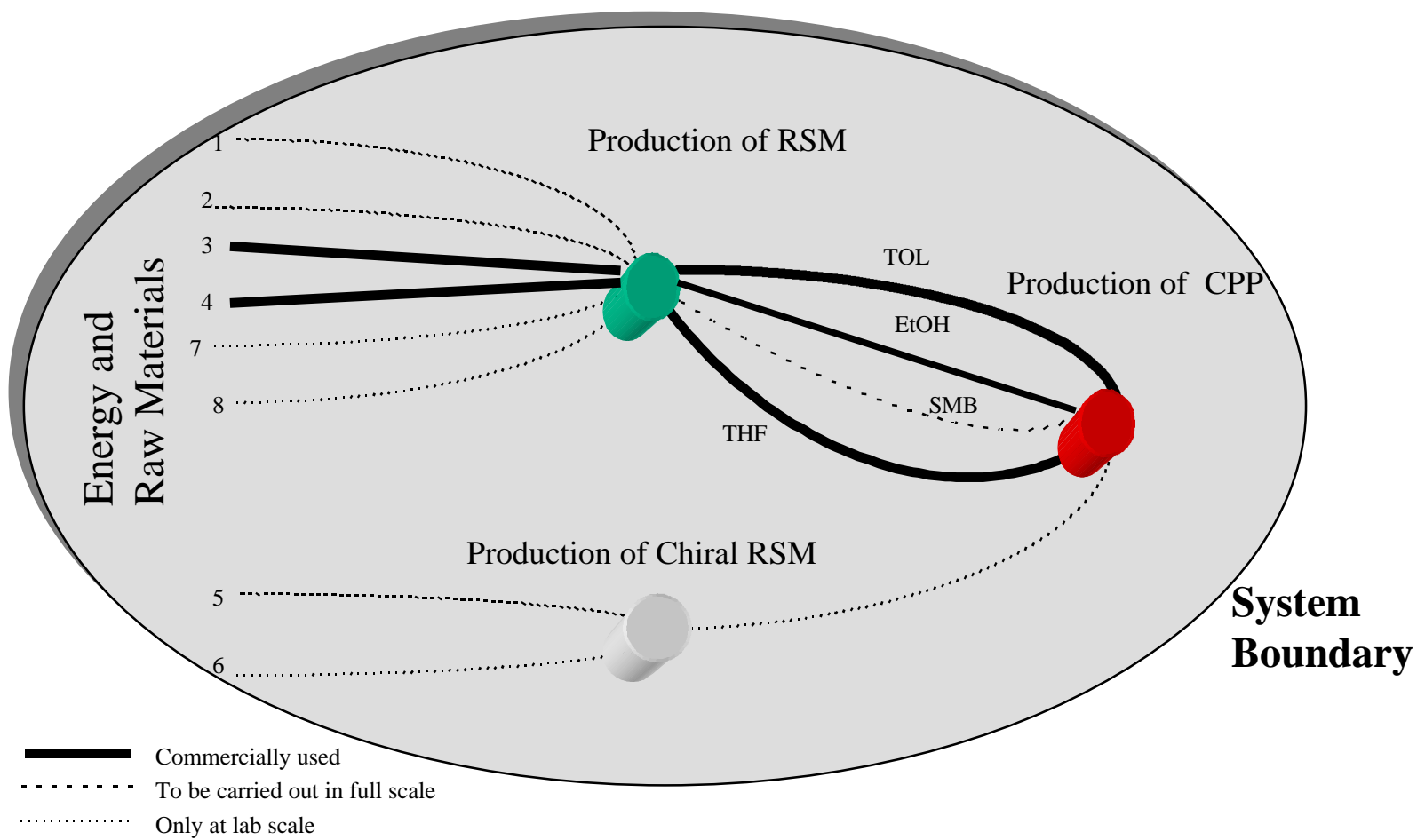


Figure 2.6. Identification of the routes (1-8) and processes under study.

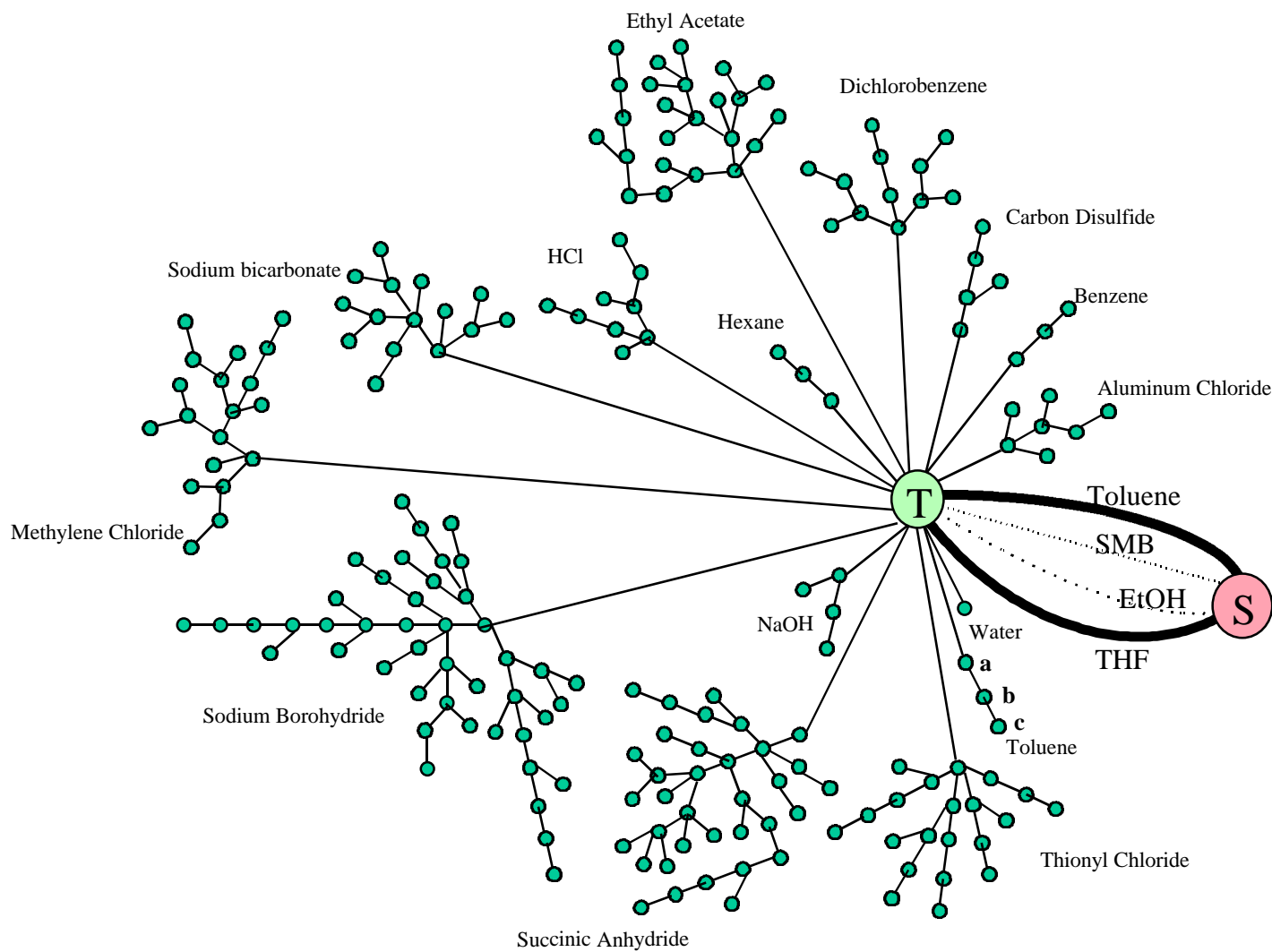


Figure 2.7. Graphical representation of the substance tree for the tetralone route 3. Each dot represents an industrial process (e.g. the three dots in the Toluene chain represent petroleum extraction, **a**; petroleum refining, **b** and toluene production, **c**)

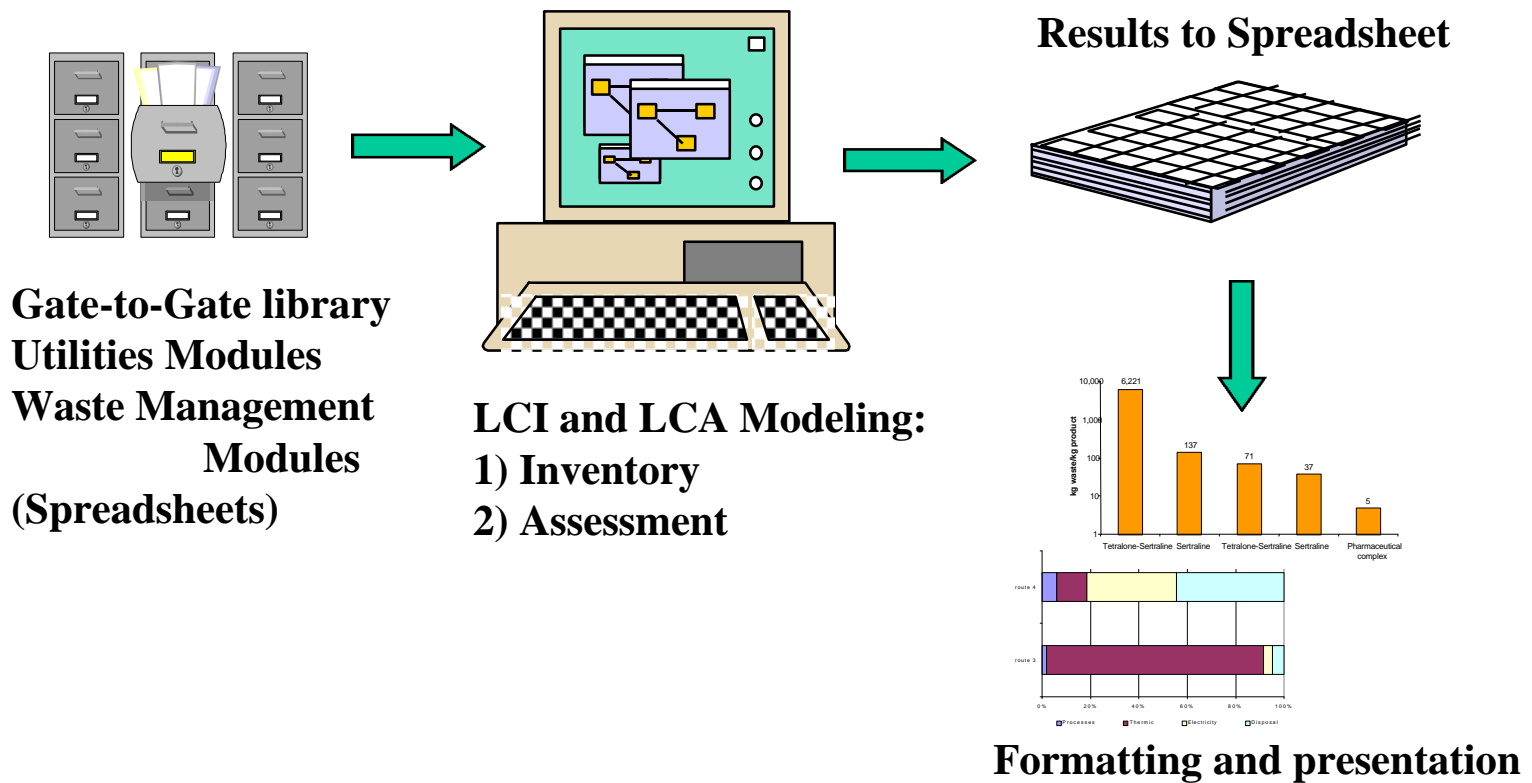


Figure 2.8. Graphic representation of the modeling phase of the study.

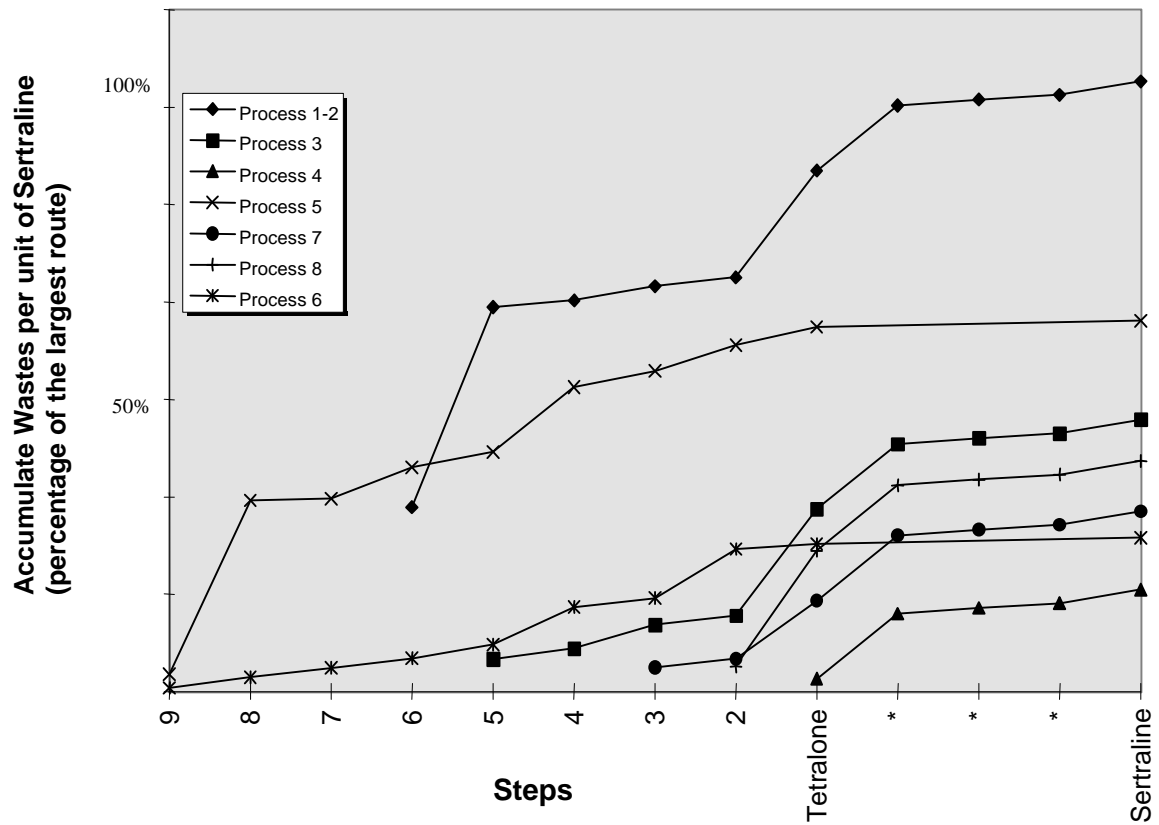


Figure 2.9. Schematic comparison Internal chemical losses of the tetralone routes (compared per unit of sertraline produced).

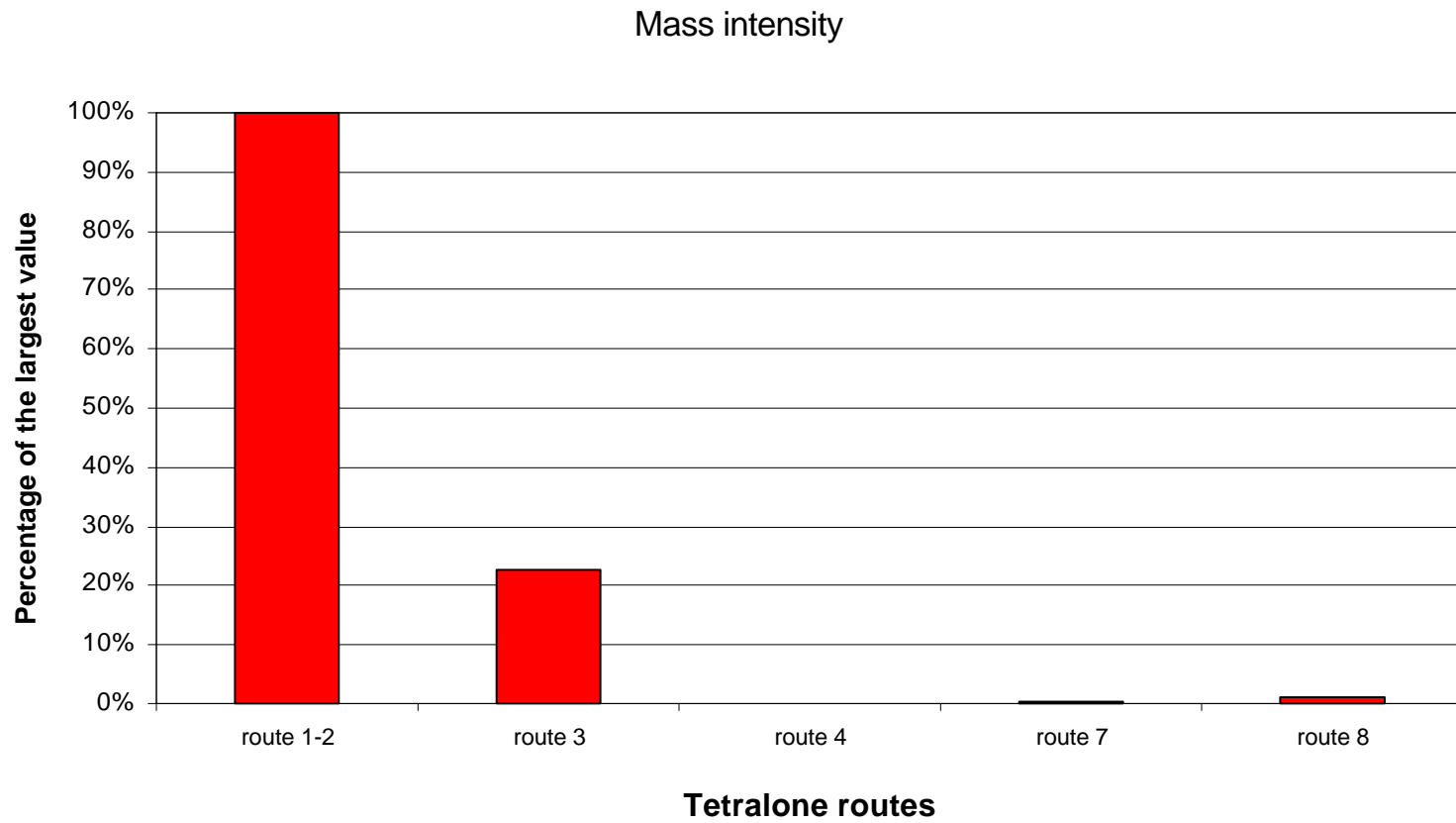


Figure 2.10. Life-cycle mass intensity for the different tetralone routes.

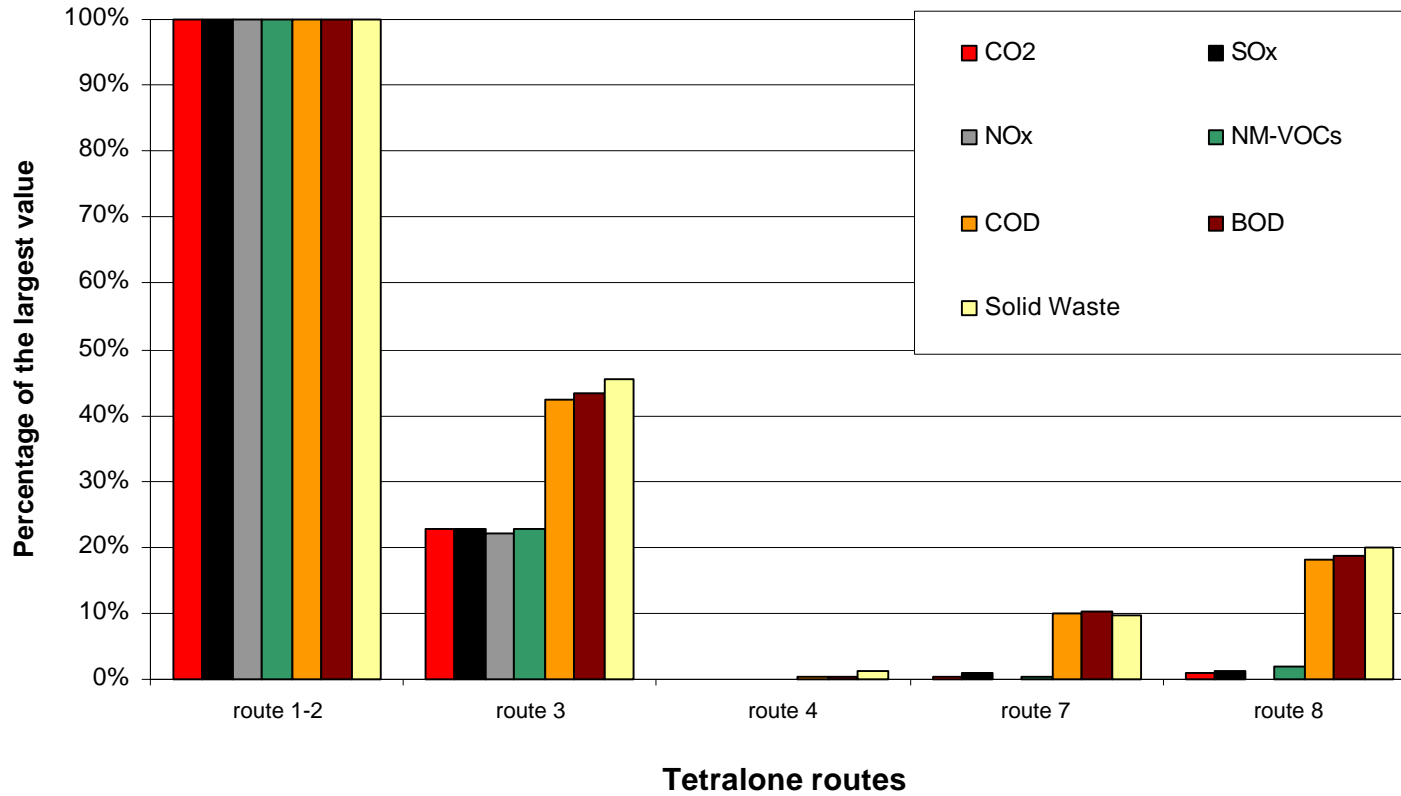


Figure 2.11. Selected Life-cycle emissions for the different tetralone routes.

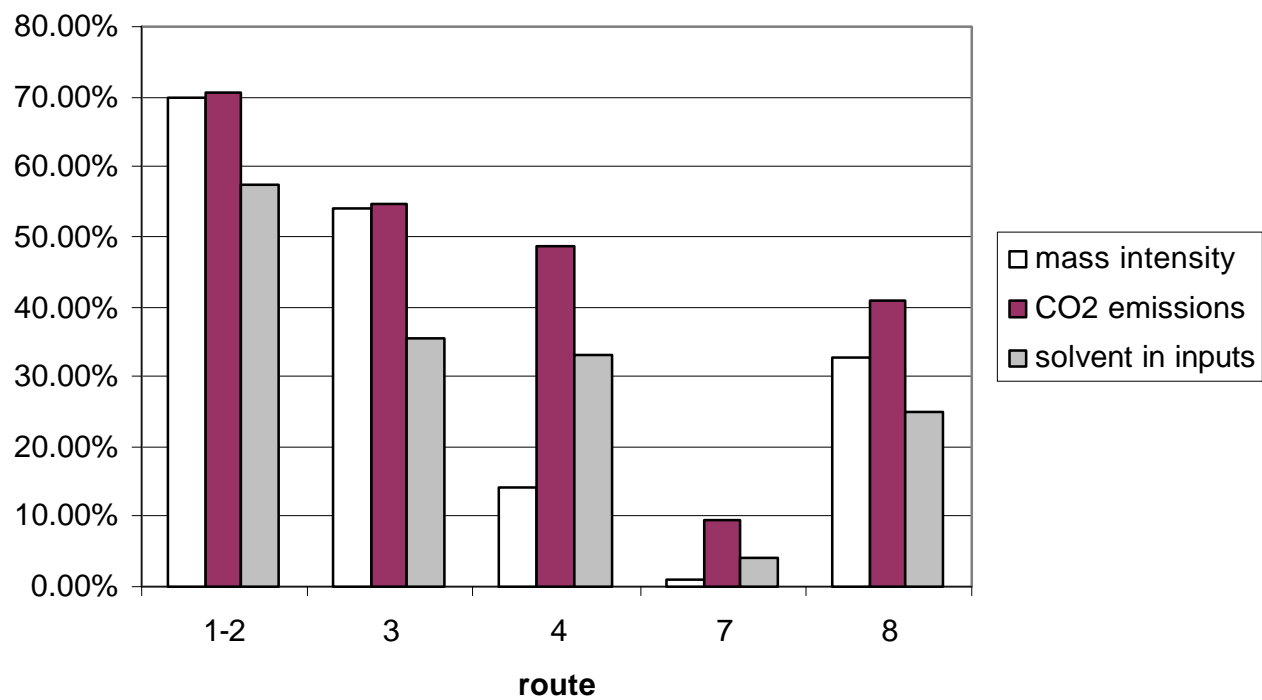


Figure 2.12. Reduction in life-cycle mass intensity and life-cycle carbon dioxide emissions with solvent recovery (75% of solvent gets recovered) in the Tetralone routes.

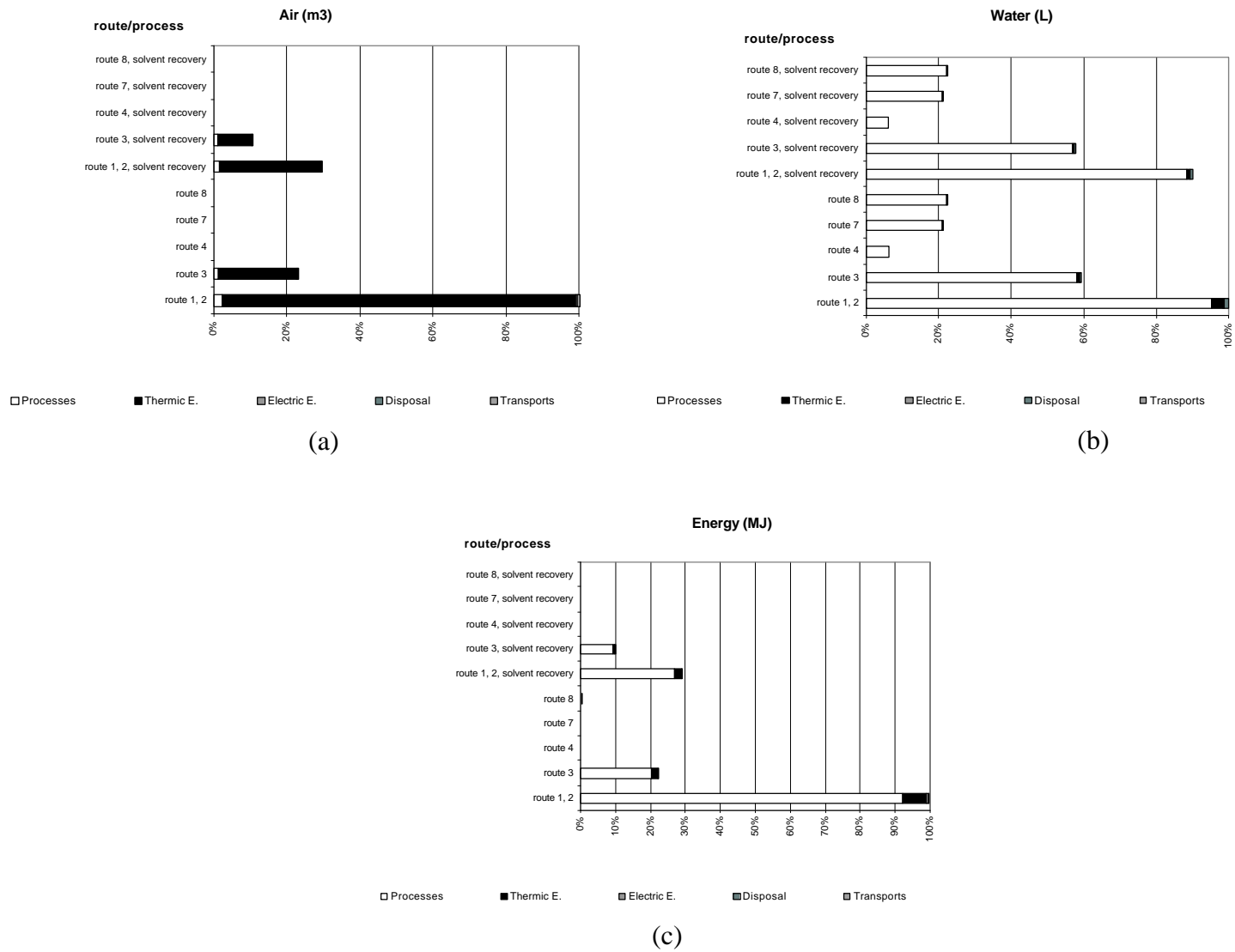


Figure 2.13 Life cycle assessment for tetralone routes: BUWAL 132 Method (1996)
 (a) Air, (b) Water, and (c) Energy.

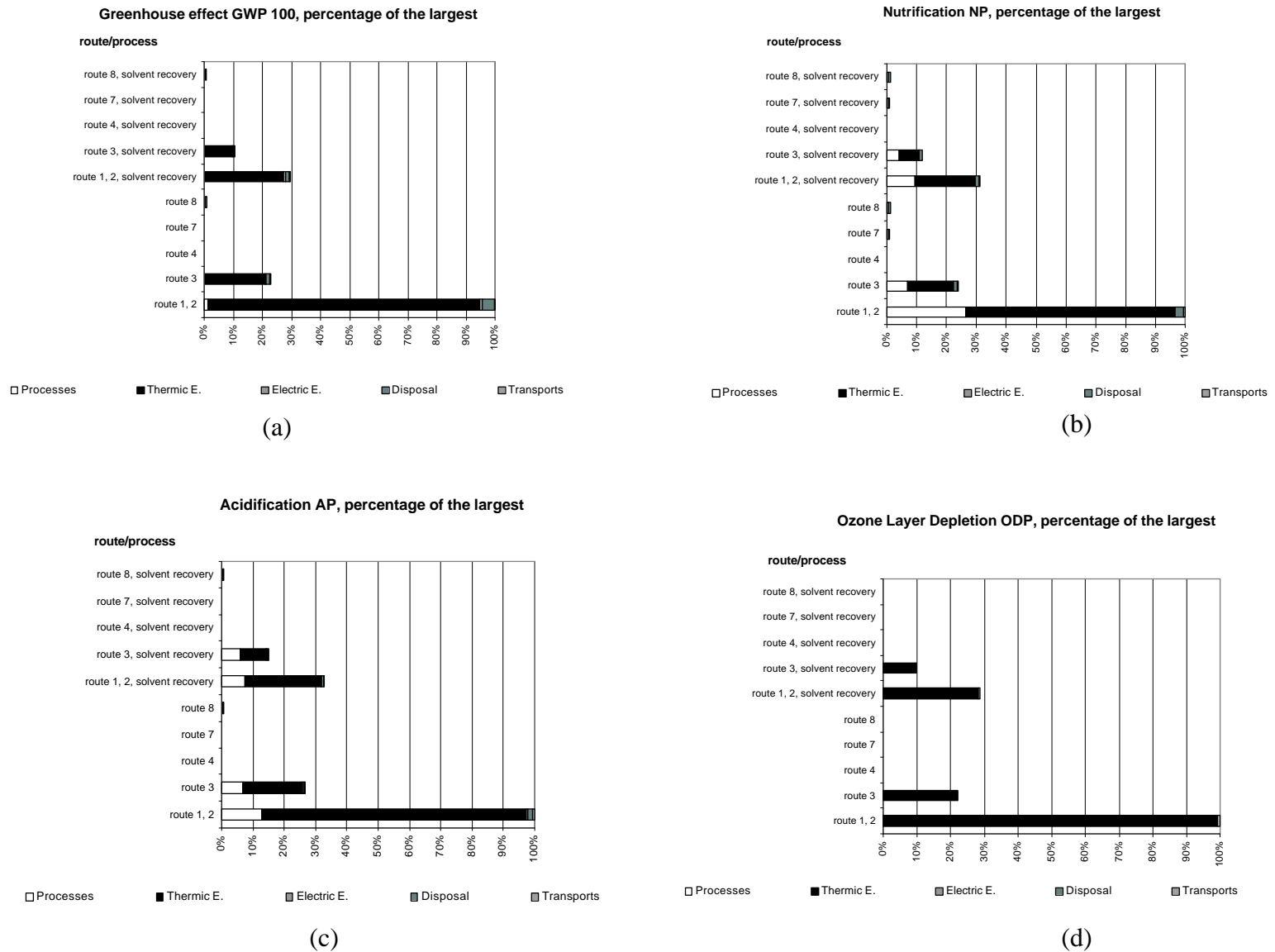
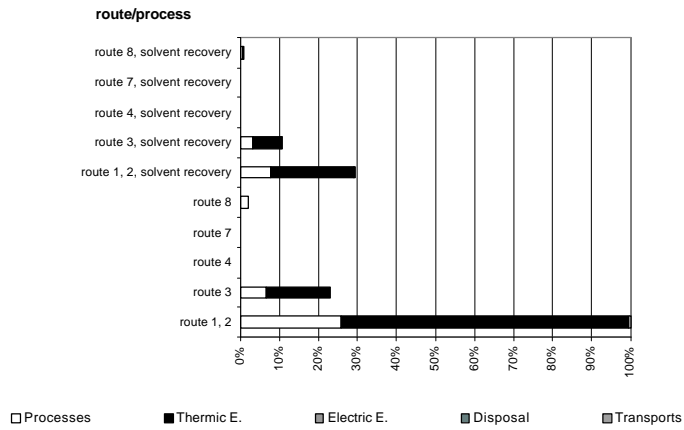
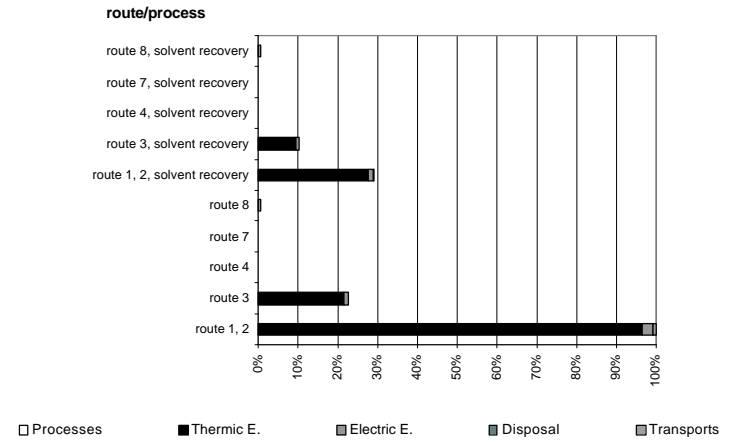


Figure 2.14 Life cycle assessment for tetralone routes: CML Method
 (a) Greenhouse effect, (b) Nutrifcation, (c) Acidification, (d) Ozone layer depletion.

Photochemical Oxidation POCP, percentage of the largest

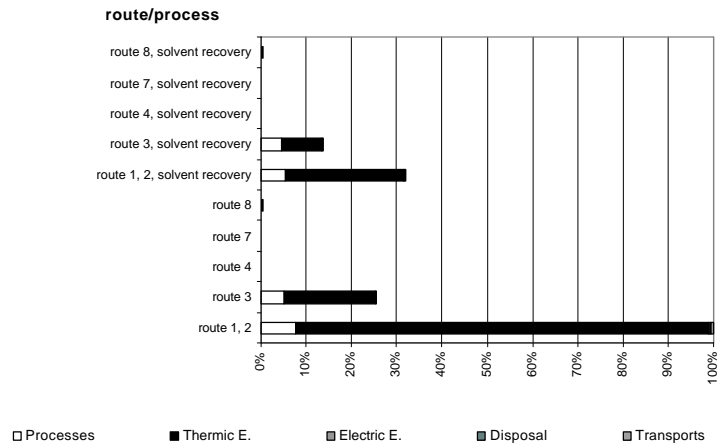


Ecotoxicity Aquatic ECA, percentage of the largest



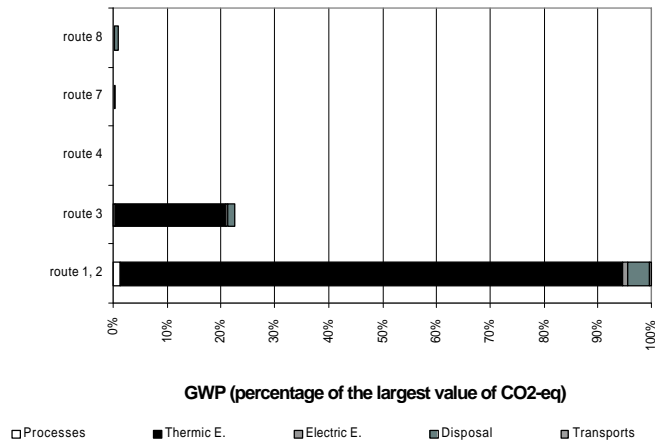
(f)

Human Toxicity, HC

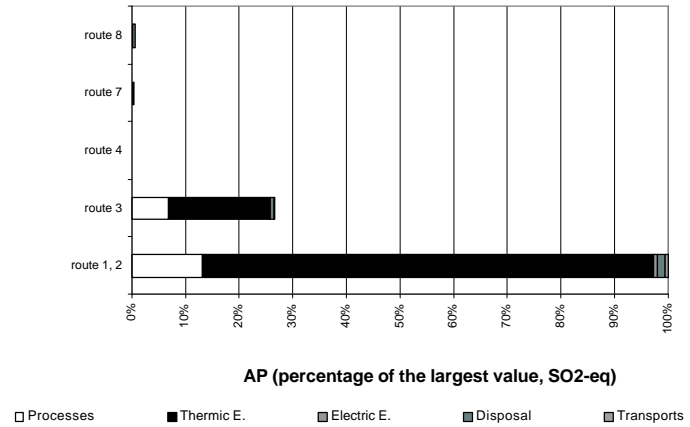


(g)

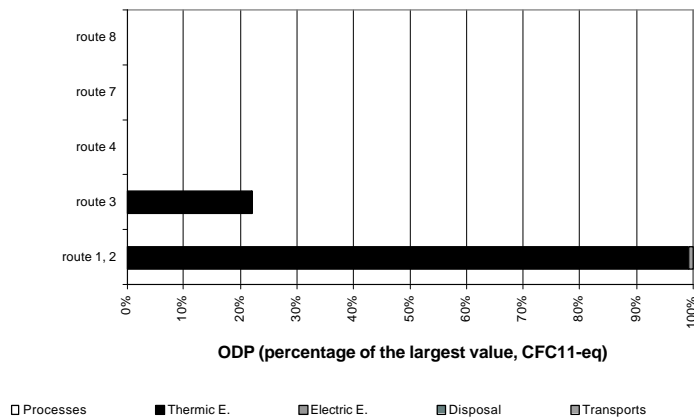
Figure 2.14 (continued) Life cycle assessment for tetralone routes: CML Method
 (e) Phototchemical oxidation, (f) Aquatic Ecotoxicity , (g) Human Toxicity.



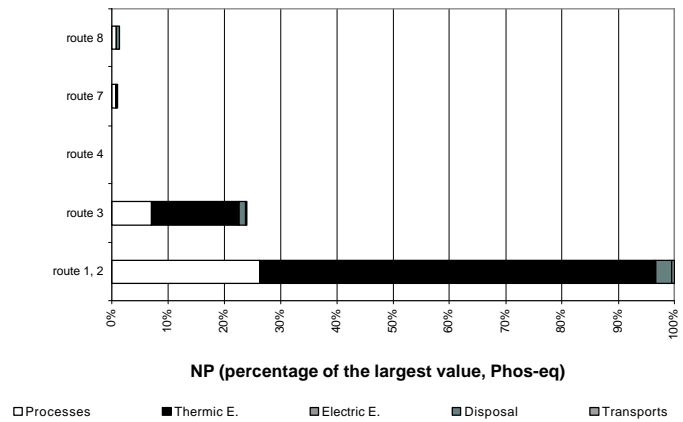
(a)



(b)

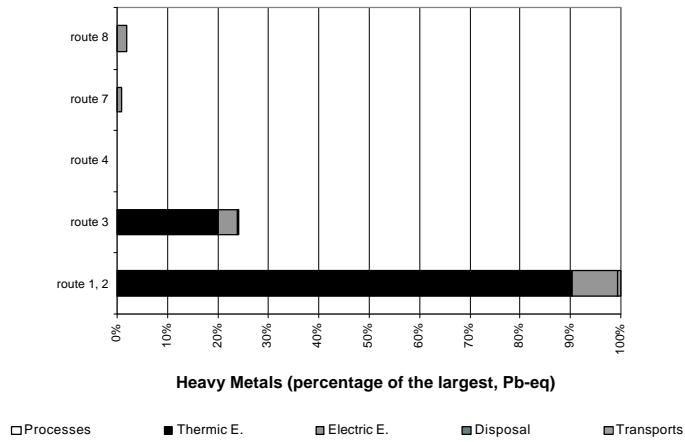


(c)

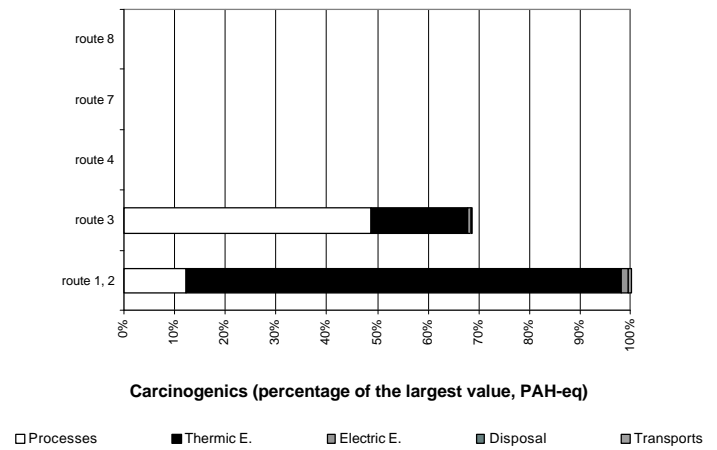


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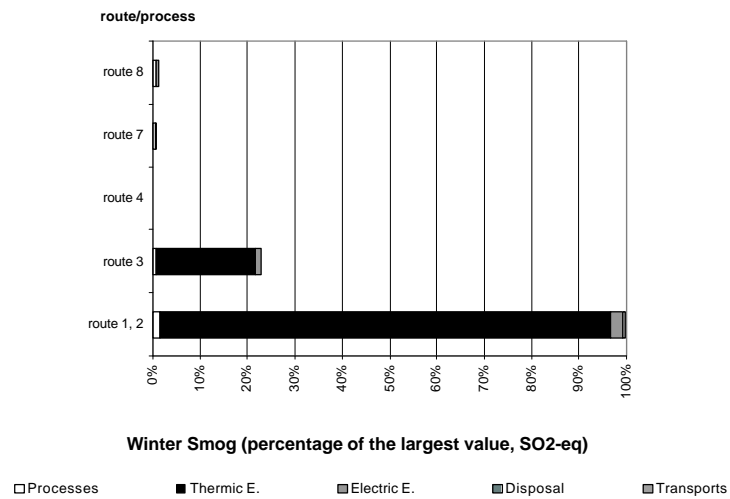
Figure 2.15 Life cycle assessment for tetralone routes: Ecoindicator 95 Method (characterization only)
 (a) Global Warming potential, (b) Acidification potential, (c) Ozone Depletion Potential, (d) Nutrifcation potential.



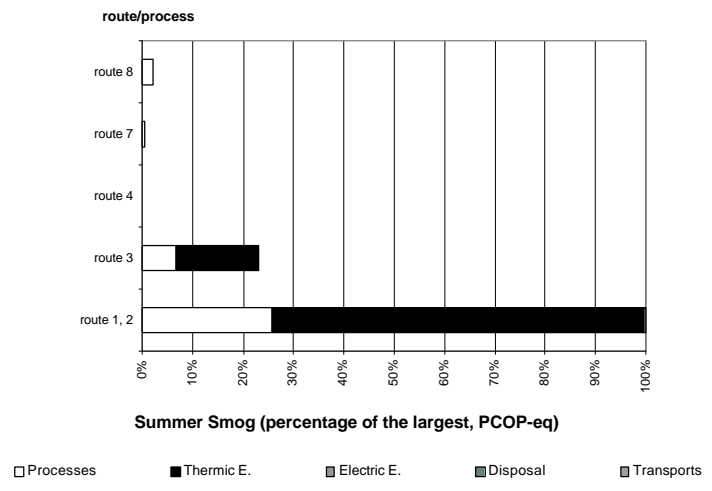
(e)



(f)

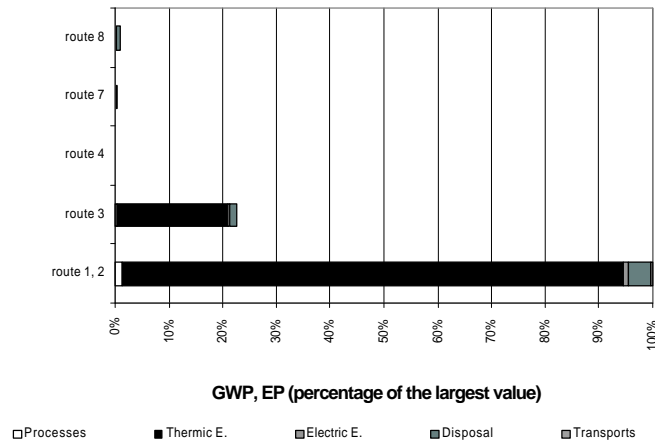


(g)

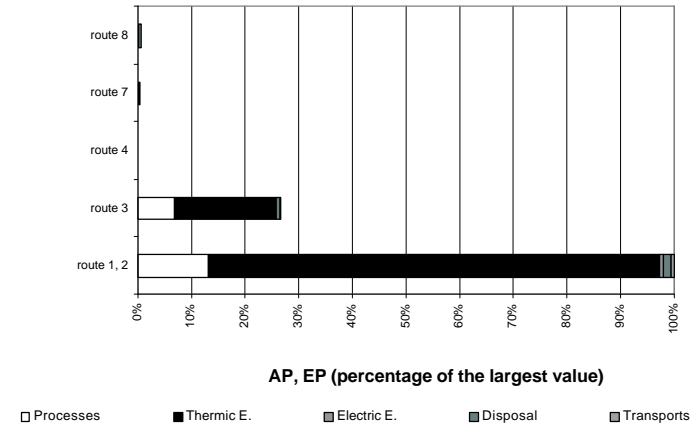


(h)

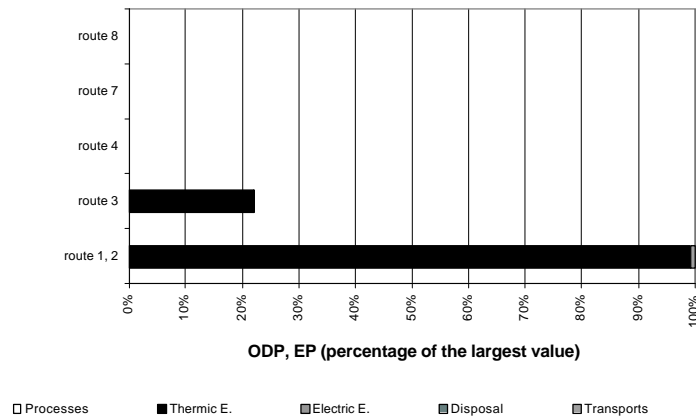
Figure 2.15 (continued) Life cycle assessment for tetralone routes: Ecoindicator 95 Method (characterization only)
 (e) Heavy metals, (f) Carcinogenics, (g) Winter Smog, (h) Summer Smog.



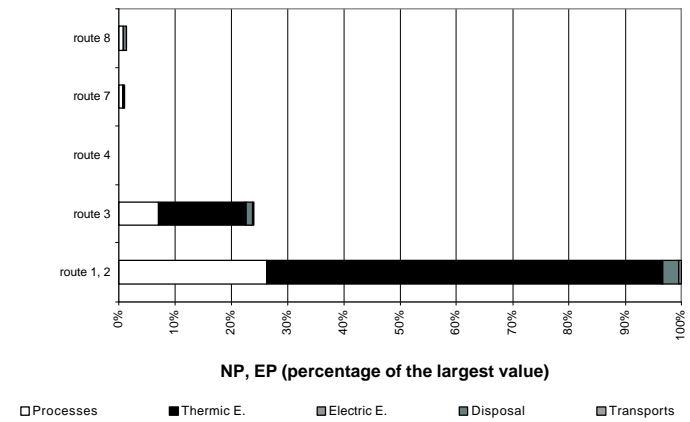
(a)



(b)

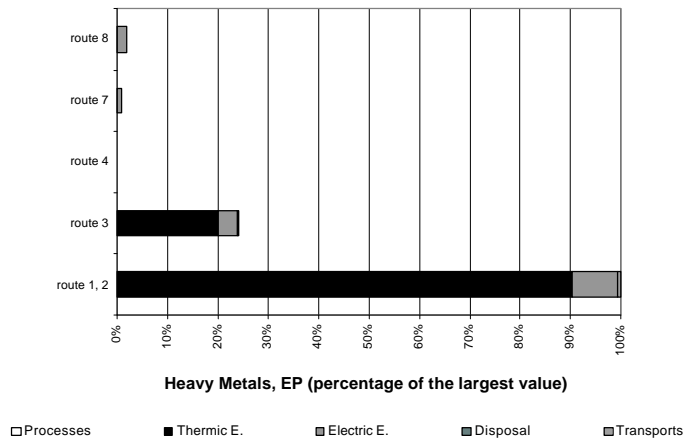


(c)

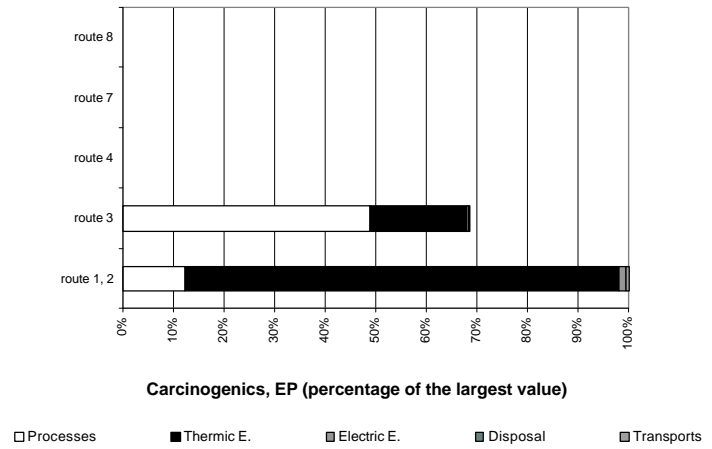


(d)

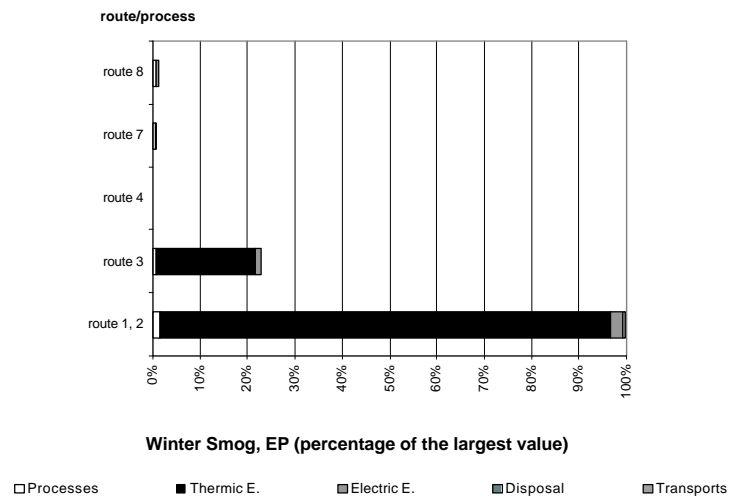
Figure 2.16 Life cycle assessment for tetralone routes: Ecoindicator 95 Method (valuation)
 (a) Global Warming potential, (b) Acidification potential, (c) Ozone Depletion Potential, (d) Nutrifcation potential.



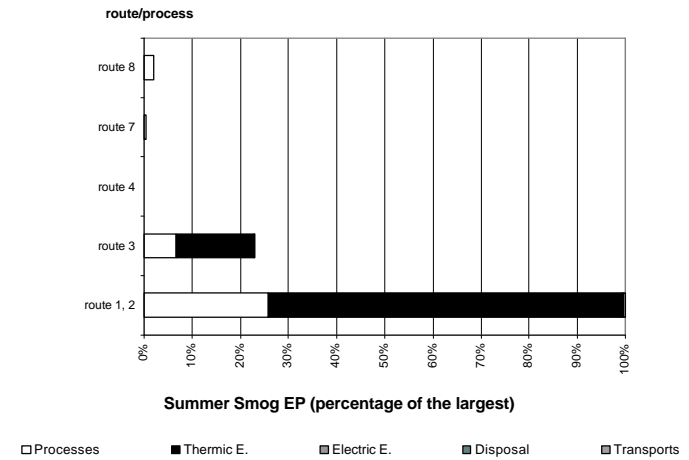
(e)



(f)



(g)



(h)

Figure 2.16 (continued) Life cycle assessment for tetralone routes: Ecoindicator 95 Method (valuation)
 (e) Heavy metals, (f) Carcinogenics, (g) Winter Smog, (h) Summer Smog.

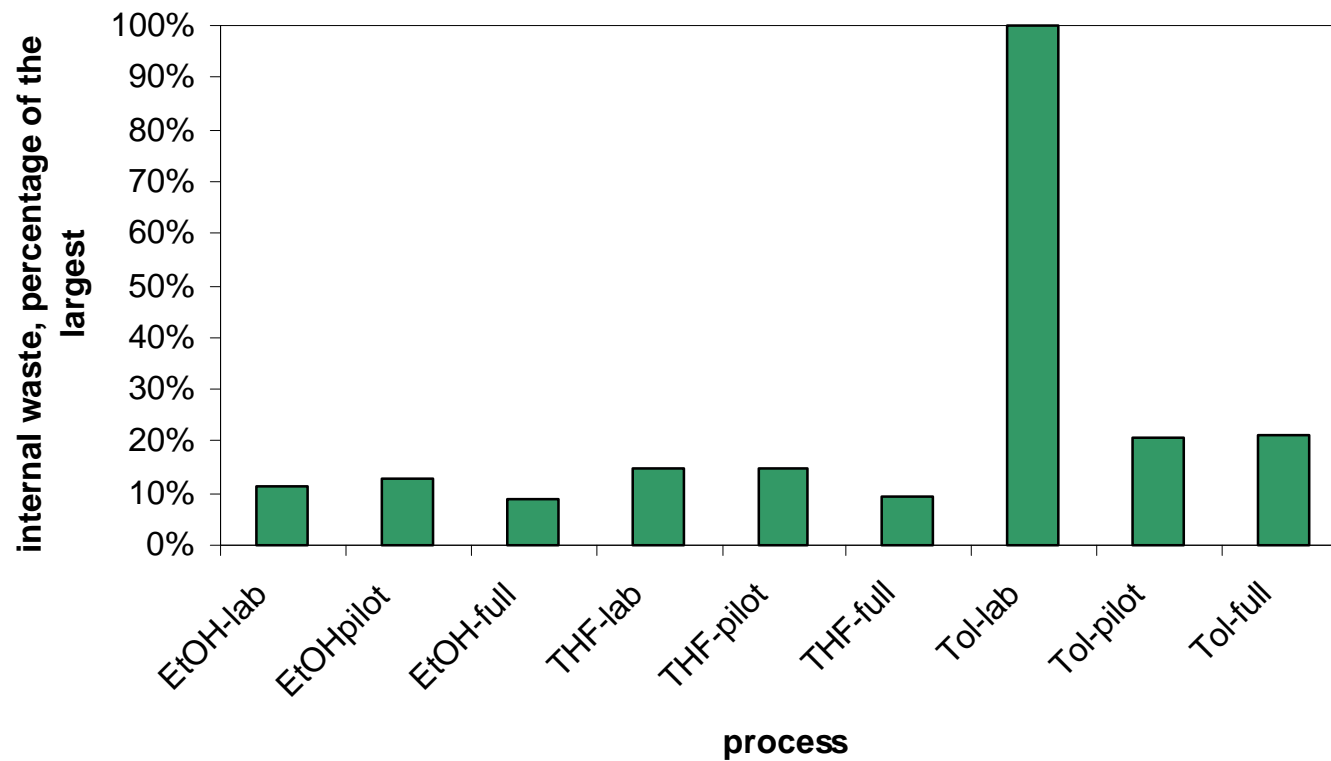


Figure 2.17 Internal chemical losses of the sertraline processes at laboratory, pilot and full scales.

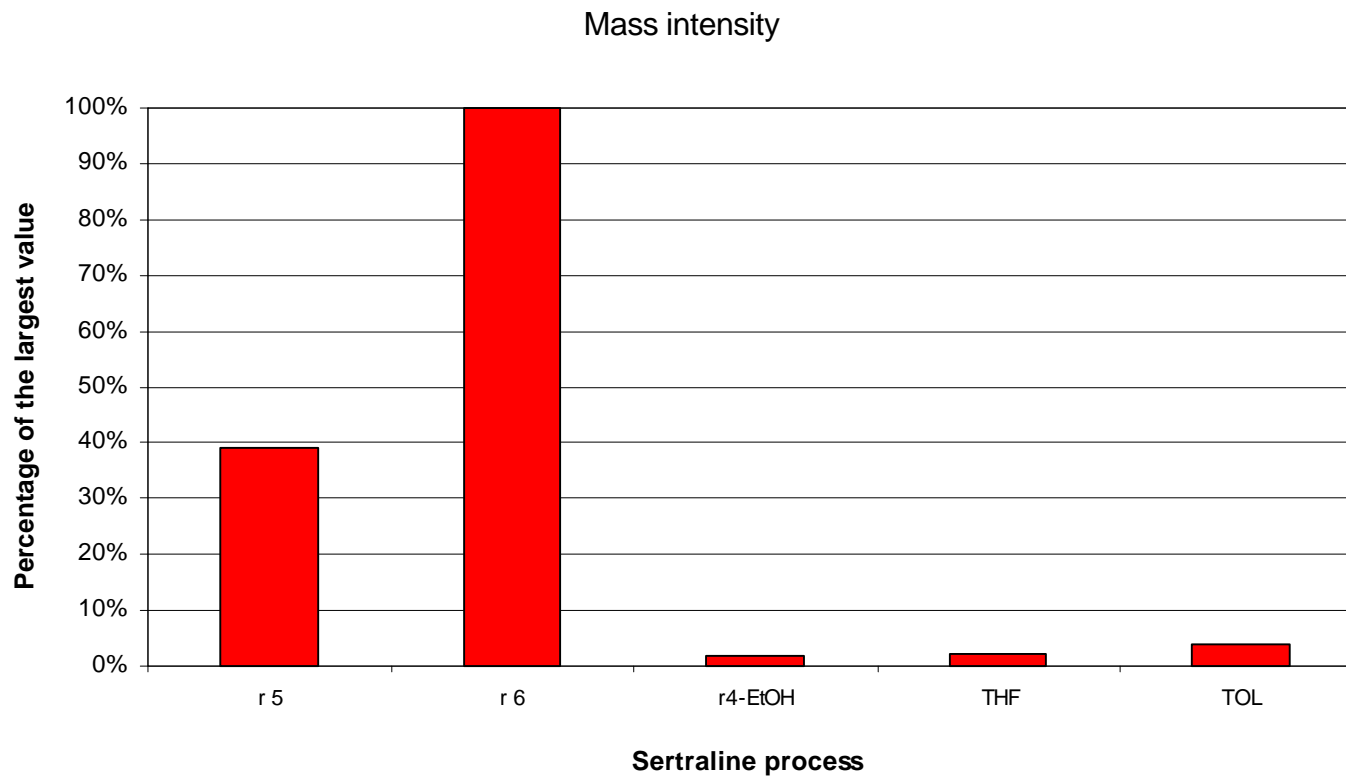


Figure 2.18. Life-cycle mass intensity for the sertraline processes.

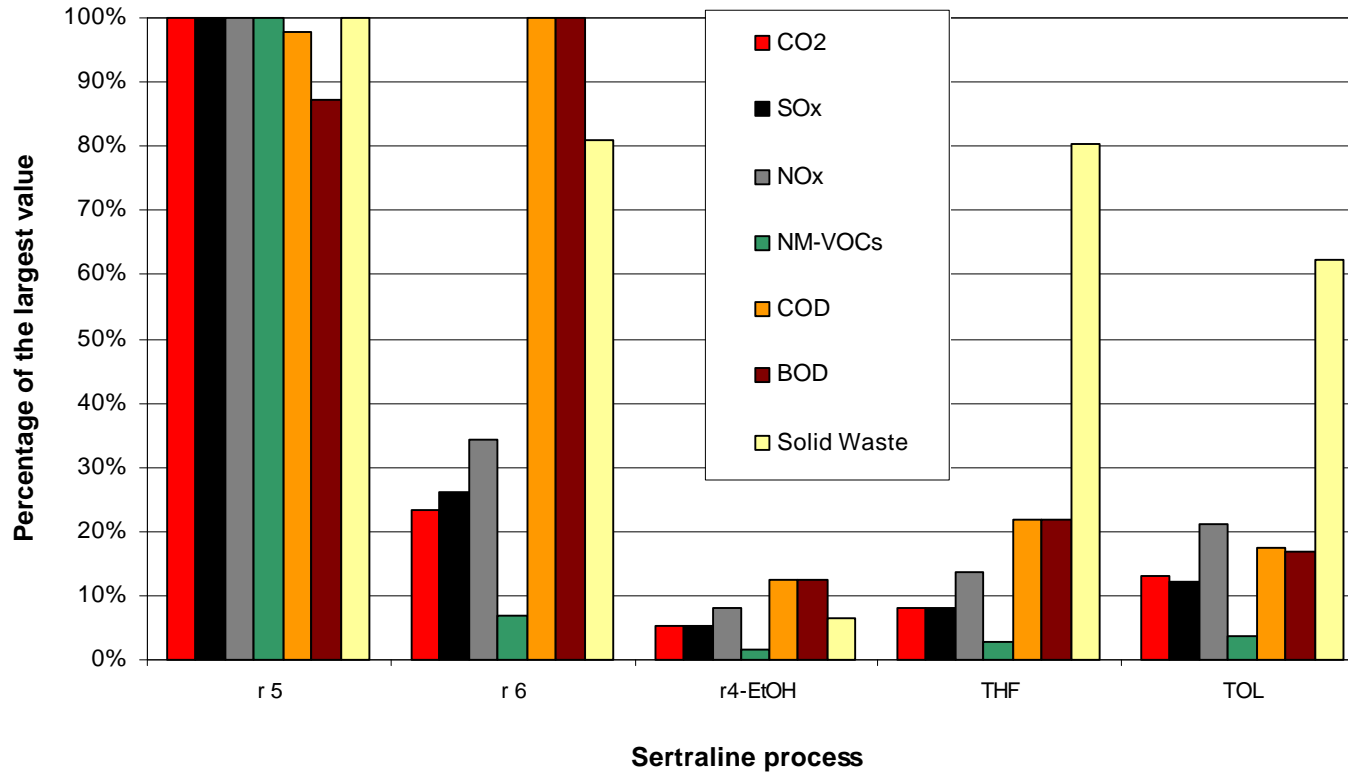


Figure 2.19. Selected life-cycle emissions for the sertraline processes.

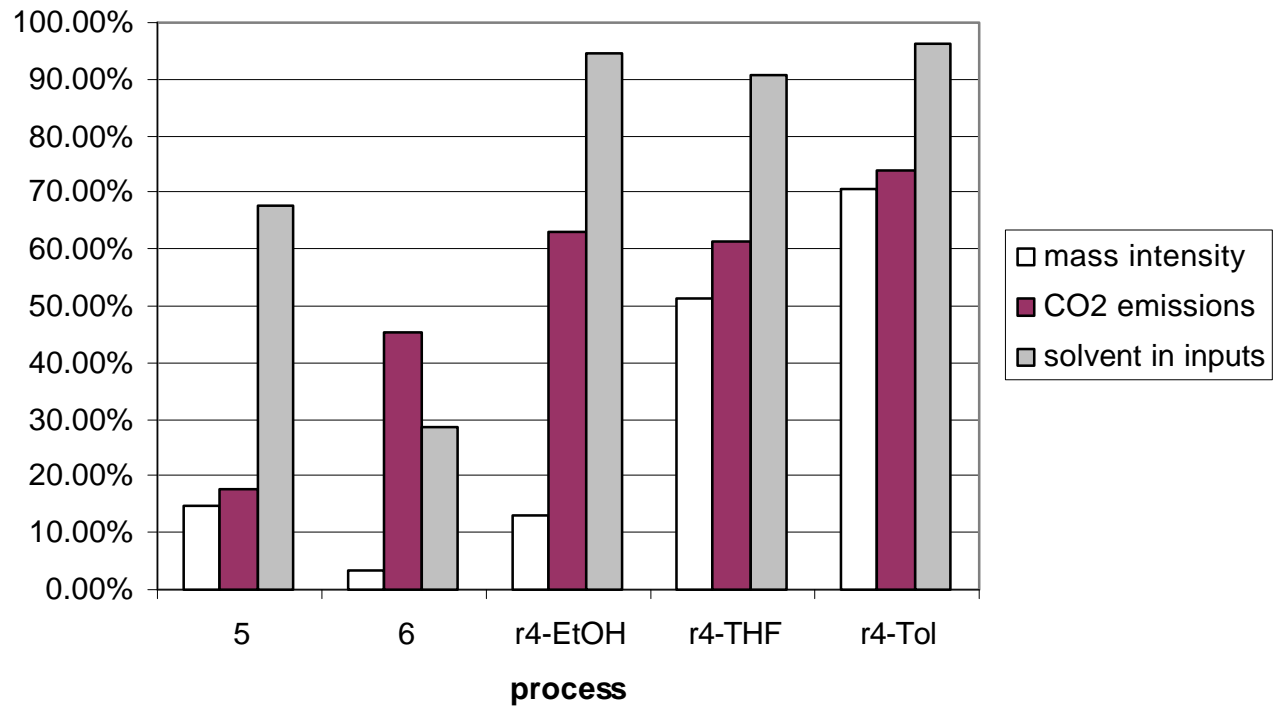


Figure 2.20. Reduction in life-cycle mass intensity and life-cycle carbon dioxide emissions with solvent recovery (75% of solvent gets recovered) in the Sertraline processes.

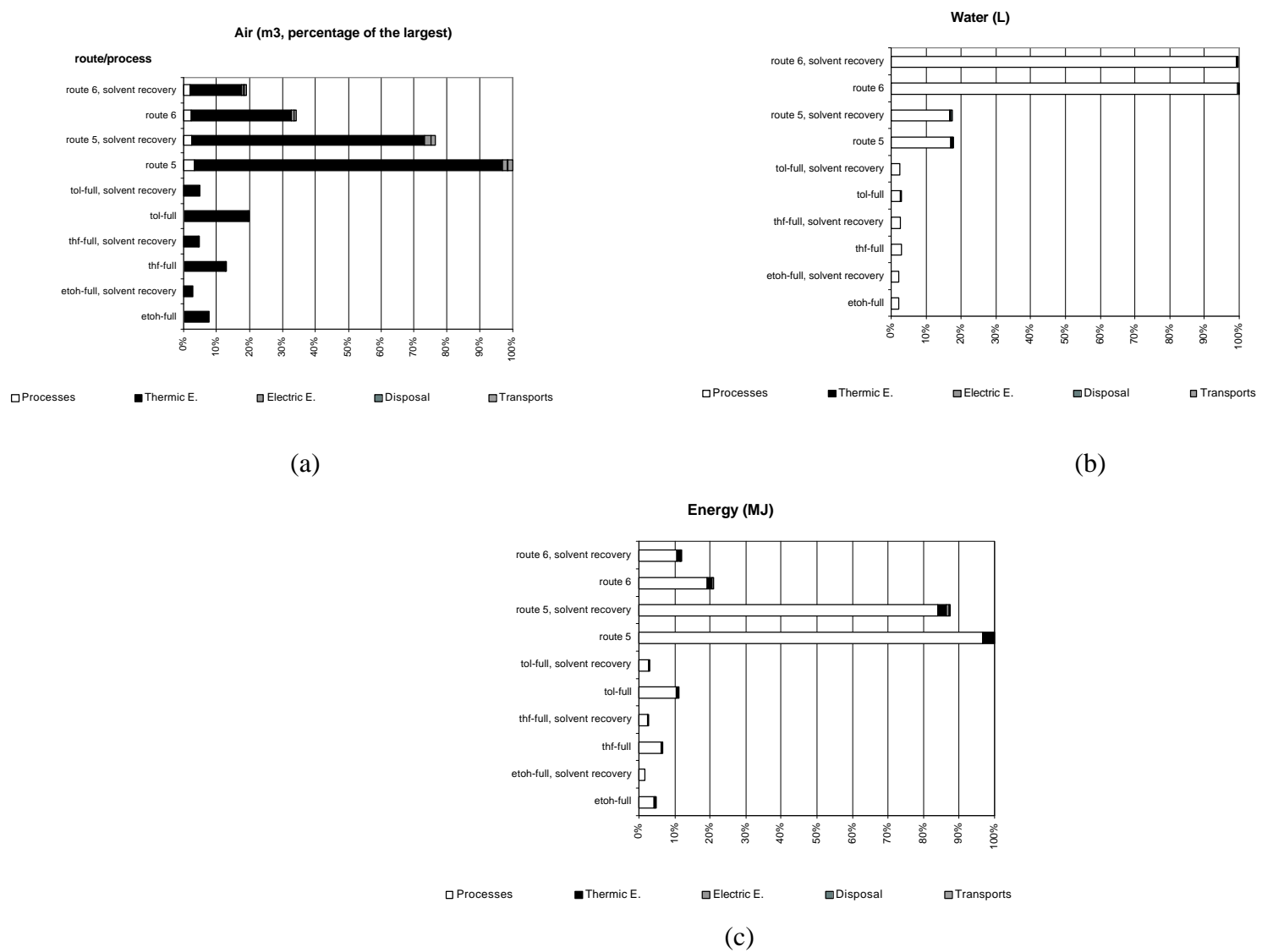
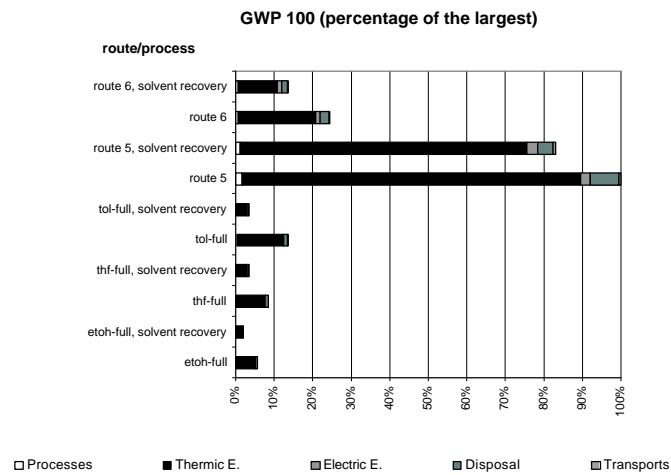
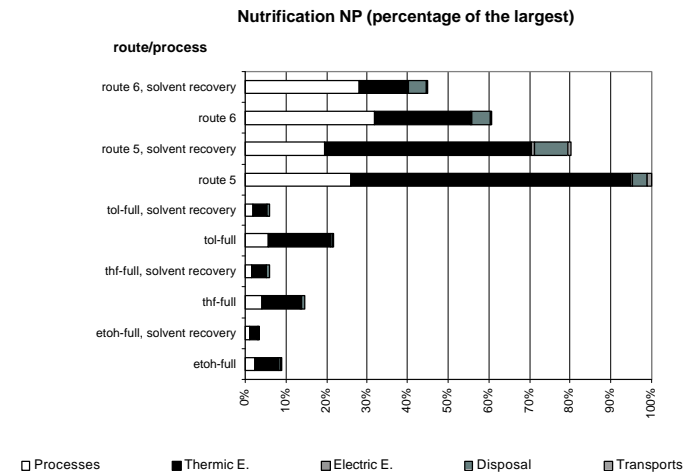


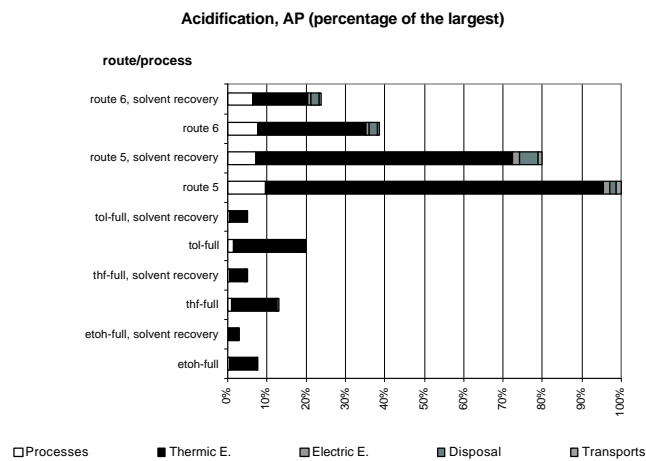
Figure 2.21 Life cycle assessment for sertraline processes: BUWAL 132 Method (1996)
(a) Air, (b) Water, and (c) Energy.



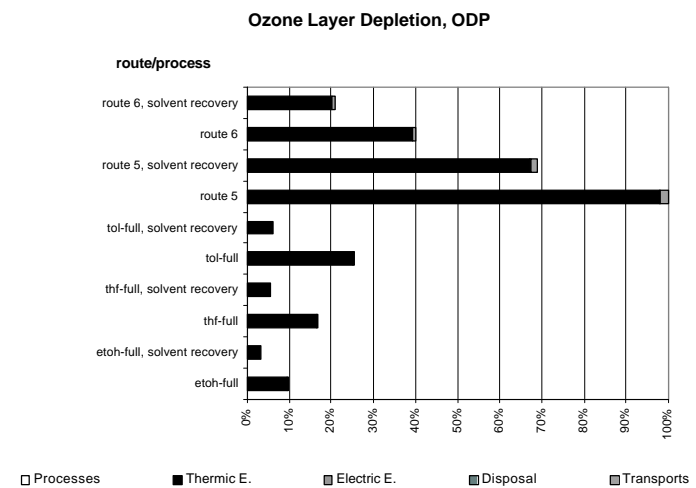
(a)



(b)

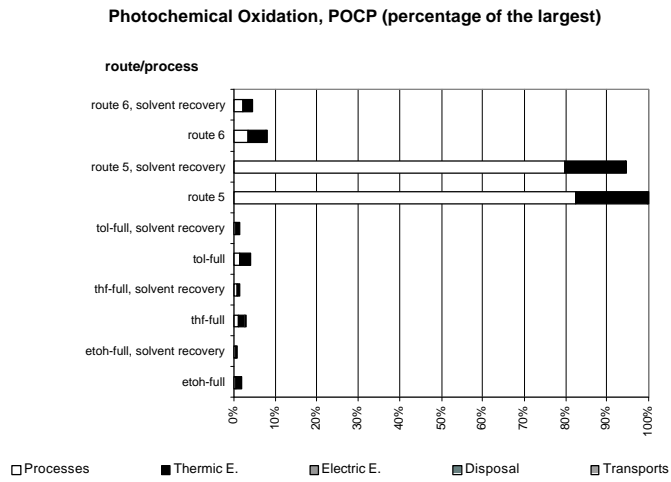


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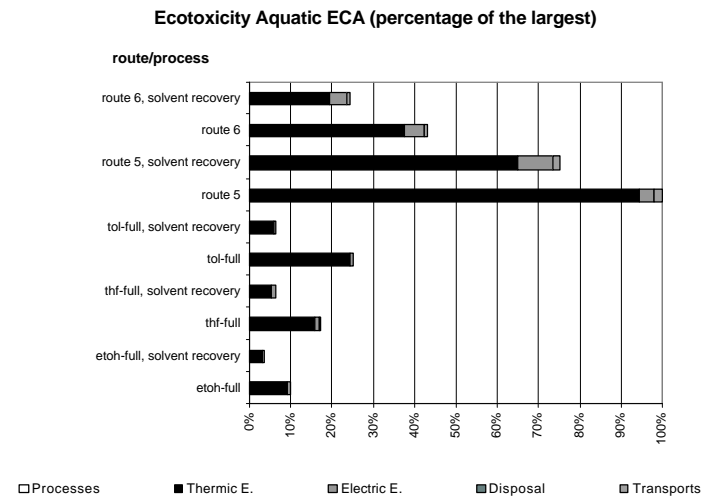


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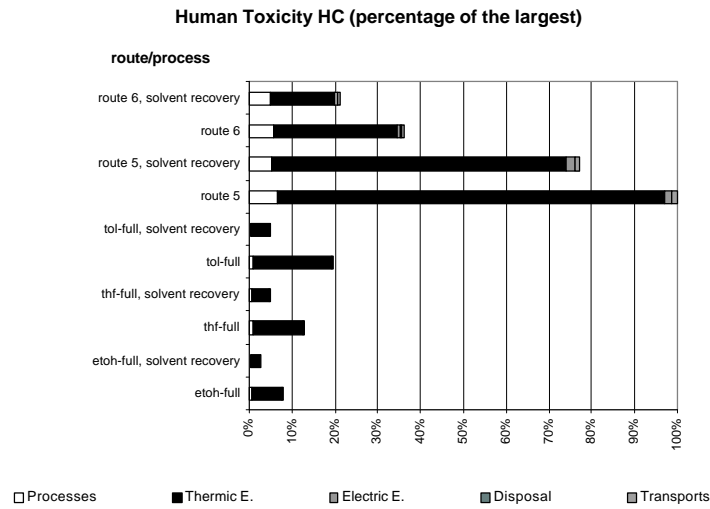
Figure 2.22 Life cycle assessment for sertraline processes: CML Method
 (a) Greenhouse effect, (b) Nutrifaction, (c) Acidification, (d) Ozone layer depletion.



(e)

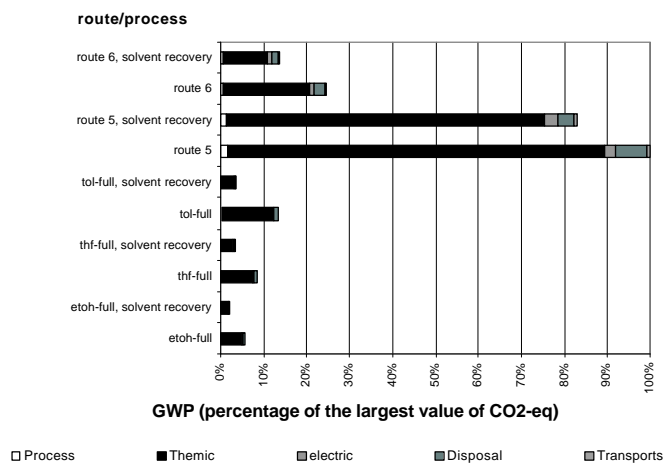


(f)

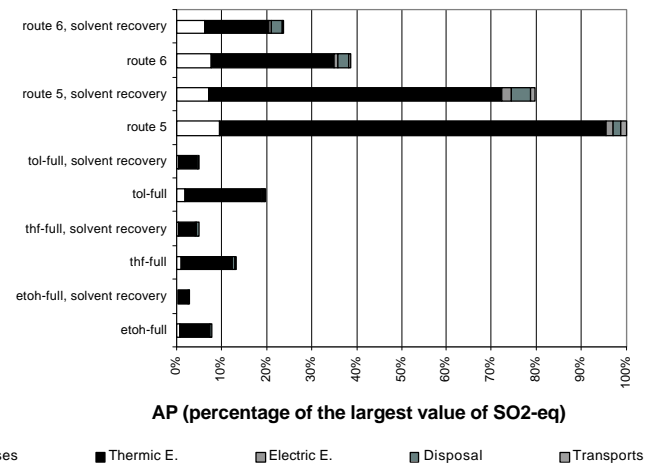


(g)

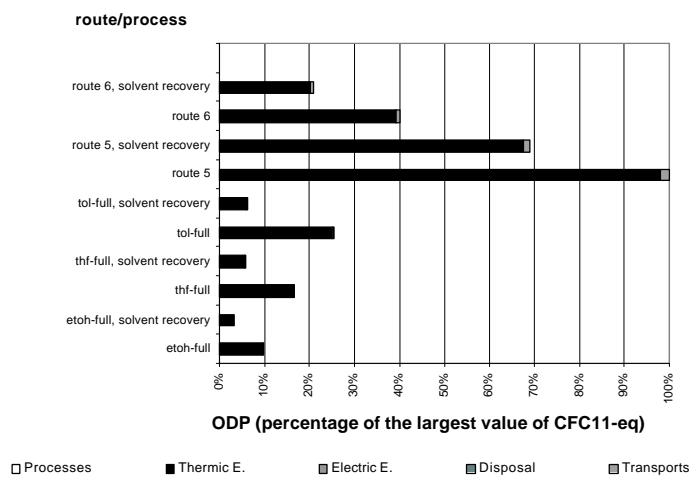
Figure 2.22 (continued) Life cycle assessment for sertraline processes: CML Method
 (e) Phototchemical oxidation, (f) Aquatic Ecotoxicity , (g) Human Toxicity.



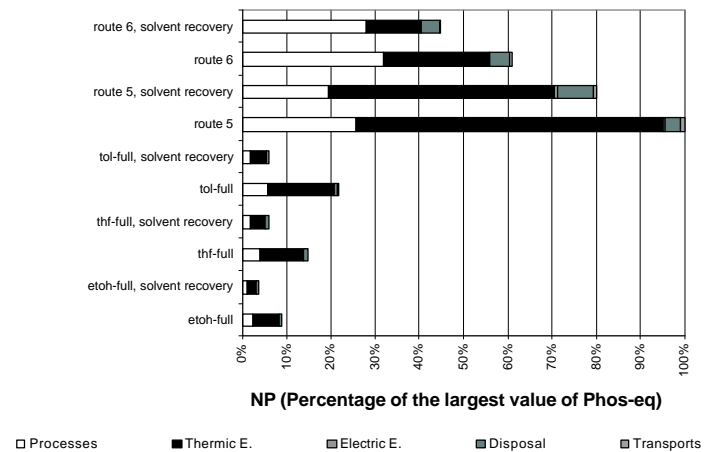
(a)



(b)

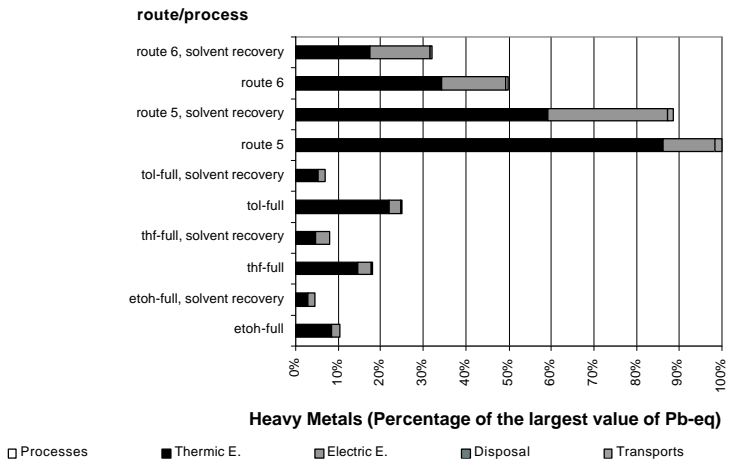


(c)

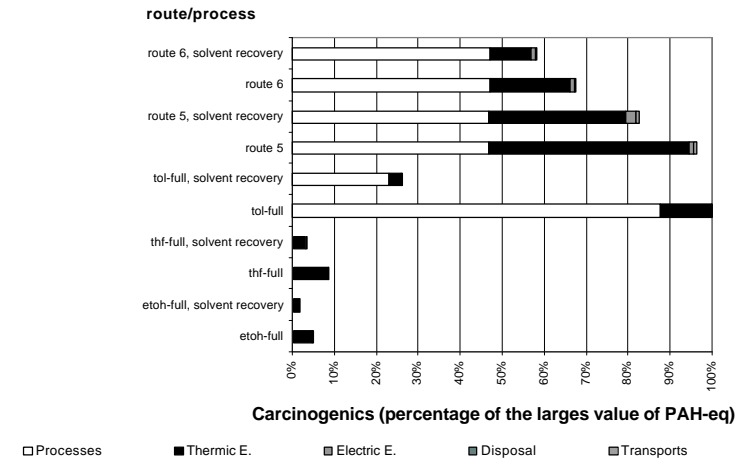


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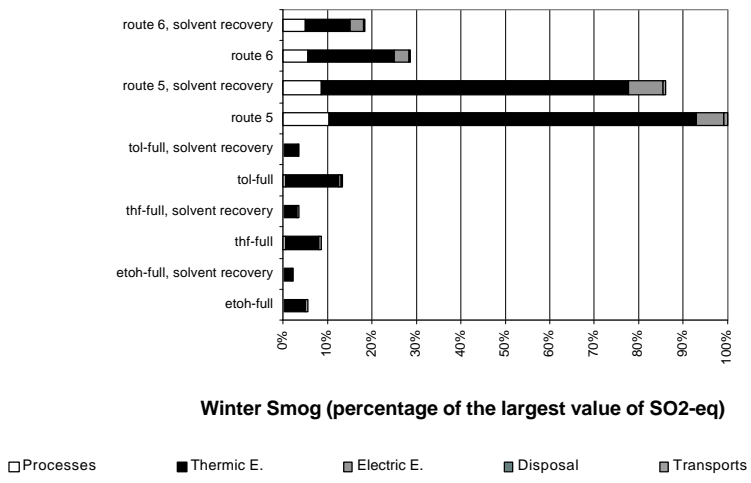
Figure 2.23 Life cycle assessment for sertraline processes: Ecoindicator 95 Method (characterization only)
 (a) Global Warming potential, (b) Acidification potential, (c) Ozone Depletion Potential, (d) Nutrifcation potential.



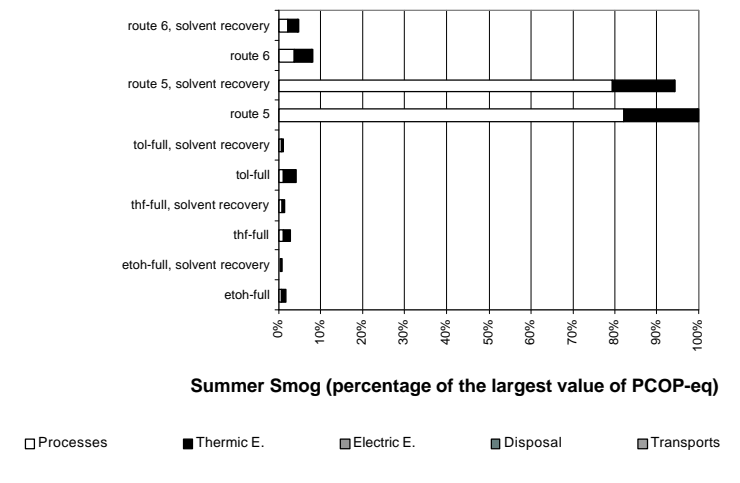
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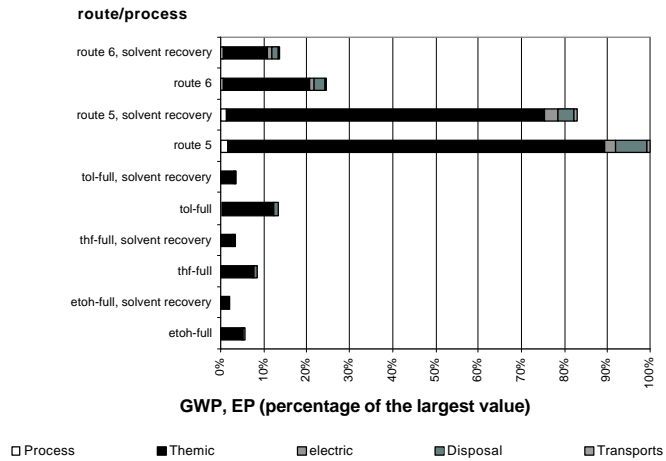


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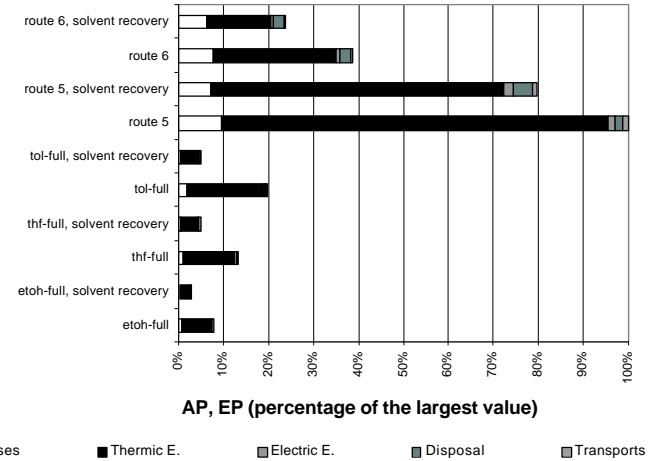


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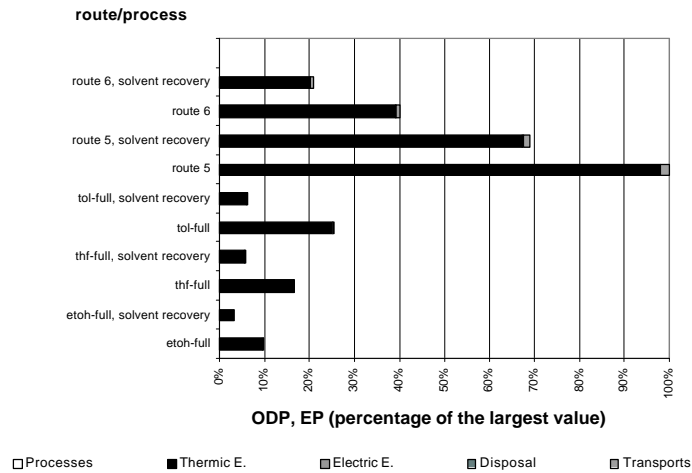
Figure 2.23 (continued) Life cycle assessment for sertraline processes: Ecoindicator 95 Method (characterization only)
 (e) Heavy metals, (f) Carcinogenics, (g) Winter Smog, (h) Summer Smog.



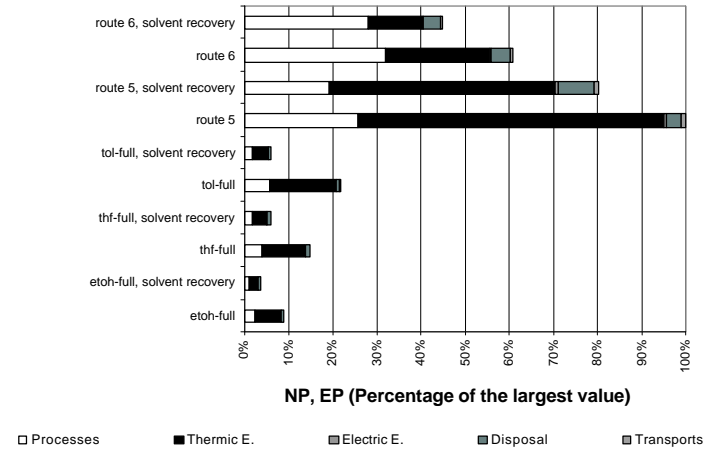
(a)



(b)

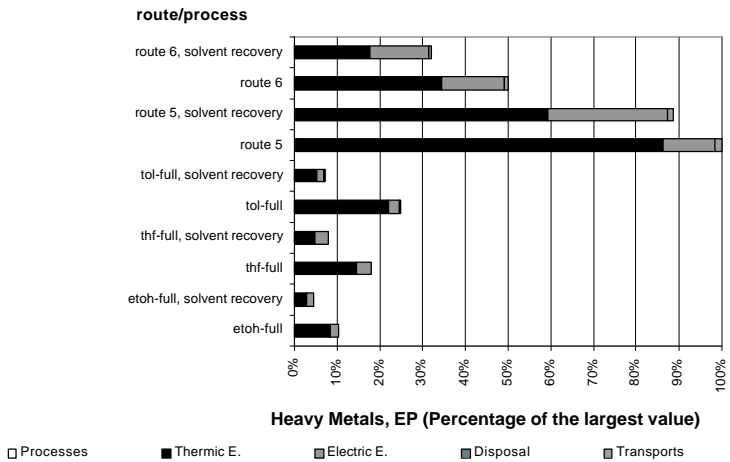


(c)

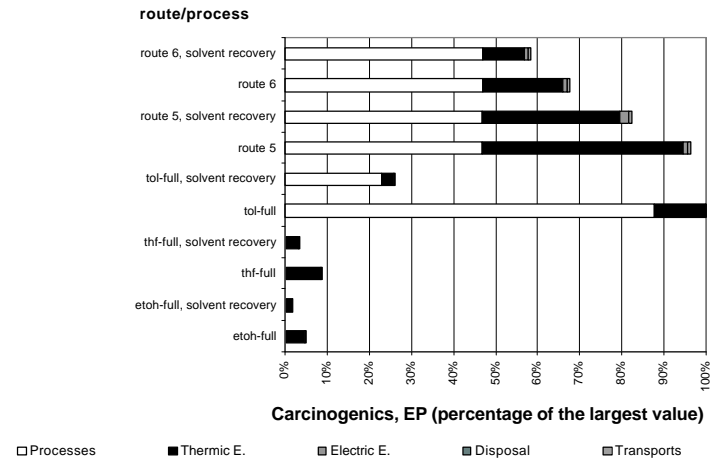


(d)

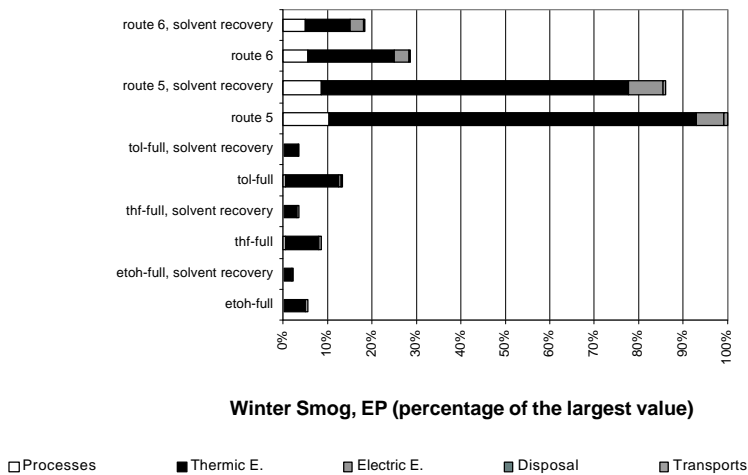
Figure 2.24 Life cycle assessment for sertraline processes: Ecoindicator 95 Method (valuation)
 (a) Global Warming potential, (b) Acidification potential, (c) Ozone Depletion Potential, (d) Nutrifcation potential.



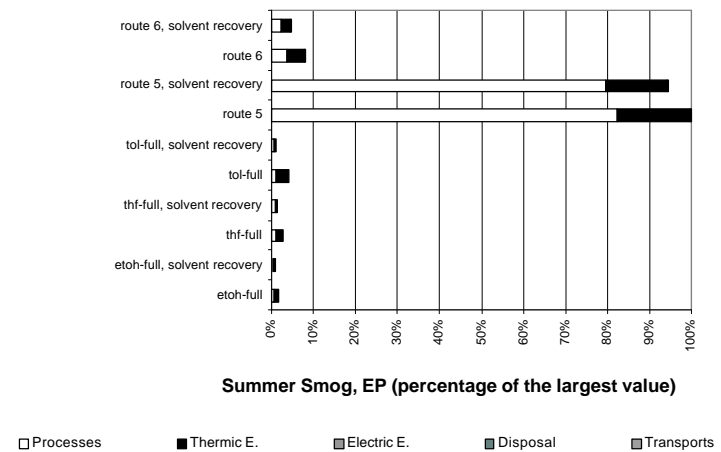
(e)



(f)



(g)



(h)

Figure 2.24 (continued) Life cycle assessment for sertraline processes: Ecoindicator 95 Method (valuation)
(e) Heavy metals, (f) Carcinogenics, (g) Winter Smog, (h) Summer Smog.

3. METHODOLOGY FOR DEVELOPING GATE-TO-GATE LIFE CYCLE INVENTORY INFORMATION

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3. METHODOLOGY FOR DEVELOPING GATE-TO-GATE LIFE CYCLE INVENTORY INFORMATION

Abstract

Life Cycle Assessment (LCA) methodology evaluates holistically the environmental consequences of a product system or activity, by quantifying the energy and materials used, the wastes released to the environment, and assessing the environmental impacts of those energy, materials and wastes. Despite the international focus on environmental impact and LCA, the quality of the underlying life cycle inventory data is at least as, if not more, important than the more qualitative LCA process.

This work presents an option to generate gate-to-gate life cycle information of chemical substances, based on a transparent methodology of chemical engineering process design (an ab initio approach). In the broader concept of a Life Cycle Inventory (LCI), the information of each gate-to-gate module can be linked accordingly in a production chain, including the extraction of raw materials, transportation, disposal, reuse, etc. to provide a full cradle to gate evaluation. The goal of this article is to explain the methodology rather than to provide a tutorial on the techniques used.

This methodology aims to help the LCA practitioner to obtain a fair and transparent estimate of LCI data when the information is not readily available from industry or literature. Results of gate-to-gate life cycle information generated using the cited methodology are presented as a case study.

It has been our experience that both LCI and LCA information provide valuable means of understanding the net environmental consequence of any technology. The LCI

information from this methodology can be used more directly in exploring engineering and chemistry changes to improve manufacturing processes. The LCA information can be used to set broader policy and to look at more macro improvements for the environment.

Keywords: ammonia production, carbon dioxide production, fugitive emissions, heat transfer efficiency, life cycle assessment, life cycle inventory, life cycle of processes, gate-to-gate life cycle, potential energy recovery, process design.

3.1. Introduction

Life Cycle Assessment (LCA) is a widely accepted tool to evaluate environmental effects of products, processes, and services (SETAC, 1993). The LCA methodology evaluates holistically the environmental consequences of a product system or activity, by quantifying the energy and materials used, the wastes released to the environment, and assessing the potential environmental impacts of those energy, materials, and wastes (Nordic Council, 1995).

A complete life cycle assessment consists of four complementary components: goal and scope definition, inventory analysis, impact assessment, and interpretation (Wenzel, 1997). The backbone of a LCA is a Life Cycle Inventory. The objective of the inventory is to create a model of the product or activity identified during the goal and scope definition.

The collection of data is the most time-consuming part in a LCA and involves a great deal of work to obtain faithful, transparent, and representative information about the

many processes in a production system. Quite often, the practitioner faces the frustration of incomplete or missing information.

When performing a LCA of a pharmaceutical or biochemical product, the amount of chemical substances involved in the supply chain increase geometrically in relation of the number of steps in the synthesis. The supply chains in this kind of production networks can reach high degrees of complexity, and therefore, the information available about the chemical substances involved is limited.

Even though the life cycle method is gradually becoming more important for industry to incorporate the environmental factor in processes, services, and products, the information about the processes is not readily available. Unfortunately, the substances that are included in the most common LCA databases represent just a part of the raw materials used in chemical and biochemical companies, and it is not easy to obtain the information from the manufacturers due to legal or intellectual property concerns. Frequently the response time from the manufacturers is extremely long, even longer than the time scope for the study.

With that background, the estimation of gate-to-gate life cycle information of chemical substances using chemical engineering process design techniques becomes a feasible and plausible LCI alternative when factual or literature information is not available for a study.

It is a normal practice that the manufacturing plants producing chemical substances use design techniques for such plants, and so no major discrepancies with reality are expected (although not proven) when used for LCI. To further overcome the later concern, the transparency of the methodology and assumptions becomes a priority.

This work presents an option to generate gate-to-gate life cycle information of chemical substances, based in a transparent methodology from chemical engineering process design. In the broader concept of a LCI, the information of each gate-to-gate module can be linked accordingly in a production chain, including the extraction of raw materials, transportation, disposal, reuse, etc.

3.2. Methodology

The methodology developed for generating gate-to-gate data suitable for creating life cycle information of chemical substances is presented schematically in Figure 3.1 and described as follows:

- 1) Search and selection of the process. In this stage the process to be evaluated is chosen. It is important to ensure that the information is as updated as possible, and it is representative of the current industrial practice and of the region under study. The phases of this first stage could be described as follows:
 - a) Investigation of the processes that have the greatest industrial importance. Collect all the information regarding the process. Patents, articles, electronic and on-line databases, industrial bulletins, and direct industrial contacts are examples of the sources of information.
 - b) Selection of the process to be used. This selection could be based on the amount, age, and scale of the information obtained, as well as on the process that is most common for the regional area under study. For the majority of chemicals there is economic competition that forces a similarity in chemical and energy efficiency.

Thus selecting any major process is probably representative, given the modest level of precision needed in complex LCI systems.

- 2) Definition of the process. This second stage determines and delimits the details of the process as such. We seek to define the mass flow of the process, the substances present in the system and the properties, and to identify the reactions involved, and the conditions of all the operations. One decides on components when there is an opportunity of selecting these (e.g. solvents), and determines the unit operations used.

The sequence of this stage could be described as follows:

- a) Description of the chemical reactions, including all names and structural formulae for reactants and products.
- b) Identification of the conditions of temperature, pressure and composition under which each operation takes place.
- c) Determination of the reaction conversion and separation efficiencies.
- d) Elaboration of the flow diagram of the process with numbered process streams indicating the temperature and pressure conditions. The utilization of standard symbols is preferred (Sandler and Luckiewicz, 1987).
- e) Search or estimation of the physical and chemical properties for all direct and indirect chemicals.

A series of rules are used in all these steps to assure a reasonable uniformity across a large number of chemicals. In this way, the rules are not manufacturer-specific as currently found, but are more universal and thus somewhat less specific than at an actual plant. These rules have been an important streamlining technique in increasing the efficiency of LCI, without losing valuable chemical

and energy information. This is a different form of streamlining from current LCI practices.

- 3) Mass Balance. In this stage, the calculations of inputs and outputs for the process are performed. All materials inputs and outputs will leave or enter the overall manufacturing system at 25 C and 1 atm., unless otherwise required specifically by the conditions of the process. This assures modules can be easily coupled without violating thermodynamic rules. The mass balance results are important from a LCI point of view since these determine the major contaminants produced in the process.

In this stage:

- a) A mass balance for a chosen basis of final product is performed. This establishes the general size of the process equipment needed in the design, normally 1,000 kg/h. This design output is intermediate between commodity chemicals and specialized chemicals, since both are included in these LCI calculations (Sandler and Luckiewicz, 1987). It is also useful to enter in the process diagram every input and output for the overall process. It is also important that an industrial scale be used, so that realistic power and equipment size are used.
- b) For estimating the chemical losses, the following are taken into consideration:
 - Any inputs not in the product or marketable by-products are process emissions. Thus mass balances of overall processes are generally achieved. The process emission amounts are defined by variables such chemical reaction conversion, the feasibility of selling by-products, the efficiency of the separation processes selected, among others.

- Material Safety Data Sheets (MSDS) are used for each major process input. This information helps to determine the major impurities entering the system to later estimate, if possible, the fate of these in the manufacturing process.
 - Fugitive losses. The rule of thumb proposed is for any liquid with a boiling point (1 atm.) of 20 to 60 C, assume a 2% fugitive loss. For any liquid with a boiling point (1 atm.) of 60-120C assume a 1% fugitive loss. For any gases assume a 0.5% fugitive loss. These percentages of fugitive losses are calculated based on the approximate overall amount of chemical present in the manufacturing system, not for each process separately and thus represent the overall manufacturing plant.
 - Any water that is in contact with the other chemicals in the manufacturing process is referred to as contaminated water, and is accounted for separately.
- 4) Energy. The results from this stage will render the amount of energy required from steam, fuel, electricity, and the energy losses of the process. In a further analysis these figures can be the basis for the calculation of the energy-related emissions (using any appropriate factors). Hence the goal is transparency. Important points to take into consideration are:
- a) Heat of reaction and heat of dilution.
 - b) Sensible heat to reach reaction conditions
 - c) Energy for separation units, which will depend on the separation chosen. The energy for every process is expressed in megajoules (MJ) per 1,000 kg of product in the final state.

- d) Energy for materials transportation. For pumps, compressors, fans, blowers, etc., the pressure needed is to transport the fluid a distance of 15m between individual processes, plus the pressure needed to move the fluid through the next unit process (pressure drop), (Walas, 1987; Woods, 1995).
- e) For all distillations use a reflux ratio, $R=1.3$ (Mix, 1978), showing separately the reboiler energy requirement and the condenser.
- f) Potential Energy Recovery. A table is prepared showing all heating requirements (positive) clearly labeled with the process name. Then all energy losses due to cooling (negative) are added, clearly labeled with the name of the process that is being cooled. Finally, an estimation of how much of this lost energy could be recovered is performed with the efficiency rules shown in Table 3.1 (Branan, 1994):

3.3. Results and Discussion

The Gate-to-Gate LCI information of the substances involved in the pharmaceutical case study formerly described were generated using the methodology described.

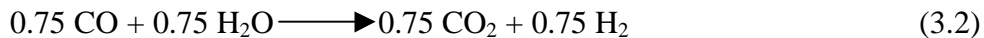
As a case study for the methodology here proposed, the results for the estimation of LCI information for ammonia are presented. Furthermore, those results obtained with the suggested methodology are compared to the values presented by commercially available databases and literature data.

3.3.1. Estimation of LCI information for ammonia production.

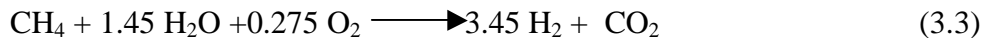
Ammonia is synthesized by a catalytic reaction of hydrogen with nitrogen (Ullmann's 1997, Slack 1973, Brykowski 1981, Kirk-Othmer 1992). The raw materials are a hydrogen source (natural gas, hydrocarbon or coal), air, and water. The process diagram for the ammonia production process is presented in Figure 3.2 where natural gas is used as a hydrogen source, and the synthesis gas is formed by a steam reforming. Carbon dioxide is also produced as a byproduct. The ammonia production process may be divided into the following sub-processes:

A) Synthesis gas preparation

The main goal of this process is to prepare a synthesis gas of nitrogen and hydrogen in the stoichiometric ratio of 1 : 3. The synthesis gas from natural gas is produced by steam reforming. Carbon monoxide is converted into carbon dioxide in a high/low temperature shift converter.



Overall reaction



B) Carbon dioxide separation/purification

The synthesis gas passes through an absorption tower to separate carbon dioxide before going to the ammonia synthesis process. Removed carbon dioxide is desorbed in a

carbon dioxide stripper. The absorbent (such as methylethylamine) is recycled to the absorption tower.

C) Ammonia synthesis

The remaining oxides of carbon in the synthesis gas are removed through a methanation process. The pure synthesis gas is compressed in a steam-turbine centrifugal compressor and combined with the recycled gas. Ammonia is synthesized by the catalytic reaction of hydrogen with nitrogen. Ammonia is refrigerated and separated by a gas/liquid separator.



The procedure shown in the methodology section was used to estimate the LCI information for ammonia production using process design techniques. A production rate of 1000 kg/hr of ammonia was taken as a basis of the calculations, thus setting the process as an intermediate size ammonia plant. Table 3.2 shows the energy requirements per process unit for ammonia production. The negative energy values in Table 3.2 represent an energy from process cooling that is recovered to use in heating steam or water. There are two types of the avoided energies – one is an avoided energy that is recovered to practically use within a process, and another is a potential avoided energy that is recovered for possible use in heating water or steam.

A summary of the LCI information for this process, including the classification of chemical losses and the estimation of potential heat recovery from the process is presented in Table 3.3. Energy-related emissions are not documented in Table 3.3. However, emissions from the combustion of the flue gas, which is recycled within the

process, in the primary reformer are taken into account. The energy-related emissions can be easily estimated by energy modules.

3.3.2. Comparison with other data

It is of interest to check the differences between estimated values and site-specific data. Since the site-specific data are not available up to now, the commercial LCA databases and the literature data are used for comparison. Table 3.4 presents the inputs, products, and emissions data from Boustead (Boustead 1996), PEMS (PIRA 1998), BUWAL 250 (BUWAL 1996) and EFMA (EFMA 1995) for the same process.

In general, it can be said that the methodology works well when compared with different published data and commercially available databases. Most of apparent differences found between the databases and the results given by the methodology seem to be related mainly to the transparency of the data.

Regarding materials, by example, the amounts of natural gas reported by BUWAL and EFMA are in the same range as the results given by this methodology. In the case of Boustead and PEMS, the amount reported includes the natural gas used for fuel. In the proposed methodology, the natural gas used for heating is 364 kg, assuming all the heating comes from steam production using only natural gas. If we add the natural gas used for fuel to the result obtained in the proposed methodology, then the total natural gas including fuel and feedstock of 810 kg of natural gas is in the range of the numbers reported by Boustead and PEMS (760kg of natural gas).

The air inputs are controlled by the stoichiometry of equation (3.4) and therefore must be on the order of 1,800 kg/1,000kg ammonia. Thus it is clear that the air inputs in

Boustead and PEMS are only of some supplementary part of the overall process (such as the air-activated control systems). The lack of transparency makes this impossible to verify, but the stoichiometry must be closer to the air requirements, as shown in our methodology and EFMA.

There is a clear lack of consistency with regard to the water input, but this may also be just an issue of transparency. The water reported in the NCSU methodology is that required to carry the chemical reaction, and it is in the same range as the data reported by BUWAL and EFMA (920-1,500 kg water/1,000 kg ammonia). This is smaller, by a factor of 10, when compared with Boustead and PEMS. On the other hand, if the cooling water is added to the reacting water (Table 3.3, inputs), the value obtained coincides pretty well with the one reported in Boustead and PEMS (11,000-12,000 kg water/1,000 kg ammonia). It is then logical to assume that the latter databases are including cooling water in the total amount of water required and reported. Thus, all five databases may be correct, but are measuring different aspects of water use and, without transparency, the differences are large. These differences would thus have a significant impact on subsequent use of ammonia LCI data.

Reporting products and by-products is also subject to a need for clarity. With the same basis, 1,000 kg of ammonia, the stoichiometry leading to CO₂ is relatively fixed. Three databases chose to identify the carbon dioxide (range, 1,150-1,300 kg/1,000 kg ammonia, Table 3.4) as a byproduct. However, two other reported the carbon dioxide as an emission.

With use of any one database for the LCI of ammonia, the variability of carbon dioxide emissions is wide, even though the underlying chemistry is similar. In the

Boustead and PEMS databases, the reported carbon dioxide emissions are remarkably larger than in the rest of the databases. Applying the reaction stoichiometry (44 kg of carbon dioxide produced by 16 kg of methane) to the total amount of natural gas required reported in these two data sets (760 kg natural gas/1,000 kg of ammonia), which includes both natural gas used for heating and for the reaction, the total carbon dioxide formed was estimated in 2,090 kg CO₂/1,000 kg NH₃, which is similar to the total amount of CO₂ reported. The latter is an indication that the carbon dioxide emissions reported by Boustead and PEMS very likely include the emissions produced during the heating of the processes. On the other hand, the carbon dioxide emission reported in this study is that which is unrecovered by the carbon dioxide byproduct processes, and thus is a residual emission.

Emissions in the case study are the sum of estimated fugitive losses and the estimated emissions from the combustion of the flue gas, which is recycled from an ammonia separation process. Since the fugitive emissions are not normally assessed in production plants, and therefore not reported, the differences in the emissions are most likely attributable to the additional estimation of fugitive emissions, which are normally not measured in many LCI studies or corporate reports. As for carbon dioxide , some of data sets treat carbon dioxide formed as an emission, while the case study reported most of it as a byproduct, which is the current industrial practice.

The other larger chemical losses to air are generally 100-fold lower than carbon dioxide, hence variability of these reported emissions would be expected to increase. Losses of argon, hydrogen, and ammonia reported in our study, are estimates of fugitive emissions often not reported in regulated permit requirements. The nitrogen oxides are

also produced in side reactions. However, there is no SO_x reported since sulfur is largely absent from the process chemistry and the above comparative analysis does not include emissions from heating.

Table 3.5 shows the energy data available in the databases mentioned above, plus some extra information found in the literature. Total energy requirement in the ammonia manufacturing process ranges from 6,094 MJ to 15,964 MJ. Steam reforming is used in Brykowski's data (Brykowski, 1981). The energy requirement depends on type of unit process, efficiency of boiler, and efficiency of energy recovery.

The calculations of the energy balance in the case study were reviewed by an industrial person. It was suggested that a compressor for the natural gas was not required, that 100% efficiency could be applied to the heat recovery A and B, that preheating air at the primary reformer was not necessary, and so on (Weimer 1999). Considering his suggestions, the energy requirement decreased by about 20% of the original calculation, and are those listed in Table 3.5.

Specific analysis of the total energy separates the needs for electricity and heating of processes and process streams. The design-based methodology yielded an intermediate value for heating, 12,559 MJ/1,000 kg ammonia (databases range, 6,094-14,696 MJ/1,000 kg ammonia). However, we have a higher electricity estimate. Since electricity is only about 4% of the total energy, the influence of the overprediction is of less consequences to total energy requirements.

3.4. Conclusions

Unfortunately, the substances that are included in the most common LCA databases represent just a part of the raw materials used in chemical and biochemical companies, and it is not easy to obtain the information from the manufacturers due to legal, or intellectual property concerns. Besides, frequently the response time from the manufacturers are extremely long, even longer than the time scope for the study.

Therefore, it is common that the practitioners suffer from incomplete or missing information. This sometimes becomes one of the uncertainty sources in the LCA outcome. Furthermore, it could make LCA practitioners give up the implementation of LCA.

LCI information from the North Carolina State University methodology (ab initio calculations) suggested in this paper is useful to LCA practitioners when the information in both foreground and background system is not available. It can reduce the uncertainty associated with the data gaps.

In general, it was found that the results obtained with the proposed methodology are consistent with the existing information. In the case study for ammonia production, the apparent differences found between this methodology and other databases are mainly due to the degree of transparency of the information presented. Another source of differences is that this methodology includes additional issues that normally are not measured (e.g. fugitive emissions), and therefore these are not likely to be reported in other databases.

The design-based approach using repeatable rules provides very comparable LCI values to the industrial measured information when one examines the large parameters,

inputs, by-products, CO₂ emissions, and specific energy requirements. An industrial verification correction of about 20% in energy led to the closer results from the design-based approach. However, even without this refinement, the major process emissions and inputs were close to field measurements and energy, within 20%. In the large scale use of LCI information for complex studies, such variation is small compared to having to use zero values because data are unavailable.

Like other methodologies, this one has uncertainties. For instance, the uncertainties may be caused by the choice of efficiency of reactor/separation, the efficiency of boiler/heat transfer, or the choice of process types. Sensitivity analysis however, can overcome those uncertainties.

It also needs to be taken into account that the methodology proposed is intended to be a dynamic tool. The “rules of thumb” here proposed are open to change with the current trends of the industrial production processes, the improvements of process operations, and of pollution prevention methods and technologies (e.g. fugitive emissions). Such changes can be done in a very transparent approach for improvement.

Another merit of this methodology is the identification of key unit within a process. Since this calculation is a microscopic analysis, it is easy to identify a key unit. Therefore, LCI information from this methodology can be used more directly in exploring engineering and chemistry changes to improve manufacturing processes.

3.5. References

- Boustead, I. (1996): Primary data for operation. Ammonia Gas Production. No. 3667.
- Branan, C. R. (1994): Rules of Thumb for Chemical Engineers, Gulf Publishing Company.
- Brykowski, F.J. (1981): Ammonia and synthesis gas, Noyes Data Corporation.
- BUWAL 250 (1996): Swiss Federal Laboratories for Materials Testing and Research. EMPA, Lerchenfeldstr. 5, CH-9014, St. Gallen.
- EFMA. (1995): Production of Ammonia, European Fertilizer Manufacturer's Association, Brussels, Belgium
- Kirk, R.E.; Othmer, D.F. (1992): Kirk-Othmer Encyclopedia of Chemical technology, 4th ed., John Wiley & Sons.
- Mix, T.J.; Dweck, JS.; Weinberg, M. (1978): CEP, [49-55]
- Nordic Council of Ministers, Nordic Guidelines on Life Cycle Assessment. (1995): Nordic Council, The Nordic Council.
- PIRA International. (1998): PEMS 4. Randall Road. Leatherhead. Surrey. England.
- Sandler, H.J.; Luckiewicz, E.T. (1987): Practical Process Engineering: A Working Approach to Plant Design, XIMIX Inc. Philadelphia, PA, 638p.
- Slack, V.; James R.G. (1973): Ammonia, Marcel Dekker, Inc.
- Society of Environmental Toxicology and Chemistry. (1993): Guidelines for Life Cycle Assessment: A Code of Practice.
- Ullmann, F. (1985): Ullmann's Encyclopedia of Industrial Chemistry, 5th ed., John Wiley & Sons.
- Walas, S. M.(1987): Chemical Engineering, March 16, [75-81]

Weimer, R.F.(1999): personal communication.

Wenzel, H.; Hauschild, M.; Alting, L. (1997): Environmental Assessment of Products.

Chapman and Hall.

Woods, D.R. (1995): Process Design and Engineering Practice. Prentice Hall.

Table 3.1. Heat recovery efficiency.

Temperature of Hot Stream Being Cooled	Heat Recovery Efficiency
>500°C	75%
301C-500°C	60%
151C-300°C	45%
60C-150°C	25%
<60°C	0%

Table 3.2. Energy requirement for each unit process and energy recovery.

<u>Energy Input (MJ/1000 kg product)</u>			<u>Cooling Requirements (MJ/1000kg product)</u>				
<u>Unit Operation</u>	<u>Energy Input</u>	<u>Cumulative Energy Input</u>	<u>Unit Operation</u>	<u>Energy Loss</u>	<u>Cumulative</u>	<u>Temp. (°C)</u>	<u>Heat Recovered</u>
Compressor A (1)	7.00E+02	7.00E+02	Secondary reformer (5)	-1.27E+03	-1.27E+03	974	-9.50E+02
Pump A (2)	3.46E-03	7.00E+02	Heat recovery A (6)	-3.52E+03	-4.78E+03	974	-3.52E+03
Primary reformer (3)	9.86E+03	1.06E+04	Heat recovery B (8)	-1.38E+03	-6.16E+03	427	-1.38E+03
Pump B (4)	3.42E-02	1.06E+04	Heat recovery C (10)	-2.27E+03	-8.43E+03	266	-1.02E+03
High Temp. Shift converter (7)	-	1.06E+04	Cooler A (12)	-3.37E+02	-8.77E+03	90	-8.41E+01
Low Temp. Shift converter (9)	-	1.06E+04	Cooler B (19)	-5.68E+01	-8.83E+03	82	-1.42E+01
Pump C (11)	4.71E-02	1.06E+04	Cooler C (23)	-2.17E+03	-1.10E+04	80.6	-5.42E+02
Gas/liquid separation (13)	-	1.06E+04	Heat recovery D (26)	-6.84E+02	-1.17E+04	313	-4.10E+02
CO2 absorber (14)	-	1.06E+04	Cooler D (28)	-3.02E+02	-1.20E+04	121	-7.54E+01
Pump D (15)	4.73E-02	1.06E+04	Cooler E (31)	-1.07E+02	-1.21E+04	177	-4.81E+01
Heat exchanger A (16)	-	1.06E+04	Cooler F (34)	-1.05E+03	-1.31E+04	93	-2.62E+02
CO2 stripper (17)	2.80E+03	1.34E+04	Heat recovery E (39)	-1.41E+03	-1.45E+04	371	-8.45E+02
Pump E (18)	1.53E-03	1.34E+04					
CO2 storage tank (20)	-	1.34E+04					
Pump F (21)	4.39E-02	1.34E+04					
Pump G (22)	5.85E-02	1.34E+04					
Heater A (24)	8.96E+02	1.43E+04					
Methanator (25)	3.36E+01	1.43E+04					
Pump H (27)	8.14E-03	1.43E+04					
Steam turbine C. Compressor A (29)	3.37E+03	1.77E+04					
Pump I (30)	2.88E-03	1.77E+04					
Steam turbine C. Compressor B (32)	1.38E+03	1.90E+04					
Pump J (33)	2.83E-02	1.90E+04					
Refrigerator A (35)	3.32E+02	1.94E+04					
Ammonia separator A (36)	-	1.94E+04					
Heat exchanger B (37)	-	1.94E+04					
NH3 converter (38)	1.80E+02	1.96E+04					
Refrigerator B (40)	4.85E+00	1.96E+04					
Ammonia separator A (41)	-	1.96E+04					
Ammonia storage tank (42)	-	1.96E+04					
Potential energy recovery		-9.15E+03					
Total		1.04E+04	Total recovery				-9.15E+03

Table 3.3. Summary of Life Cycle Inventory Information.

Product:	Ammonia
Basis:	1,000 kg/h ammonia
Reference:	Slack, V. and James R.G., Ammonia, Marcel Dekker, Inc., 1973. Brykowski F.J. Ammonia and synthesis gas, Noyes Data Corporation, 1981.
Comments:	All mass and energy units per hour are equivalent to per 1,000 kg of ammonia.

Inputs	Amount	Units	Comments
Air	1,796.85	kg/hr	688.6 kg of air is used in burning flue gas.
Natural gas	446.75	kg/hr	
Water	1,200	kg/hr	12,000 if cooling water is included with the water used in reaction.
Total	3,443.6		

Product	Amount	Units	Comments
Ammonia	1,000	kg/hr	99 % purity (9.4 kg/hr water)
Carbon dioxide	1,179	kg/hr	100% purity

Process emissions*	Amount				Units	Comments
	Air	Liquid	Solid	Solvent		
Ar	13.29				kg/h	
CH4	2.23				kg/h	
CO	2.9				kg/h	
CO2	52.54				kg/h	
H2	3.07				kg/h	
NH3	6.42				kg/h	
NO	3.52				kg/h	
NO2	5.39				kg/h	
Mass balance difference	-30.72				kg/h	

Water (513 kg/h), oxygen (27kg/h) and nitrogen (560 kg/h) are not included in this table as process emissions.

Energy Requirements	Amount	Units	Comments
Electricity	7.00E+02	MJ/hr	
Heating – Steam	9.00E+03	MJ/hr	Includes a heat transfer efficiency of 85%
Heating fuel	9.86E+03	MJ/hr	Includes a heat transfer efficiency of 85%
Cooling refrigeration	-	MJ/hr	
Cooling water	-1.08E+04	MJ/hr	
Potential Heat Recovery	-9.15E+03	MJ/hr	
Net Energy**	1.04E+04	MJ/hr	

Notes:

* Oxygen and nitrogen are not included;

** Energy requirement minus potential heat recovery from cooling systems

N/A not applicable for this chemical process

Table 3.4. Comparison of inputs, products and emissions per 1,000 kg of ammonia produced. Data are only the process for production of ammonia.

Parameter	Case Study	BUWAL 250	Boustead	PEMS	EFMA^d
Process type	Steam reforming	Steam reforming	n.r.	n.r.	Steam reforming
Inputs					
Natural gas, kg	446.75	467	760 ^a	760 ^a	458
Air, kg	1,796.85	n.r.	5.02	6.6	1,100
Water, kg	1,200 (12,000 ^c)	920	11,166	11,000	1,500
Products					
Ammonia, kg	1,000	1,000	1,000	1,000	1,000
CO ₂ , kg	1,179	1,156	^b	^b	1,150 – 1,300
Emissions					
Ar, kg	13.29	n.r.	n.r.	n.r.	n.r.
Methane, kg	2.23	7.14	n.r.	16 ^c	n.r.
CO, kg	2.9	0.025	0.002	0.04 ^c	<0.03
CO ₂ , kg	52.54	436.1	1,975 ^d	2,055 ^d	500
Non-methane VOC, kg	n.r.	0.928	n.r.	n.r.	n.r.
Hydrogen, kg	3.07	n.r.	n.r.	n.r.	n.r.
Ammonia, kg	6.42	n.r.	0.001	0.001	n.r.
NO _x (as NO ₂), kg	8.91	0.304	1.17	2.6 ^d	0.6 – 1.3
SO _x (as SO ₂), kg	n.r.	0.010	0.036	0.78 ^d	< 0.01

n.r. Not reported.

^a Sum of fuel and feedstock

^b Reported as emissions

^c Includes transport emissions. No transport distance is indicated.

^d Emissions are sum of process-related emissions and energy-related emissions.

^e If cooling water is added to reaction water.

Table 3.5. Comparison of energy per 1,000 kg of ammonia produced. Data are only the process for production of ammonia.

Parameter	Total Heating [MJ]	Electricity [MJ]	Total Energy [MJ]
Energy			
Case study	12,559	700.15	13,259
BUWAL 250	6,094	n.r.	6,094
PEMS	11,294	320 ^a	11,614
Boustead	11,294	330	11,624
EFMA	n.r.	n.r.	8,000 – 10,000
Brykowski	14,696 ^b	475	15,171

n.r. Not reported.

^a Calculated using the European Grid (medium voltage) reported in PEMS

^b Potential energy recovery rule in this study is adopted to modify the energy calculation for energy recovery within the process or plant.

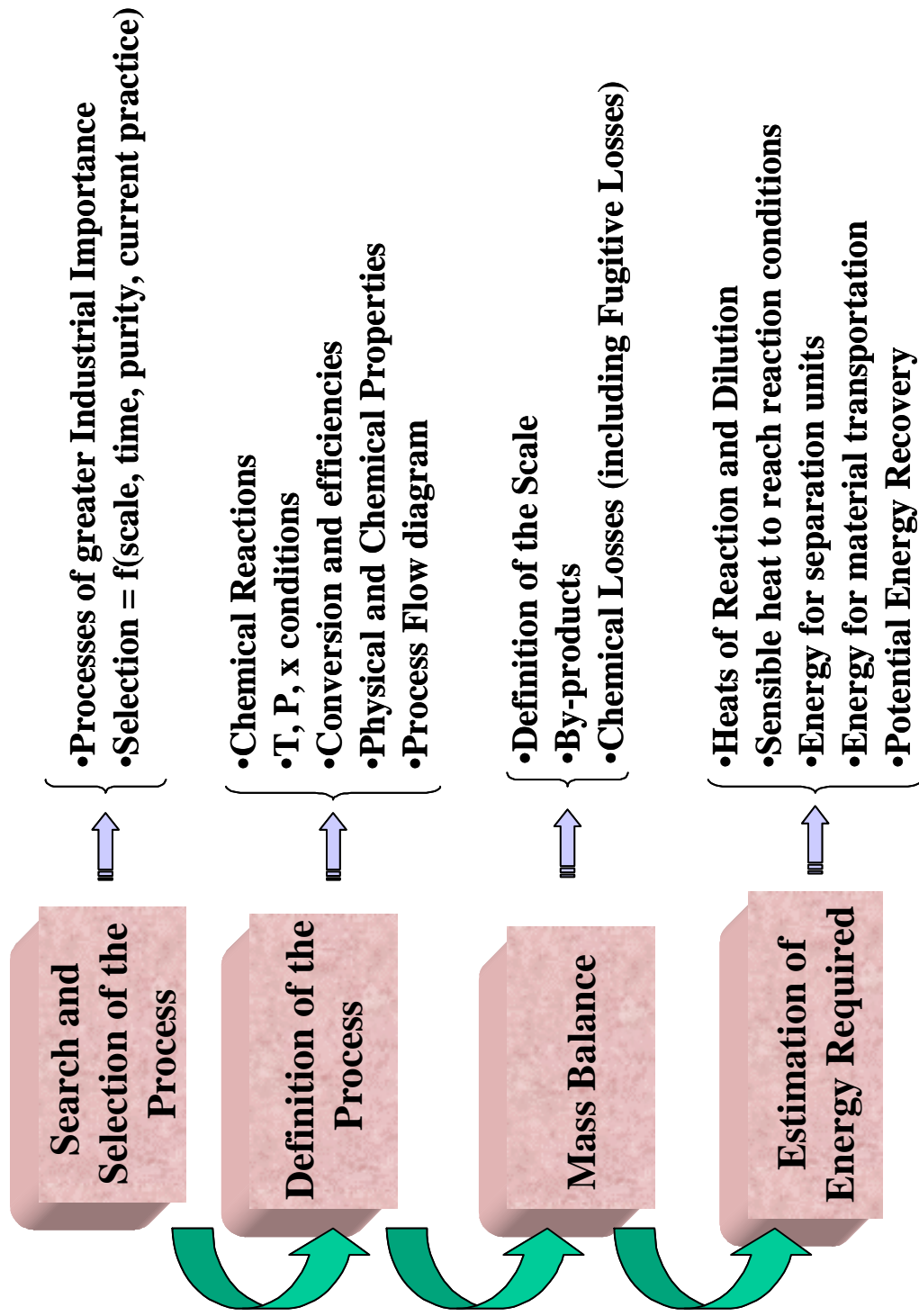


Figure 3.1. Methodology for developing Gate-to-Gate Life Cycle Inventory information.

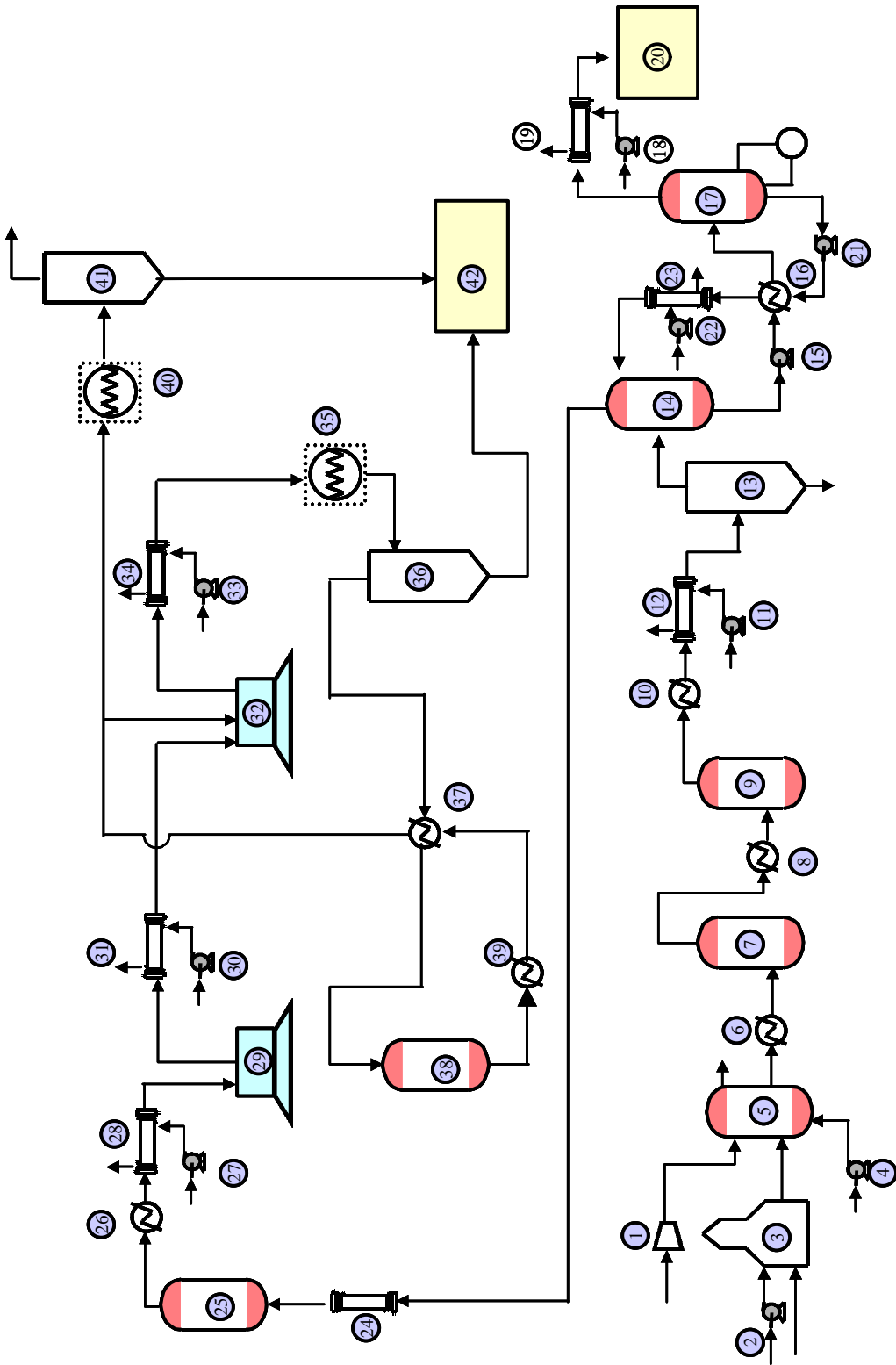


Figure 3.2. Process diagram for ammonia manufacturing process. The process operations are indicated in Table 2

4. ENERGY SUB-MODULES APPLIED IN LIFE CYCLE INVENTORY OF PROCESSES

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4. ENERGY SUB-MODULES APPLIED IN LIFE CYCLE INVENTORY OF PROCESSES

Abstract

The heating and cooling of unit processes (utilities) are often the most significant energy fraction of a gate-to-gate life cycle inventory (LCI) for individual chemicals. Electricity usage is typically a smaller factor. An LCI of a manufacturing process for a specific chemical has been used to identify the heating and cooling requirements.

This paper demonstrates the sub-modules used to convert these utilities into actual energy-related emissions for use in the LCI of a specific chemical. Assumptions and results of the unit operation inventory data and of the potential life cycle burdens are clearly stated to foster the objective of transparency.

A user may substitute another energy grid, fuel sources, or efficiencies based on some site-specific data. The sub-modules utilize a design basis for calculating the utility emissions. Results may be used in LCI studies in the chemical, biochemical and pharmaceutical industries.

Keywords: life cycle of processes, energy-related emissions, energy sub-modules, gate-to-gate life cycle inventory, utilities

4.1 Introduction

Life cycle analysis techniques (LCA) have emerged in the last 30 years and are now growing in applications for environmental issues (Colberg and Overcash 1996). A LCA is defined as “a process to evaluate the complete environmental burdens associated with a product, process or activity.” (SETAC 1993)

A complete life cycle study consists of three complementary components: inventory analysis, which is a compilation of all material and energy requirements associated with each stage of product manufacture, use and disposal; impact analysis, a process in which the effects of the inventory on the environment are assessed; and improvement analysis which is aimed at reducing the product impact on the environment (Pistikopulos 1994).

The life cycle inventory (LCI) can be used in process analysis, material selection, product evaluation, product comparison and policy-making. Also, it can be used internally and externally to an organization, with the external application requiring a higher standard of accountability (USEPA 1993). When performing a life cycle inventory or assessment to compare two production processes, or when estimating data in gate-to-gate LCIs, the practitioner would very likely face situations in which energy transfer occurs, due to necessary changes in temperature of the streams involved, chemical reactions and process specification, among others. This situation is true especially in the chemical, biochemical and pharmaceutical industries.

Within a manufacturing plant, as one evaluates an LCI it is common to document the amount of heating and cooling required. This is often the largest energy component in chemical manufacturing. The aim of this paper is to present representative engineering modules which link the requirements for heating and cooling to the environmental emissions

and basic utilities needed. In a sense, these modules reflect the inefficiency (chemical and thermal) in achieving heating or cooling in manufacturing. Process sub-modules for cooling and heating requirements were developed for a cooling tower, refrigeration cycles, dowtherm heat exchange, and steam generation. The calculations of energy emissions related to the generation of electricity are not included in the scope of this paper.

This methodology employs either field information that might be readily available from the site under study, standard chemical engineering process design techniques, or both. For this reason is expected to provide a transparent and flexible tool to estimate the energy-related emissions that are specific to a given production process. The transparency of the tool resides in the fact that all the assumptions made for the calculations will be available to the user of the LCI and will also be based on the same standard techniques that are normally used to design and build the production processes. The methodology is intended to also be flexible in such a way that when the conditions of the process change (e.g. using 120 C saturated steam vs. 300 C superheated steam), the calculations should be easy to modify to the new situation.

4.2. Methodology

4.2.1. The concept of energy sub-modules.

A process requires of material and energy inputs to produce typical chemical products. The energy required is mostly thermal or mechanical, with the latter provided by electricity in a great number of cases. These requirements translate into “heating requirements” and “electricity usage”, respectively.

At the same time, heat has to be dissipated to fulfill the functions of the system or to comply with regulations or standards. The necessity of dissipating thermal energy has been labeled as “cooling requirements”.

To satisfy the electricity usage and heating and cooling requirements, another process must take place to provide energy sources or sinks (Figure 4.1). Those processes will have materials as inputs and outputs that can be readily traced back until extraction from the earth (e.g. natural gas, coal, potential energy of water). Moreover, these energy requirements can be easily broken down into material inputs and outputs (e.g. electricity, burning oil). In the case of heating requirements, the process for production of steam is an example. In the case of cooling requirements, we use a cooling tower as a representative example. (Figure 4.1)

The set of information about a process that satisfies energy requirements has been called an energy sub-module. The energy sub-module comprises the amount of material inputs and outputs for that sub-module, as well as the amount of the energy required that can easily be converted into material inputs and outputs (primary sources of energy) or that can be addressed via an electricity sub-module.

The development of an electricity sub-module is not part of the present work, since there is a reasonable amount of life cycle information about electricity generation, including regional and national grids, and different generation processes (Dumas 1997; EMPA 1997; PIRA 1998; Pre Consultants 1998).

The energy sub-modules presented in this work were selected as the most common for heating and cooling in chemical manufacturing. These are cooling tower, refrigeration cycle using a fluid such as SUVA 123, refrigeration cycle using ammonia, heating using

Dowtherm A, steam generation using natural gas and finally steam generation using No. 2 oil. The operating temperature ranges for these energy sub-modules, are shown in Table 4.1.

The energy sub-modules contain information on material inputs and outputs, and the energy required for the sub-module is broken down to the primary energy carrier (e.g., gas, oil) and electricity usage. Electricity usage is not further converted into inputs and outputs at this stage, so as to allow the flexibility for use of various electricity sub-module models that fit the characteristics of the process in the best way.

Once the energy sub-modules were completed, a comparison of the main potential environmental burdens of all of these was performed using the methodology of Ecoindicator 95, with the calculation aid of the environmental life cycle analysis tool “ECOPRO”. This comparison included the environmental burdens of the extraction and production of the fuels and raw materials.

A description of the process conditions and assumptions for the development of energy sub-modules in this work is presented next.

4.2.2. Cooling Tower

This sub-module is an example of using a combination of specific data with process design calculations. It was developed as part of a site-specific life cycle study, but data were also developed for a general case. The cooling tower scheme and the normal temperatures of the inlet and outlet water for both the site-specific and the generic sub-module are shown in Figure 4.2.

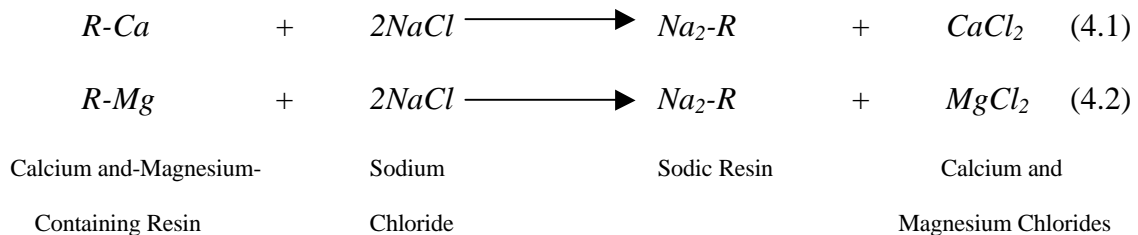
In the site-specific case, an actual cooling tower was taken as a basis for the calculations. The cooling tower has design flow of 10,000 gallons of water per minute

(37.85 m³/min), and operates, on average, at a heat load of 10,300,000 ton-hr of cooling/year (a ton of cooling is equal to 211 kJ/min), which gives an average of 6.6 kJ of cooling/ kg cooling water flow. The total average electricity usage is 1,540,000 kWh per year.

The main material input for this sub-module is the water introduced to the tower to make-up for the evaporative losses, the water that gets “carried-over” by the air, and the blowdown. The other inputs considered are the pre-treatment chemicals added to the water. The air flow into the cooling tower was not considered as an input or output because it is readily available from nature and it is returned to nature with no major thermal difference of conditions. The outputs considered are the water losses, water blowdown, and the pretreatment waste.

The average water make-up rate according to company’s records is 59.6 gpm (0.226 m³/min). The blowdown was considered as a 5% of the make-up water with 95% being evaporation and water carried over into the air (McKelvey 1959, Willa 1987).

Ionic exchange pretreatment for make up water was taken as a calculation basis (Fountain 1982). A total hardness of 100 mg/L of Ca²⁺ and 155 mg/L of Mg²⁺ was assumed in the water to be pretreated (Hill 1990). An efficiency of 100% in hardness removal was assumed in the calculations. The ion exchange resin replacement was neglected because it is continuously regenerated. The input considered was the sodium chloride solution used for resin regeneration, estimated as 555 mg of NaCl/L of water treated (Hill 1990), based on the following equations:



The output from the water pretreatment consisted of 4.92 g of sludge/L of water treated, containing 5.6% w/w of calcium chloride and 4.4% w/w of magnesium chloride and 4.4% of Na⁺ in solution. The volume of this sodium chloride solution was fixed in a quantity equal to the estimated amount of sludge leaving the pretreatment unit.

As it is shown in Figure 4.2, the temperature difference between the input and output water in this site-specific tower is only 1°C (nominal value), not representing the typical operation range for a cooling tower. Therefore, to obtain a generic cooling tower sub-module, all the inputs and outputs for the site-specific tower were scaled-up for a temperature range of 25°C (Walas 1987; Willa 1987), taking as basis the same water flow. The latter conditions correspond to an average of 88 kJ of cooling/ kg cooling water flow for the generic tower.

4.2.3. Refrigeration Cycle

Two refrigerant fluids were considered for this sub-module: ammonia and SUVA 123 (Ethane, 2,2-dichloro-1,1,1-trifluoro-). Figure 4.3 shows the general scheme for this sub-module, with the temperatures and pressures corresponding to SUVA 123.

For SUVA 123 a typical saturated refrigerant cycle was assumed (Lemmon et. al. 1997; Sibley 1983), with a vaporizing temperature of -23°C (1.46 psia, 10 kPa), and condensing temperature of 20°C (11 psia, 75.8 kPa). Under these conditions the heat of vaporization of SUVA 123 for the cycle is 22.26 kJ/mol and consequently a flow of refrigerant of 87 kg refrigerant/h-ton of refrigeration is needed (6.86×10^{-3} kg SUVA 123/kJ of refrigeration). The condensation energy is assumed to be released by a cooling tower (1.22 kJ/kJ of refrigeration).

For ammonia, a typical saturated refrigerant cycle was assumed with the same operating temperatures as in the sub-module with SUVA 123. The vaporizing temperature was also of -23°C (24.23 psia, 167 kPa), and condensing temperature of 20°C (89.27 psia, 615.3 kPa). Under these conditions the heat of vaporization of ammonia for the cycle is 20.20 kJ/mol and consequently a flow of ammonia of 10.6 kg ammonia/h-ton of refrigeration is needed (8.45×10^{-4} kg ammonia/kJ of refrigeration). The condensation energy is assumed to be released by a cooling tower (1.16 kJ/kJ of refrigeration).

For both refrigeration fluids a compressor efficiency of 50% was used in the calculations (Dosat 1997; Olivo 1990). The material inputs considered were the refrigerant added to make-up for the losses, and the maintenance materials (oil and filters). The refrigerant losses were calculated assuming an average make-up of 10% of the refrigerant mass per year (Chacón, 1997), and the maintenance wastes regarding oil and filter changes for the compressor were estimated in an average of 0.4 kg/HP of compressor.

The pumping requirements for the refrigerant and the condensing liquid were calculated with the general equation presented by Perry (Perry, 1997). Two pumps for the refrigerant stream and one pump for the condensing fluid were assumed. A total head of 13 ft of H₂O for each refrigerant pump and 14 ft H₂O for the condensing liquid were used in the calculations (Dosat 1997; Olivo 1990).

4.2.4. Steam

The steam sub-module consists of the generation of saturated steam using a package boiler, assuming an ion-exchange pretreatment for the input water (Figure 4.4). The sub-module was developed with two fuels for combustion: natural gas and No.2 Oil. The system

was modeled for production of saturated steam at two pressures: 50 lb/in² and 135 lb/in² (345 and 931 kPa., respectively).

For the estimation of steam requirements, it is assumed that during the heat exchange process, the vapor enters as saturated steam and leaves as saturated liquid. Water entering the boiler is assumed to be at 71°C, which accounts for the heat losses during piping and storage, and the mixing with make-up water at 20°C. A boiler efficiency of 80% (MJ steam produced/MJ fuel used) was assumed (Cohen-Hubal 1992). This efficiency accounts for the possible heat recovered from the emissions in a preheater for gas and air.

The material inputs considered were fuel, air, chemicals for water pretreatment, and water for make up. The material outputs taken into consideration were combustion emissions, blowdown, evaporative losses and waste from water pre-treatment.

Combustion gases were calculated using material and energy balances. The heat value of the natural gas used was 54,200 kJ/kg, and 47,585 kJ/kg for the oil. An air excess of 25%, on a molar basis, was used in the case of natural gas, and 22% in the case of oil (Cohen-Hubal 1992; Perry 1997).

Blowdown was estimated as 5% of boiler capacity (kg steam produced/MJ); evaporative losses as 8% of boiler capacity and electricity requirements of 3.87×10^{-3} kWh/kg of generated vapor (or 1.40×10^{-2} MJ/kg of generated vapor); with 62% used for water pumping and the rest for fuel pumping (Cohen-Hubal 1992).

For pretreatment chemicals, the same assumptions for the pretreatment of cooling tower water were applied.

4.2.5. Dowtherm A

Figure 4.5 shows the flow diagram for the sub-module for heating with Dowtherm A. The whole system is maintained at atmospheric pressure, and the vaporizer utilizes natural gas as primary energy carrier. Pumping is needed for the return of the Dowtherm. The Dowtherm is assumed to leave the vaporizer as saturated vapor and return to it as saturated liquid. The heat exchange efficiency for the vaporizer is assumed to be 80%. This efficiency accounts for the possible heat recovering from the emissions in a preheater for gas and air. Under these conditions the heat of vaporization of the Dowtherm A is 290.5 kJ/kg, and consequently a flow of Dowtherm A of 3.44 kg Dowtherm/MJ of heating is needed.

The inputs included natural gas (for the vaporizer) and electricity. The outputs considered were the combustion emissions of natural gas. Electricity requirements are considered for pumping the return stream and for natural gas and air blowers are included. The heat value of the natural gas used was 54,200 kJ/kg. Dowtherm losses are assumed to be negligible in the calculations.

4.3. Results and Discussion

The unit operation inventory results for the sub-modules corresponding to the cooling tower and refrigeration cycle are shown in Table 4.2. For the refrigeration cycle, two refrigerant fluids were used; ammonia and SUVA 123.

The type of chemicals for pretreatment and the composition of the pretreatment waste can change depending upon the kind of pretreatment that the input water has undergone. In this case the chemical needed is make-up sodium chloride solution for the ion exchanger regeneration; and the waste consists of a suspension of calcium chloride and magnesium

chloride. Also, the concentrations would vary if there is a different condition of hardness in the input water.

Table 4.3 shows the outputs that result of burning 1 kg of natural gas or No. 2 oil with the indicated amount of air. In the stricter sense of the definition, these results can be taken as a separate energy sub-module, if the energy source consists of the combustion of either fuel. During the assessment phase of a life cycle, outputs as nitrogen or oxygen would not represent any environmental burden.

Table 4.4 presents the sub-modules for heating with steam and Dowtherm A. It can be noted that with the amount of steam make-up water, pretreatment and blowdown are the same for the same steam pressure. This is because those quantities are calculated proportional to the steam required per energy unit (MJ heated); and that depends on the condition of the steam. The considerations about pretreatment are the same as for the cooling tower.

As described in the methodology, a comparison of the main potential effects was performed, including the extraction and production of electricity, fuels and raw materials. For the NaCl used in resin regeneration and the ammonia make-up, life cycle inventory information was taken from the database of ECOPRO. For the make-up of SUVA 123 (CF_3CHCl_2), production data of refrigerant R-134a ($\text{CF}_3\text{CH}_2\text{F}$) was taken as an approximation, since data for SUVA 123 were not available (Rice 1999). For electricity, the average national grid for the USA was used in the calculations (Dumas 1997).

The life cycle inventory information for natural gas and oil were taken directly from the ECOPRO database. Tables 4.5 to 4.8 show the summarized data used as life cycle inventory information for NaCl, ammonia, SUVA 123 and electricity, respectively (LCI data

for gas and oil are not shown here, but were considered using the information from EMPA, 1996).

The potential effects were analyzed using Ecoindicator 95 (characterization only). As an illustration, the results of global warming, nitrification, acidification and the contributions to winter smog and summer smog are shown in Figures 4.6 to 4.10.

In this analysis, Global Warming Potential (GWP) is expressed in CO₂ equivalents (CO₂-eq), Nitrification Potential in phosphate equivalents (Phos-eq), Acidification and Winter Smog Potentials are expressed in sulfur dioxide equivalents (SO₂-eq) and Summer Smog Potential is expressed in photochemical ozone creation potential equivalents (POCP).

Figure 4.6 shows that the potential effect in global warming is the largest for the steam generated by oil combustion, followed by refrigeration using SUVA 123 and steam generated by natural gas combustion. It is important to note that for all the heating sub-modules, the major contribution of the GWP comes from fuel combustion, while for cooling sub-modules those are derived from electricity requirements.

For acidification and winter smog, the sub-module that exhibits the larger potential burdens is refrigeration with SUVA, as shown in Figure 4.7 and 4.8. In general, for all the categories analyzed, there is lower potential environmental burdens for refrigeration with ammonia when compared to refrigeration using SUVA 123.

Furthermore, all the potential environmental burdens for the generic cooling tower are negligible in comparison with the rest of the energy sub-modules analyzed and the impacts of the site-specific cooling tower are considerably smaller than heating sub-modules and refrigeration. This is consistent with the considerably smaller amount of electricity required than the other sub-modules, and the fact that no combustion or significant oil is required.

It can also be noted that for heating with steam, the potential environmental burdens are proportional to the pressure of the steam. That is, steam at a higher pressure will represent a larger potential environmental burden in all the categories. Also, most of the potential environmental burdens appear to be less for Dowtherm A than for any of the steam sub-modules analyzed, as shown in Figure 4.6 to 4.10.

On the other hand, the utilization of one steam pressure instead of another, or steam instead of a thermal fluid; will depend on the conditions of the processes, such as the desired temperature and the plant conditions to handle pressure. Nevertheless, using boilers operated with gas instead of boilers operated with oil, when possible, brings a reduction in the overall energy-related emissions, as well as in the potential environmental burdens, according to the model presented here.

Any of the options presented here could be used directly in an analysis or could be modified to suit some specific system. Using one alternative instead of the other (e.g. ammonia vs. SUVA 123, or natural gas instead of oil) would depend on the conditions of the system. Therefore, when there is no information available about the characteristics of the sub-module needed, or when the objective of the analysis is to decide about the kind of utility to use, a sensitivity analysis is recommended to complement the results of this study.

4.4. Conclusions

The present work provides an alternate methodology for estimating energy-related emissions by relating the energy requirements of a specific process to the energy sub-modules. A summary is provided of the potential life-cycle burdens associated with these sub-modules (process utilities).

The energy sub-modules allow flexibility and transparency for any required change or adjustment to the process conditions. These can be constructed, using factual data, theoretical designs or a combination of both. The modules would be used as a part of a design-based approach to life cycle inventory studies, in which heating and cooling are specified. In general, information on utilities (steam, refrigeration, etc.) are more available, and these modules can then be used to calculate actual emissions.

For the energy sub-modules evaluated here, the generation of steam by oil combustion has the largest GWP, followed by refrigeration using SUVA 123 and finally, steam generation using natural gas. For the heating sub-modules, the major contribution to the GWP derives from fuel combustion, while for cooling sub-modules it derives mostly from energy consumption.

Moreover, the potential environmental burdens of heating with steam vary in a proportional manner with the pressure of the steam. Furthermore, lower potential environmental burdens are produced by refrigeration with ammonia in comparison with refrigeration with SUVA 123. The potential environmental burdens of the cooling tower sub-modules are considerably smaller than the impacts for the other sub-modules. Thus, using the most efficient system in each case, there will be far less environmental burden per MJ to cool than to heat.

Nevertheless, the performance of a sensitivity analysis to evaluate the effect of any change in the sub-modules over the system under study is strongly recommended, to justify the direct utilization of the results here presented or to perform any necessary adjustment to the current conditions.

This energy sub-module methodology is expected to have applications primarily in the generation of gate-to-gate life cycle information in chemical, biochemical and pharmaceutical processes.

4.5. References

Chacón, Miguel Angel, personal communication, Oct. 15, 1997.

Cohen-Hubal, E.A.: Net waste reduction analysis applied to air pollution control technologies and zero-water-discharge systems. Raleigh NC: NCSU MS Thesis, 1992

Colberg, M., Overcash, M.: Life Cycle Assessment of Solvent Manufacturing and Use. New Orleans: Presented at AIChE 1996 Spring National Meeting, 1996

Dosat, R. J: Principles of Refrigeration. 4th. Ed. New Jersey: Prentice Hall, 1997

Dumas, R. D: Energy Usage and Emissions Associated with Electric Energy Consumption as Part of a Solid Waste Management Life Cycle Inventory Model. Raleigh, NC: NCSU, Department of Civil Eng., 1997

EMPA: ECOPRO, Life Cycle Analysis Software. St. Gallen, Switzerland: EMPA (Swiss Federal Laboratories for Material Testing and Research, 1996

Fountain. R.L.: Water Treatment Plant Operation, Chemistry for Operators. Michigan: Ann Arbor Science, 1982

Hill, G.B: Cooling Towers, Principles and Practice. 3rd. Ed. London, Boston: Butterworth-Heinemann, 1990

Lemmon, E. W., McLinden, M.O., Friend, D.G.: Thermophysical Properties of Fluid Systems. NIST Standard Reference Database Number 69. Eds. WG Mallard and P J Linston. National Institute of Standards and Technology. (<http://webbook.nist.gov>), August 1997

McKelvey, K. K.: The Industrial Cooling Tower. New York: Elsevier Publishing Company, 1959

Olivo, C. T.: Principles of Refrigeration. 3rd. Ed. Albany, NY: Delmar, 1990

Perry, R.H.: Chemical Engineer's Handbook. 7a. Ed. New York: McGraw Hill, 1997

PIRA: PEMS, Life Cycle Analysis Software. Surrey, UK: Pira International, 1998

Pistikopulos, E. N. et. al.: A methodology for Minimum Environmental Impact Analysis.

Pollution Prevention via Process Modifications. New York: Halwagi and Petrides, Ed., 1994

Pre Consultants: SIMAPRO, Life Cycle Analysis Software. Amersfoort, The Netherlands:

Pre Consultants B.V., 1998

Rice, G.: The Application of Life Cycle Assessment (LCA) to Industrial Process Selection

and The Application of Life Cycle Thinking to Industrial Process Improvement.

Engineering Doctorate in Environmental Technology Thesis. Guildford, UK:

University of Surrey at Center for Environmental Strategy, 1999

Sibley, H. W.: Selecting Refrigerants for Process Systems. Chemical Engineering, May 16

(1983) 71-76

Society of Environmental Toxicology and Chemistry: Guidelines for Life-Cycle Assessment:

“A Code of Practice”. Pensacola, Florida: SETAC, 1993

USEPA: Life Cycle Assessment: Inventory Guidelines and Principles. EPA/600/R-92/245,

1993

Walas, S. M.: Rules of Thumb Selecting and Designing Equipment. Chemical Engineering,

March 16 (1987) 75-81

Willa, J. L.: Improving Cooling Towers. Chemical Engineering, Nov. (1987) 92-96

Table 4.1 . Operating Temperature Ranges for the energy sub-modules .

Energy Sub-module	Temperature Range
Steam, 50 psia	Up to 140°C
Steam , 135 psia	Up to 200°C
Dowtherm A	Up to 250°C at 1 atm, Up to 380°C at 10 atm
Cooling Tower	Down to 25°C
Refrigeration-SUVA 123	Down to –30°C
Refrigeration-ammonia	Down to –40°C

Table 4.2 . Unit Operation results for the energy sub-module for cooling a process stream.

	Sub-modules			
	Cooling Tower Generic	Cooling Tower Site-Specific	Refrigeration using ammonia	Refrigeration using SUVA 123
Inputs				
Electricity (kWh/MJ cooling potential)	8.9E-4	1.18E-2	9.01E-2	1.37E-1
(MJ/MJ cooling potential)	3.2E-3	4.2E-2	3.24E-1	4.93E-1
Water make-up (kg/MJ cooling potential)	7.0E-2	9.33E-1		
11.2% NaCl solution for water pretreatment: (kg/MJ cooling potential)	3.45E-4	4.60E-3		
Cooling from cooling tower (MJ/MJ cooling potential)			1.16	1.22
Refrigerant make-up (kg/MJ cooling potential)			9.62E-6	7.84E-5
Maintenance supplies (kg/MJ cooling potential)			1.33E-5	1.83E-5
Outputs				
Blowdown (kg/MJ cooling potential)	3.50E-3	4.67E-2		
Water losses to air (kg/MJ cooling potential)	6.65E-2	8.87E-1		
Pretreatment waste: 10% wt. CaCl ₂ /MgCl ₂ sludge (kg/MJ cooling potential)	3.45E-4	4.60E-3		
Maintenance waste (spent oil and filters) (kg/MJ cooling potential)			1.33E-5	1.83E-5
Refrigerant Losses (kg/MJ cooling potential)			1.60E-7	1.31E-6

Table 4.3. Results of the combustion mass balance for natural gas and No. 2 oil. Data do not include pre-combustion emissions.

	Natural Gas	Fuel No. 2
Air Required (kg/kg fuel)	21.10	17.56
Carbon Dioxide (kg/kg fuel)	2.71	3.2
Sulfur Oxides (kg/kg fuel)	0	6.2E-3
Nitrogen Oxides (kg/kg fuel)	1.2E-2	2.8E-3
Water Vapor (kg/kg fuel)	2.31	1.26
Nitrogen (kg/kg fuel)	16.11	13.4
Oxygen(kg/kg fuel)	0.96	0.73

Table 4.4. Unit operation results for the energy sub-module for heating a process stream with steam or Dowtherm A.

	Dowtherm A	Fuel No. 2		Natural Gas	
		135 psia (931 kPa)	50 psia (345 kPa)	135 psia (931 kPa)	50 psia (345 kPa)
Inputs					
Air Required (kg/MJ heating potential)	0.49	0.56	0.52	0.60	0.55
Oil Required (kg/MJ heated)		3.21E-2	2.97E-2		
(MJ/MJ heated)		1.53	1.41		
Natural Gas required (ft ³ /MJ heated)	1.13			1.39	1.29
(kg/MJ heated)	0.023			0.029	0.026
(MJ/MJ heated)	1.25			1.53	1.41
Water make-up (kg/MJ heated)		0.063	0.060	0.063	0.060
Electricity (kWh/MJ heated)	2.12E-4	1.92E-3	1.81E-3	1.93E-3	1.81E-3
11.2% NaCl solution for water pretreatment (kg/MJ heated)		2.97E-3	2.80E-3	2.97E-3	2.80E-3
Outputs					
Blowdown (kg/MJ heated)		0.024	0.023	0.024	0.023
Pretreatment waste: CaCl ₂ /MgCl ₂ 10% sludge (kg/MJ heated)		2.97E-3	2.80E-3	2.97E-3	2.80E-3
Evaporative Losses (kg/MJ heated)		0.039	0.037	0.039	0.037
Carbon Dioxide (kg/MJ heated)	6.31E-2	1.03E-1	9.52E-2	8.0E-2	7.0E-2
Sulfur Oxides (kg/MJ heated)	0	1.99E-4	1.84E-4	0	0
Nitrogen Oxides (kg/MJ heated)	2.8E-4	8.99E-5	8.33E-5	3.70E-4	3.43E-4
Water Vapor (kg/MJ heated)	5.30E-2	4.05E-2	3.75E-2	7.0E-2	6.0E-2
Nitrogen (kg/MJ heated)	0.375	0.43	0.40	0.46	0.42
Oxygen (kg/MJ heated)	2.2E-2	2.35E-2	2.18E-2	2.7E-2	2.5E-2

Table 4.5. Summary of the life cycle information for 1 kg of NaCl.

	Value
Raw materials	
Limestone (kg)	1.4E-2
Sand (kg)	6.0E-5
Rock salt (kg)	1.07
Water (kg)	4.6
Energy Resources	
Hydroelectric (MJ)	0.045
Lignite (MJ)	0.069
Natural gas (MJ)	1.69
Mineral coal (MJ)	0.297
Oil (MJ)	0.699
Uranium (MJ)	0.210
Others (MJ)	0.024
Emissions to the air	
Dust (mg)	320
Carbon dioxide (mg)	175,000
Carbon monoxide (mg)	90
Sulfur oxides (mg)	1,100
Nitrogen oxides (mg)	1,500
Hydrogen chlorides (mg)	10
Methane (mg)	370
Non-methane VOC's (mg)	1,630
Emissions to the water	
COD (mg)	14
BOD (mg)	1
Metals (mg)	7
Chloride ions (mg)	34,000
Suspended solids (mg)	1,290
Sulfate ions (mg)	7,000
Sodium ions (mg)	90
Inorg. Salts and acids (mg)	30
Solid waste	
Municipal waste to incineration (g)	0.06
Mineral waste (g)	21
Regulated chemical waste (g)	0.02
Waste to landfill (g)	14

Table 4.6. Summary of the life cycle information for 1 kg of Ammonia.

	Value
Raw materials	
Natural gas (m ³)	0.584
Water (kg)	0.92
Energy Resources	
Natural gas (MJ)	0.151
Emissions to the air	
Carbon dioxide (mg)	436,109
Carbon monoxide (mg)	25
Sulfur oxides (mg)	10
Nitrogen oxides (mg)	304
Methane (mg)	7,140
Non-methane VOC's (mg)	928

Table 4.7. Summary of the life cycle information for 1 kg of 1,1,1,2-Tetrafluoroethane or R134a (used as an approximation of SUVA 123).

	Value
Raw materials	
Renewable resources (kg)	0.21
Water (kg)	32.3
Air (kg)	27.2
Open loop inputs (kg)	10.6
Energy Resources	
Hydroelectric (MJ)	4.03
Natural gas (kg)	0.37
Mineral coal (kg)	11.35
Oil (kg)	1.15
Uranium (MJ)	45.55
Others (kg)	0.001
Emissions to the air	
Dust (mg)	1
Carbon dioxide (mg)	37,785
Carbon monoxide (mg)	7.73
Sulfur oxides (mg)	375
Nitrogen oxides (mg)	123
VOC's (mg)	117
Other (mg)	1,243
Emissions to the water	
Metals (mg)	1.81
Waste water (kg)	0.032
Suspended solids (mg)	8.2
Inorg. Salts and acids (mg)	276
Solid waste	
Open loop outputs (g)	3.78
Waste to landfill (g)	1.62
Other (g)	4.91

Table 4.8. Life cycle inventory information for electricity. National grid for the USA.

USA National Grid for Electricity	%
Production.	
Coal	56.45
Natural Gas	9.75
Oil	2.85
Nuclear	22.13
Hydro	8.59
Wood	0.24
<hr/>	
Emissions	Emission Factor (kg/kWh electricity)
Atmospheric Emissions	
Particulates	2.62E-03
Nitrogen Oxides	6.86E-03
Hydrocarbons (non CH4)	1.93E-04
Sulfur oxides	1.36E-02
Carbon Monoxide	2.25E-03
CO2	1.56E+00
Ammonia	1.00E-07
Lead	2.78E-11
Methane	9.81E-06
Hydrochloric acid	3.01E-09
Solid waste (ash)	1.90E-01
Waterborne Emissions	
Dissolved Solids	2.66E-04
Suspended Solids	2.34E-07
BOD5	2.56E-07
COD	1.28E-06
Oil	5.07E-06
Sulfuric Acid	1.15E-03
Iron	2.85E-04
Ammonia	3.49E-08
Chromium	1.28E-11
Lead	3.74E-11
Zinc	5.58E-10
Water flow	4.06E-01

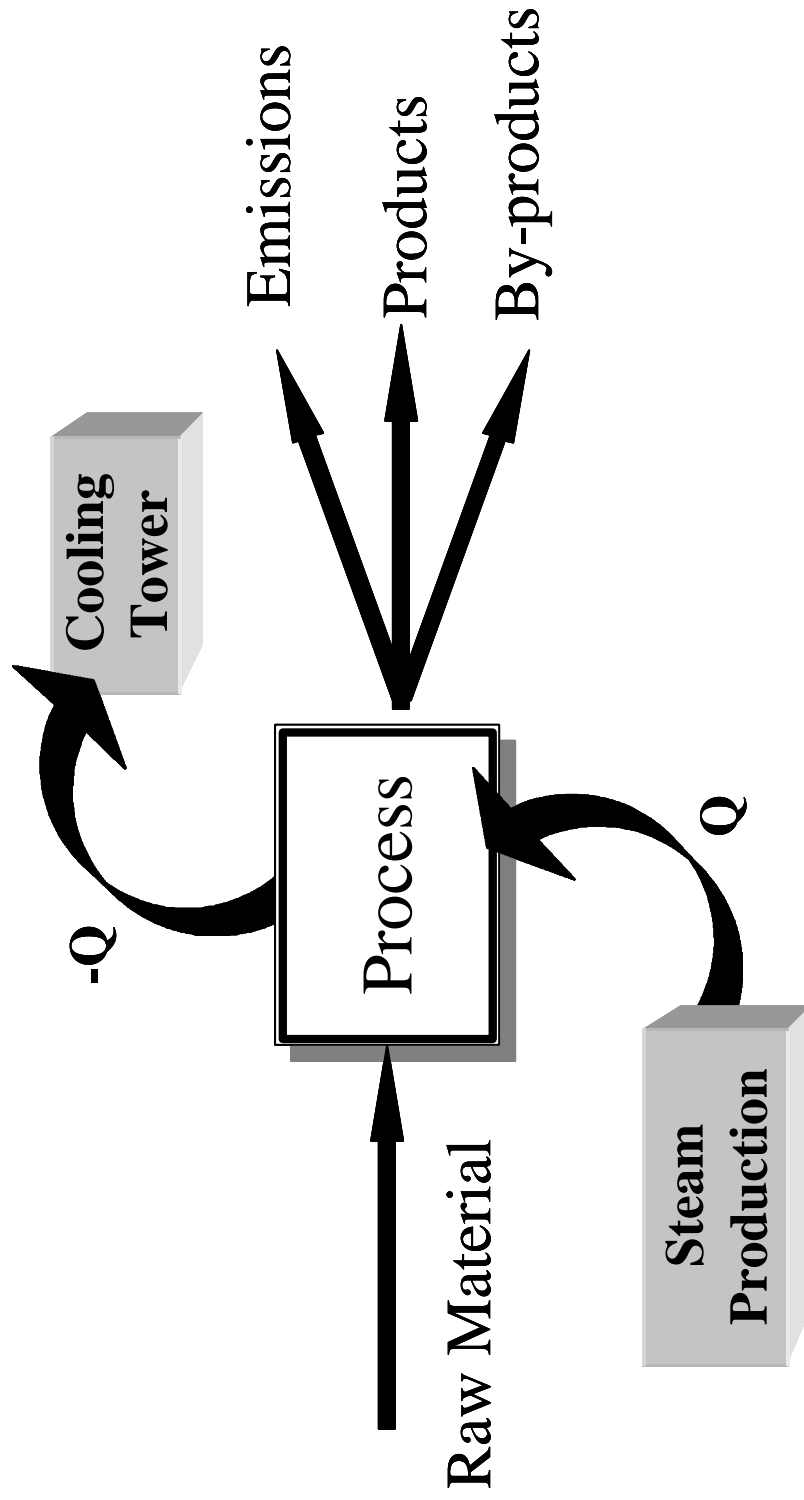


Figure 4.1. Graphic representation of energy sub-modules. It can be seen in the figure that the Steam production sub-module acts as an energy source, while the cooling tower sub-module acts as an energy sink

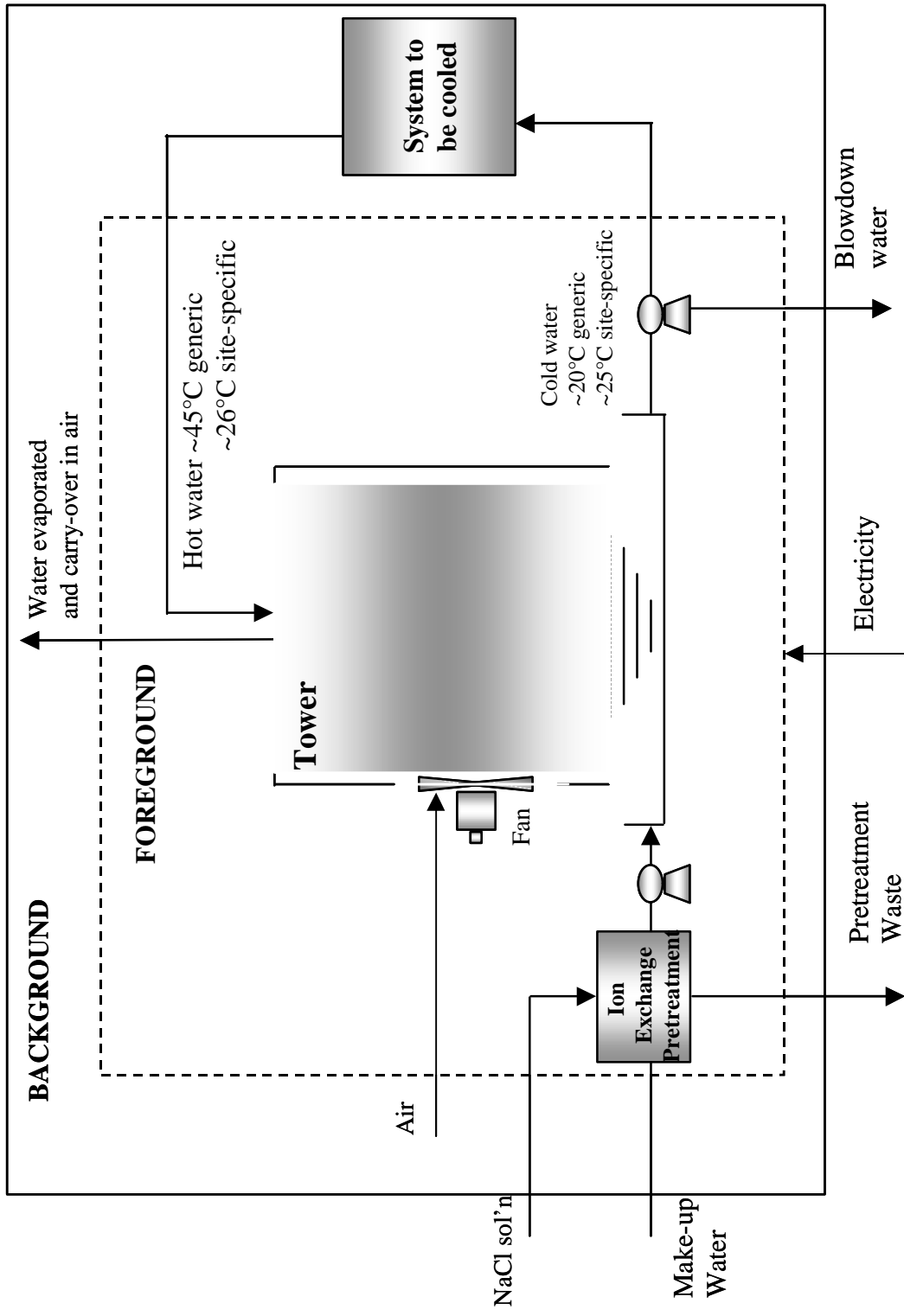


Figure 4.2. Schematic of site-specific and generic cooling water sub-module

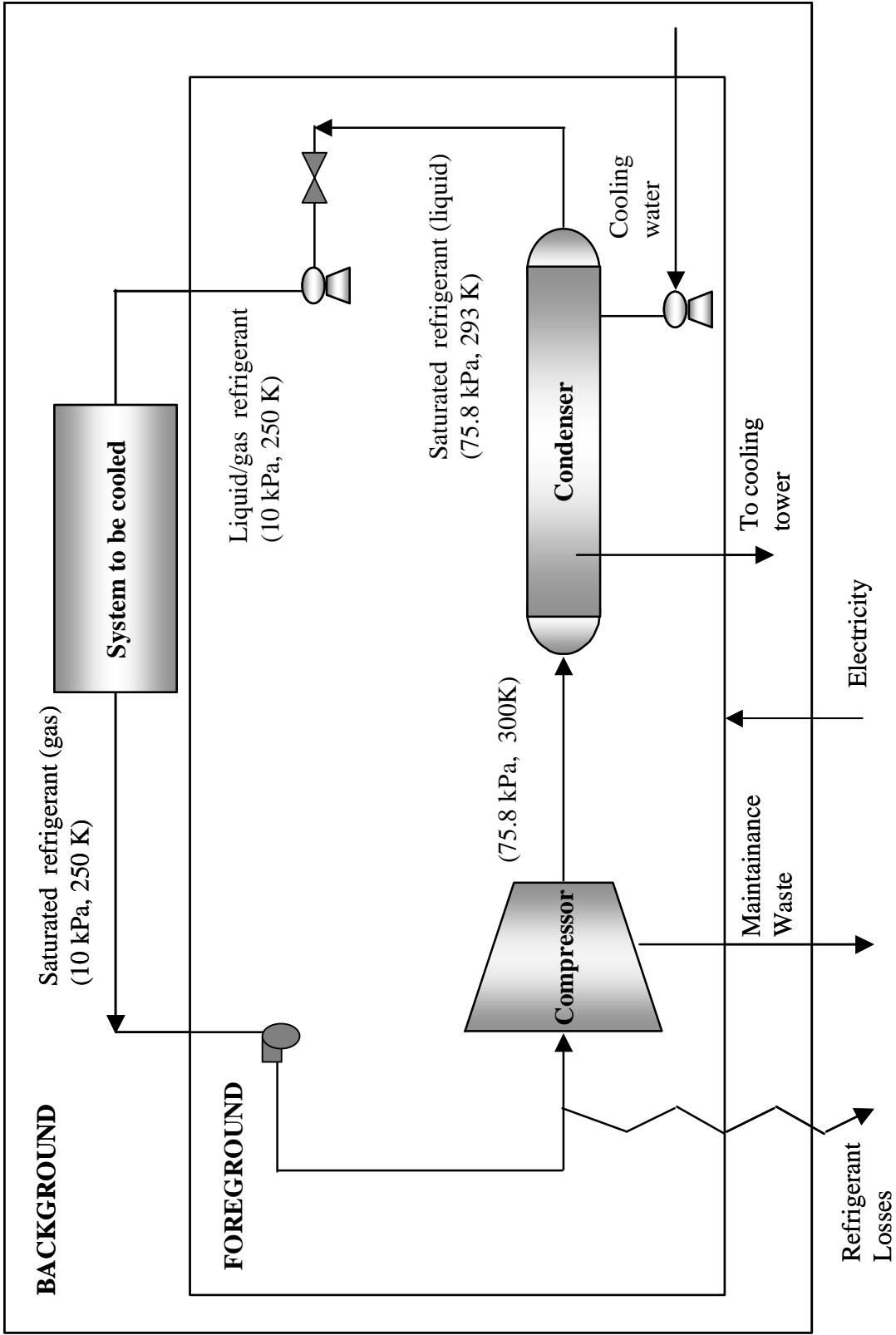


Figure 4.3. Schematic of the refrigeration cycle sub -module for SUVA 123

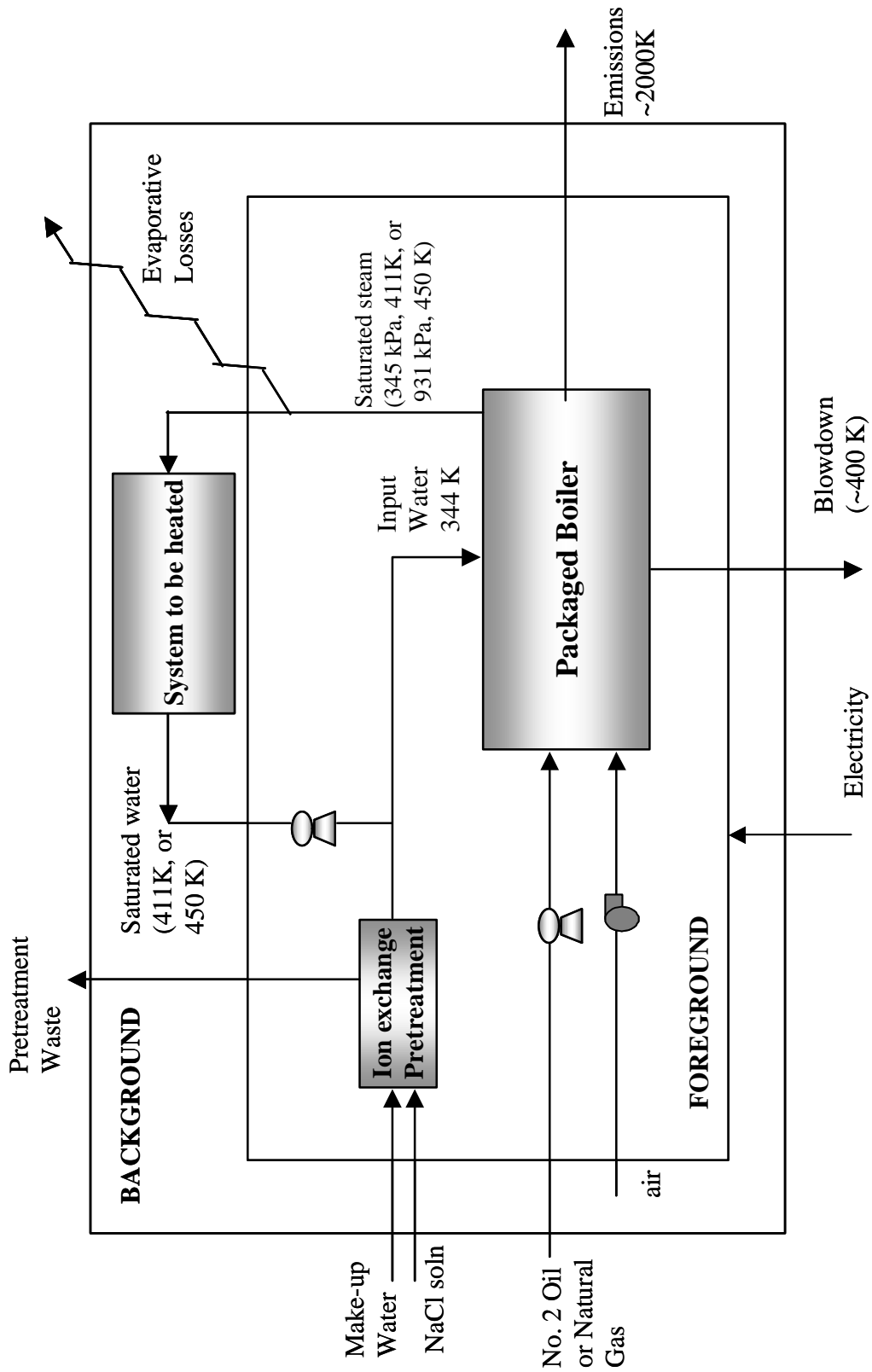


Figure 4.4. Schematic of the steam production sub-module

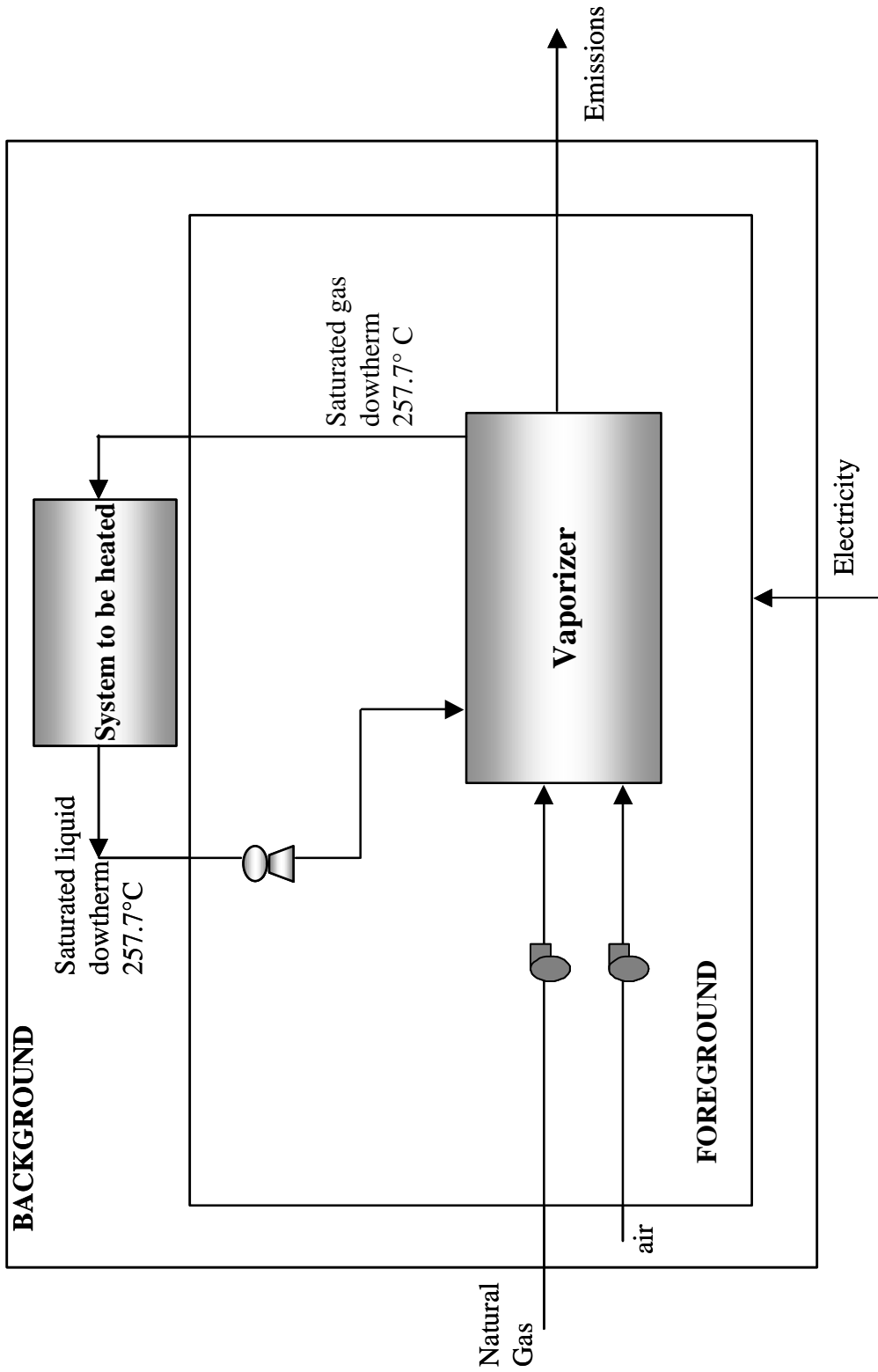


Figure 4.5. Schematic of the Dowtherm A heating sub-module

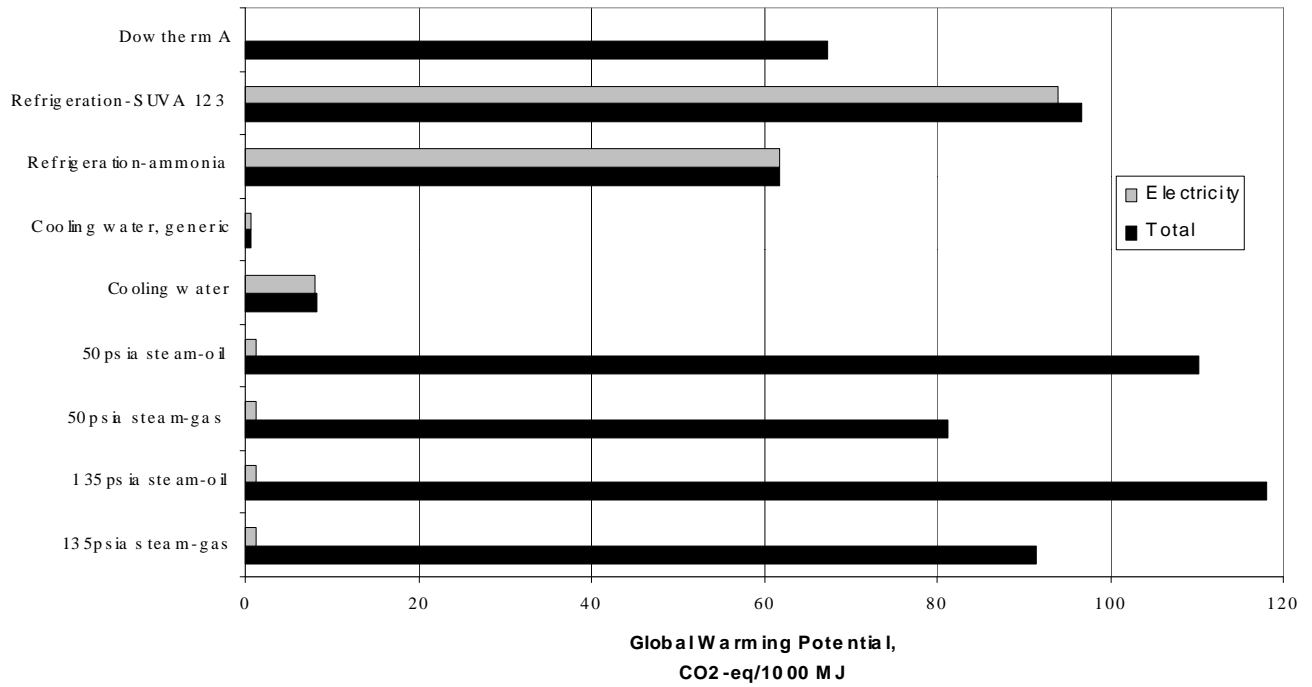


Figure 4.6. Comparison of Global Warming Potential for the energy sub-modules.

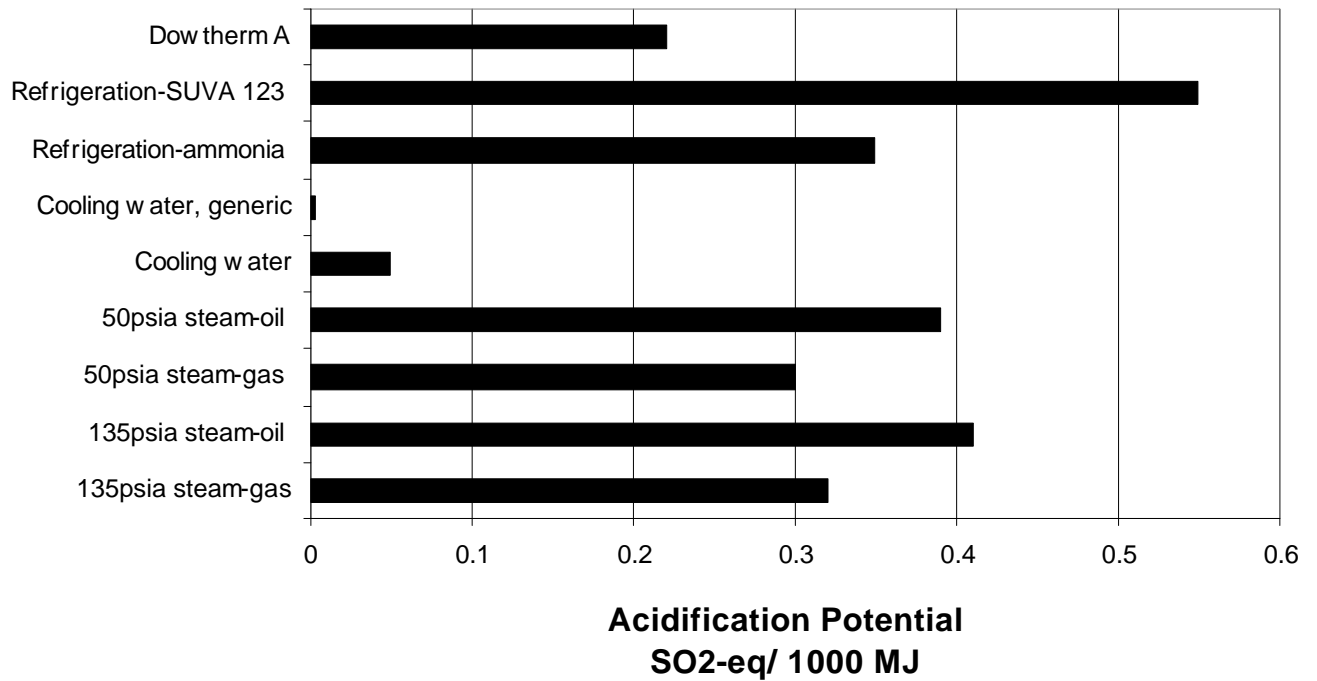


Figure 4.7. Comparison of Acidification Potential for the energy sub-modules.

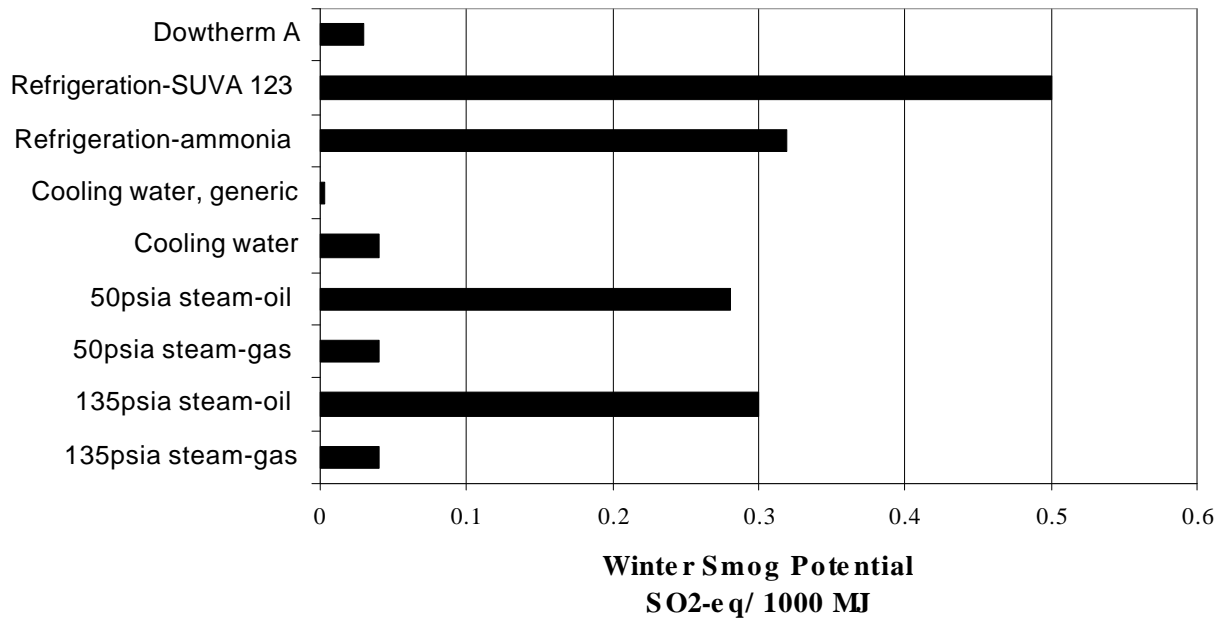


Figure 4.8. Comparison of Winter Smog Potential for the energy sub-modules.

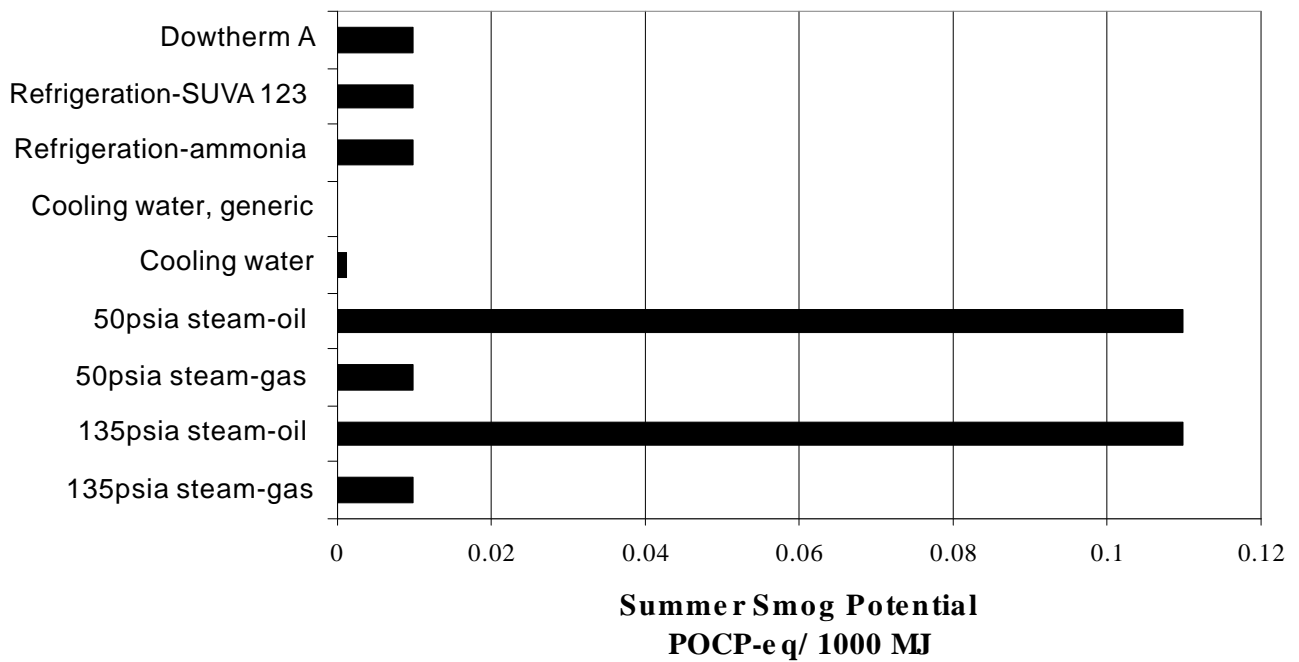


Figure 4.9. Comparison of Summer Smog Potential for the energy sub-modules.

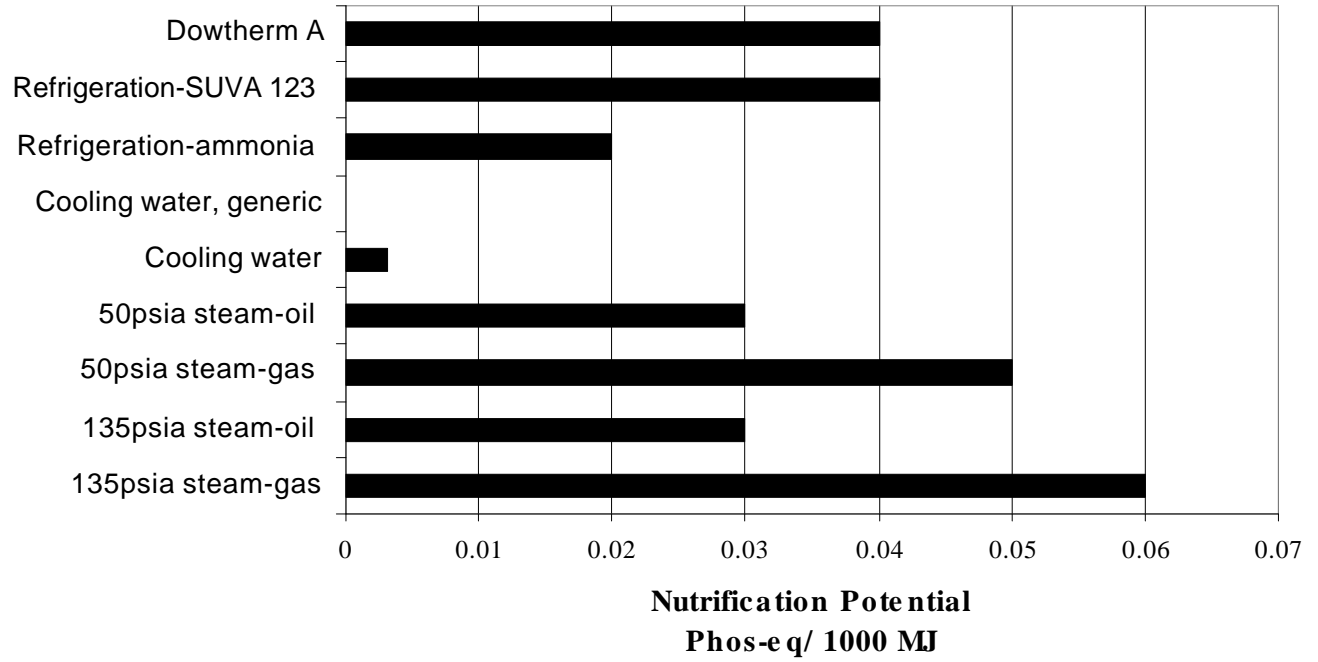


Figure 4.10. Comparison of Nutrifaction Potential for the energy sub-modules.

**5. LIFE CYCLE INVENTORY (LCI) OF REFINERY PRODUCTS:
REVIEW AND COMPARISON OF COMMERCIALY AVAILABLE
DATABASES**

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5. LIFE CYCLE INVENTORY (LCI) OF REFINERY PRODUCTS: REVIEW AND COMPARISON OF COMMERCIALY AVAILABLE DATABASES

Abstract

A great deal of energy carriers and a vast amount of industrial chemicals have a starting point from products of a refinery; and thus the life cycle inventory (LCI) data for a refinery is extensively used during the development of a life cycle assessment (LCA). Assessing the variability and reliability of the LCI data for the refinery process is a relevant issue, since the use of poor refinery LCI data could result in erroneous conclusions drawn from an LCA using such information.

The purpose of the present work is to review and compare the LCI results for refinery products among several available databases, evaluating the level of variability and technical consistency among data sets. Another objective of the present research is to highlight the need of greater transparency and standardization in LCI databases.

For the data sets evaluated, it was found that, in general, the transparency of petroleum refinery LCI data is at a relatively low level. The apparent variability in air and water emissions among the LCI databases analyzed is large (50% to 150% for air emissions, and over 1,000% for water emissions). The solid waste categories presented are extremely irregular, but the total solid waste variability is about 30%. Furthermore, the amount reported for some water emissions appeared to be technically erroneous. Such apparently erroneous results and high variability can erode the credibility of LCI investigations. This argues strongly that for a critical LCI module such as the refinery, an international effort is needed to clarify and prepare a more representative LCI for refineries.

Keywords: Life cycle assessment, life cycle inventory, refinery products.

5.1. Introduction.

In the life cycle (LC) field, the direct products of a refinery are important elements in constructing the LCI of virtually all products. The importance may be use of oil as a process heating fuel, gasoline in transport, or petrochemicals as reactants. Thus understanding the LCI of a representative refinery is a common need in this field and in the evaluation of sustainability indices.

If LCI data representing the widely used products of a refinery have significant variation, then the conclusions for all LC studies have high variability. Thus it is important to reduce the variability in information, particularly if it results from differences in reporting formats, assumptions, and even in definition of terms. A critical review of refinery LCI information is a necessary step to improvement in LC research. Improved LCI information will allow more credible distinctions between technology or policy alternatives, the goal of decision making in LC evaluation.

The LCI of a refinery appears in a number of databases used in the LC field. Often users take an LCI generated in various papers or reports for products such as plastics, solvents, automobiles, solar cells, etc., in which the refinery LCI is an imbedded part. This exchange of LCI information makes it important to understand the underlying data, such as refinery products. It is generally true that the LCI databases of refineries were collected from primary data, but in subsequent use lose transparency and thus develop apparent variability. In a search of over 400 LC articles, not a single article comparing refinery LCI data or for that matter, any other chemical LCI data comparisons were found. Thus a review of refinery LCI data is unique. Since most LCI databases are proprietary and are not primary data, a

comparison can only be of the published version. However, these published refinery LCI data are what most researchers are using for the increasing application of LC studies.

5.2. Objectives

The European evaluation of life cycle technology has identified the diversity and quality of LCI data as a major barrier or future need (Clark and Leeuw 1999). This is particularly true for the LCI of petroleum refining, because of the ubiquitous inclusion of refinery products in virtually all LC studies.

The overall goal is to provide a comparison of LCI data from the perspective of a user or researcher, dependent on published LCI data. This is a dominant perspective as the LC field grows and fewer groups have access to primary data for refinery LCI. The specific objectives are:

- 1) To prepare a common format, related to actual refining technology, for comparison of refinery LCI data.
- 2) To utilize chemical engineering principles to extract further information.
- 3) To establish the level of variability for major and minor emission from refineries.
- 4) To examine the refinery LCI databases for technical discrepancies.
- 5) To highlight the importance for greater transparency and unity in LCI databases.

5.3. Methodology

The data sets evaluated are shown in Table 5.1. Refinery LCI data were obtained from commercial databases, journal publications or reports (Table 5.1). The broader sources of the specific refinery data could not be defined. The individual primary data from actual

refineries were not available in these publications, hence the underlying variability was not given. Only the variability at the user level was determined in this paper. Again, when one draws on published sources to construct the LC of a higher order product (such as a tire or solvent) these user level data represents the practical variability among representations of refinery products.

In overview, a refinery is principally a collection of processes used to separate crude petroleum into product classes. This separation is principally by heating in unit processes. The distribution of products is routinely varied (within some broad ranges) to meet consumer demand. Processes that crack or reformulate are used to change the product distribution, along with the selection of crude oil sources. Despite the apparent complexity of the changing product mix the refinery still conforms to mass balance principles. Thus for 1000 kg of input crude, the amount of saleable product is 940-970 kg with 30-60 kg of crude being used as energy for the refinery processes (average of refinery database comparisons found by this evaluation). In fact, excluding the use of crude as energy, the refinery is highly efficient with chemical losses of only ~0.3%-0.5% (Amoco, 1995). In addition, water is a refinery input that then appears as wastewater. Therefore, the crude oil input is close to the product output. Using a “per kg product basis” for the calculations, is thus a stable reference frame even though the distribution of product can vary (say, between the amount of gasoline versus fuel oil). In the LC field, the refinery process and energy emissions are allocated to each product on the basis of the mass (kg) of product. Thus, a kg of one product has the same allocated emissions as a kg of another product and so the distribution of products is less influential. Since a mass allocation technique is used in the present work, representing emissions or energy on a kg of product, kg naphtha, kg diesel, etc. are equivalent.

First, LCI data were collected from each data set regarding energy usage, raw materials, air emissions, water emissions and solid waste. These values included pre-combustion data. The data were not available in the same categories or may have been aggregated information and so an interpretative analysis was first needed. At the beginning, it was not clear how many of these data sets are actually independent, therefore a comparison of the manner of presenting the information in each database was done.

The data sets present the energy usage information in energy units (MJ of fuel: gas, oil, coal), or mass units (kg of fuel), but rarely in both energy and mass units. To overcome this difference and to make the data standard, the calculation of the corresponding mass or energy values for fuel usage were performed. The heat values used were 45 MJ/kg for oil, 30.3 MJ/kg for coal, and 54.3 MJ/kg for gas (39 MJ/m³). The density value used for natural gas was 0.72 kg/m³. This allowed for a full picture of both mass (kg) and energy (MJ) terms by using these interconversion factors.

The next step to unify the databases was to differentiate how much of the inputs and emissions reported in each data set were related to electricity production, fuel for heating (and transportation), and from refinery processes. Only ECOPRO-Naphtha and BOUSTEAD data sets have explicitly described these information, while some other data sets had partial explanations. For the rest, further calculations (given in the following sections) were required to estimate the distribution of energy use or the results for emissions. These calculations were found to be useful as a cross examination of the data presented.

When the total electricity and other energy amounts were not reported; then calculations were needed. The disaggregation of the LCI data was conducted with the following logic. Each refinery database reported the overall amounts of coal, oil, natural gas,

hydro, and nuclear energy use. As an example, the energy data in SIMAPRO-Naphtha, Average Europe are shown in Table 5.2.

The energy includes the amounts for electricity, refinery fuel consumption for heating processes, and transportation (if reported). The emissions also correspond to those resulting from electricity consumption, combustion of fuel for heating, and emissions from the actual refinery processes.

Since refineries do not have direct hydro or nuclear facilities, these energy sources could only represent the electricity used from the grid. Thus these were used to back calculate the electricity consumption (MJ/kg refinery product) for each life cycle database, separately. Using the European electrical grid distribution, the approximate level of hydro power is 0.21 MJ hydro/MJ of electricity delivered (PRE 1998, PIRA 1998, EMPA 1996).

The refinery electricity required is estimated with the following relationship:

$$E=H/F_{\text{Hydro,SIMAPRO}} \quad (5.1)$$

Where:

E= Refinery electrical energy (MJ/kg Naphtha or other refinery product)

H= Hydro Power (MJ hydropower/kg Naphtha), as reported in the database for the refinery (e.g. SIMAPRO)

$F_{\text{Hydro,Europe}}$ = Average factor for hydropower in electricity production in Europe = 0.21 (MJ hydropower/MJ electricity produced, (See Table 5.3)

Therefore, the estimated electricity is $E= (0.01/0.21)=0.048$ MJ electricity/kg Naphtha produced in refinery. The electricity needs of each refinery were calculated utilizing the factor for hydropower as described above. Hydro was selected because the overall variability across the various LCI databases was lower (about 5-fold) than that for

nuclear for which the variation was about 100-fold. That is, if one calculates the electricity usage per kg of refinery product, as in (5.1), across all databases the variation using hydro is 5-fold while nuclear is 100-fold. Such variation between electricity values when determined by hydro versus nuclear is an uncomfortable inconsistency for which LCI practitioners should be aware. In the case of a refinery, since electricity use is low, the impact of this inconsistency in the interpretation is not large. Alternatively, LCI databases for refinery products could achieve much higher transparency by reporting directly electricity usage.

Knowing the electricity use per kg of refinery product, the estimation of electricity-related emissions were made using the emission factors of each database (Table 5.3). The underlying variability of electric power generation emissions is not reported for the individual databases.

$$L_{i,Elect.} = EF_{i,DATABASE} \quad (5.2)$$

Where:

$L_{i,Elect}$ = Electricity-related life cycle chemical i emission at a refinery, chemical i /kg of refinery product.

E = Electrical energy used (MJ/kg refinery product)

$F_{i,DATABASE}$ = Chemical i emission Factor per MJ European electricity production in SIMAPRO database (Table 5.3).

Following the example above, the estimated carbon dioxide emissions for electricity production $L_{CO_2,Elect} = EF_{CO_2,SIMAPRO} = (0.048 \text{ MJ electricity/kg Naphtha})(1.33E+05 \text{ mg CO}_2/\text{MJ electricity}) = 6,384 \text{ mg of CO}_2 \text{ related to electricity/kg refinery product}$. Similar calculations for each chemical emission to air, to water and as solid waste allows one to

establish the amount of electricity-related emissions that are attributable to a kg of refinery product.

From the estimate of electricity use calculated above for each LCI database, the mass of oil, natural gas, and coal used for that electricity production (coal use is not typically large in refineries) was calculated (See Table 5.3 for the power grid used to back calculate the mass of these fuels ascribed to refinery electricity use). Subtracting the amount of oil, natural gas, and coal used for electricity from the total oil, natural gas, and coal reported per kg of refinery product, gives the amounts of these fuel types that are utilized for heating the various refinery unit processes. Then by difference we knew the amount of oil, natural gas, and coal used in the refinery for process heating (combustion of fuel). Using the typical combustion profiles of emissions from each of these three fuels (Table 5.4) one can separately calculate the amount of the total refinery emissions attributable to heating the various refinery processes (fuel combustion).

For example, with SIMAPRO-Naphtha, the reported oil use per kg of refinery product is 1.41 MJ. The calculated oil use (expressed as MJ) attributable to the generation of electricity/kg of refinery product (based on earlier hydro information) is 0.017 MJ. Thus the amount of oil consumed by heating (diesel combustion) is 1.41 MJ minus 0.017 MJ, or 1.39 MJ. Based on the oil heating value of 45 MJ/kg (Table 5.5), the amount of oil used in heating refinery processes is 0.031 kg oil/kg of refinery product (for the SIMAPRO-Naphtha database). Following a similar calculation, the energy and mass for refinery process heating is 3.327 MJ/kg of refinery product for natural gas, and 0.102 MJ/kg of refinery product for coal. (which translates into 6.12E-02 kg gas and 4.65E-03 kg coal).

Now, with the amount of oil, natural gas, and coal used for refinery heating, the individual chemical emissions attributable to heating were determined utilizing the emissions factors (see Table 5.4, PRE 1998).

$$L_{i,\text{Heating}} = \sum_{j=1}^n C_j F_{i,j} \quad (5.3)$$

Where:

$L_{i,\text{Heating}}$ = Heating-related life cycle chemical i emissions at a refinery, kg of chemical i

C_j = Combustible fuel j (oil, natural gas, or coal mass, kg fuel j /kg refinery product)

$F_{i,j}$ = Emission Factor for chemical i from burning fuel j (Table 5.4)

For SIMAPRO Naphtha data as an example, the emissions for carbon dioxide due to heating were estimated as follows:

$$\begin{aligned} L_{\text{Carbon Dioxide, Heating}} &= \frac{0.0309 \text{ kg oil}}{\text{kg naphtha}} \left| \frac{3,760,000 \text{ mg CO}_2}{\text{kg oil}} \right. + \\ &\quad \frac{0.0612 \text{ kg gas}}{\text{kg naphtha}} \left| \frac{3,188,339 \text{ mg CO}_2}{\text{kg gas}} \right. + \\ &\quad \frac{0.0046 \text{ kg coal}}{\text{kg naphtha}} \left| \frac{2,840,000 \text{ mg CO}_2}{\text{kg coal}} \right. \\ &= 324,851 \frac{\text{mg CO}_2}{\text{kg naphtha}} \Rightarrow 114\% \text{ of total reported CO}_2 \text{ emissions} \end{aligned}$$

The percentage of each chemical emission per kg of refinery product was determined separately for electricity use and for heating use. Finally the difference between total chemical constituent emission (as reported in each LCI database) and that for electricity plus heating-related emissions is the emission directly from the processing and refining of crude oil into the various refinery products. These are referred to as process emissions.

Comparing the heating-related carbon dioxide emissions (see example), the estimated percentage of the total refinery carbon dioxide emissions from heating was determined as 114%. A percentage greater than 100% could be caused by rounding errors and different combustion profiles, but in either case it indicates that most of the carbon dioxide emissions are produced during heating processes, with a small contribution of electricity production, and practically none from processes, as expected for carbon dioxide. For the SIMAPRO-Naphtha example, the carbon dioxide emissions were determined as 2% from electricity, 114% from heating and -16% from processes, which in practical terms would translate to ~2% from electricity, ~98% from heating and ~0% from processes.

These disaggregation methods were applied to each of the LCI databases found for refinery products. With this diversity of databases, one can examine issues of variability and technical inconsistencies. These comparisons were the objective of an in-depth review of the refinery product LCI databases. The various databases were analyzed to give arithmetic average, median and standard deviation, see following discussion. In general, the median values for emissions or percentages were judged as more representative.

5.4. Results - Assessment Based on Comparative Concepts

As LCI studies are typically conducted, few projects have collected all their data independently. More typically, projects must import other specific LCI results that were collected by other investigators. Thus, in utilizing different LCI results, the underlying modules such as refinery production of fuels or feedstocks are a mixture of databases. Hence there is a need to appreciate the diversity in quantitative LCI results from published studies. This is where the issue of transparency is the most critical. Transparency reduces the need to disaggregate LCI data and permits clear changes in assumptions. By using comparative

concepts, the implications of variation among LCI databases can be illustrated, Table 5.1. The Boustead naphtha and ECOPRO Naphtha are examples of the more transparent LCI databases.

From Table 5.1, there may only be five independent sets of data. Data from SIMAPRO were taken from the PWMI report, and from BUWAL 250. Data from PEMS were taken from the PWMI Report and from ETH-ENET Eco-inventory. Nevertheless, even in data sets with the same primary source, the level of detail presented varies, hence the transparency is not similar.

The electricity required in most of the databases (reported directly or estimated using hydro) lies between 0.01 and 0.075 MJ/kg of refinery product, with a median of 0.05 MJ/kg of refinery product. However, the estimated electricity for the naphtha and diesel data seems to be higher than the electricity for the rest of the data (average of 0.224 MJ/kg of refinery product).

The feedstock needed to produce a kilogram of refinery products is relatively constant. The exceptions are EMPA-Naphtha and EMPA-Diesel, which present a higher consumption of feedstock oil (Table 5.5).

Regarding the fuel used for heating refinery processes, Figure 5.1, PEMS Naphtha, PEMS Diesel and EMPA Naphtha represent a significantly larger amount of oil and coal. The higher use of oil does not appear to be a trade off with natural gas usage, since the total fuel used is still larger for these three LCI data sets. For the rest of the databases, it appears that the oil and coal required for heating is larger for diesel than for naphtha (Figure 5.1). If this is true then direct allocation according to mass of product was not used for these products, again an opportunity for transparency. SIMAPRO Diesel is the exception (Figure

5.1), but it can be explained because the data presented for diesel are the same data for the average refinery product, which is consistent with mass allocation principles. The fuel usage pattern then explains the pattern for CO₂ emissions (Figure 5.2).

The magnitude of the carbon dioxide variation is significant as EMPA, SIMAPRO, ECOPRO and FRANKLIN are important databases. As a percentage of the median, the variation in the largest single mass emission, CO₂, is from 50% to 150% of the average or median. In LCI studies for which the emissions from refinery products are important, the sensitivity analysis typically conducted would have to allow for such a magnitude of variations.

The rest of the air emissions follow the same pattern as the fuel requirement and the CO₂ (Figure 5.3). The largest chemical emissions variation among the LCI databases were for SO_x and methane (150% for SO_x and 70% for methane). Thus the intermingling of LCI databases with importance for refinery products may have variations of these magnitudes for SO_x (leading to acid rain) and methane (leading to global warming influences).

Refinery waterborne emissions are generally much lower than air emissions. The data sets for diesel, PEMS-Naphtha and EMPA-Naphtha exhibit comparatively larger water emissions, especially oil (Figure 5.4). This cannot be completely attributed to a larger fuel requirement for diesel, since the proportion among the chemical parameters is not the same. Therefore it can be concluded that more process emissions were allocated to diesel in comparison to naphtha, increasing the amount of water emissions for diesel.

As it has been discussed before, the methodology of allocation can produce very different results in a refinery (Furuholt 1995). In general, the variation among databases for water emissions from the refinery were much larger than for air emissions. The reason for

this can not be established just from the data as presented in the LCI databases. Part of the variation may be related to the generally lower amount of the water emissions (mg of chemical/kg refinery product) than reported air emissions, hence greater possibility of error. The water emission parameters of chloride, suspended solids, dissolved solids, and sodium have such high variability (over 1000%) as to question whether such data are of much value in subsequent impact analysis. Alternatively, the water and air emissions argue strongly for a reevaluation of the important refinery LCI to achieve a less variable representative LCI.

This last point is also supported by our disaggregation into the different sources of the emissions. The strength of the disaggregation of the emissions produced by heating, electricity generation and processes is that it becomes clear that most of the air emissions are produced during heating and electricity generation, while most of the water emissions and solid waste are produced from the refinery processes (Figure 5.3).

Most of the emission distributions calculated, as explained in the methodology section, produced results as expected, and that are consistent with the actual technology used in a refinery. However the disaggregation transparency identified that the emissions of NO_x are a notable exception. Refinery processes, as distinct from heating and electricity uses, would produce no significant NO_x emissions. Yet, when disaggregating the sources of NO_x, a large number of the LCI databases showed the largest contribution (60%-80%) was from refinery processes (Table 5.3). An explanation for this might be that the reported emission factors for nitrogen oxides derived from fuel burning are not consistent with the reported data for the refinery, therefore underestimating the emissions caused by fuel burning.

Another possibility is that some important details were lost when transferring the data from the primary source of information, thus creating inconsistencies in the LCI databases.

On the other hand, three of the databases did report a distribution of emissions consistent with refinery processes, with the majority of NO_x emissions attributable to burning fuel for heating (Boustead, EMPA-Naphtha, and EMPA-Diesel). For the NO_x emission distribution shown in Figure 5.5, the average of Boustead, EMPA-Naphtha, and EMPA-Diesel was used (instead of the average of all LCI databases). As of now, there is no other defensible estimate of the emission factors for NO_x, nor an explanation of the factors taken into consideration for data generation in the other databases and hence corrected NO_x values are used (Figure 5.3). Again an argument for transparency as a means to improve the LCI literature.

The solid waste data presented are extremely irregular throughout the data sets. In some databases the waste is classified at a relatively high detail, in some it is grouped together and some do not even report solid waste (Figure 5.4). Even when the databases have the same primary source of information, the classification of solid waste is rearranged and there is not a clear definition of the kind of waste included. In Figure 5.4 a comparison of the solid waste data provided in each data set is shown, including the classification used. The least variation (30%) among LCI data sets, occurred when all types of solid waste were added together to give total solid waste. This is done assuming there is no reporting of solids in more than one category and hence the sum is a reflection of the total. As a technical consideration, no percent moisture is reported, hence it is very unclear what mass (dry solids or wet mass) is actually represented by these solid waste values. For now, it is best to utilize total solid waste in characterizing the refinery products.

5.5. Results - Assessment Based on Technical Issues

An examination of the emissions reported in all the LCI databases for a refinery can also be used to assess the underlying technical validity of LCI information. Using the median values for the chemical constituent emissions to air, water and as solids, a technical analysis was undertaken. For the larger air emissions, the results seem to have no chemical or technical inconsistency (such as a disproportionate ratio of SO_x to CO₂). The only inconsistency was found with metals for which refinery metals lost to the air were significantly lower than would be found by combusting the same amount of oil and natural gas (Table 5.4). Since the total amount of metals (principally from burning oil for heating) is very low, the influence of this inconsistency may not have a great impact on life cycle assessment interpretations of refinery-related results.

In contrast, a number of technical inconsistencies were discovered for water emissions. First, the median dissolved solids (known as total dissolved solids, TDS) was found to be very much lower (14 mg/kg of refinery product) than the summation of the typical reported ions that comprise the actual TDS value, according to the chemical protocol (APHA, 1980) ($\text{Ca}^{++} + \text{Na}^+ + \text{Cl}^- + \text{SO}_4^{--} + \text{K}^+ + \text{Mg}^{++} = 3,600 \text{ mg/kg}$ of refinery product). Second, the total organic carbon was 10-fold to 30-fold larger (TOC around 500 mg/kg of refinery product) than the reported chemical oxygen demand (COD around 14 mg/ kg of refinery product). Also the oil emission (around 1,000 mg/kg of refinery product) was 10-fold to 70-fold larger than the reported chemical oxygen demand (COD around 14 mg). These results are again not technically possible based on the actual analytical test performed to measure these parameters. It is not possible with these technical inconsistencies to

determine which parameters are actually correct, but it illustrates the need for more technical review of such databases in order to maintain credibility.

5.6. Conclusions

The LCI information for petroleum refineries is vital to a large number of studies involving transportation fuel, electricity generation, plastics, and many products containing organic chemicals. Petroleum refining is thus a critical module in life cycle evaluations and in terms of understanding the environmental emissions from the petroleum refining industry. In addition the life cycle inventory databases represent a large number of sources and so can be investigated with regard to absolute data and variability. This investigation of the petroleum refining LCI databases concluded the following:

- 1) By disaggregating the LCI data for the largest chemical emission, CO₂, about 2% of the emissions are from electricity generation and consumption in the refinery, 98% from combustion of petroleum products to heat refinery unit processes, and a negligible amount originates from the actual refinery unit processes.
- 2) Other dominant air emissions such as NO_x, SO_x, CO and CH₄, are also mostly from heating.
- 3) Emissions to air of hydrocarbons and non-methane VOC were predominantly from refinery processes.
- 4) For water emissions the hydrocarbons, oils, COD, BOD₅, nitrogen and sulfate were primarily from the refinery processes and not heating or electricity-related emissions.
- 5) Variability in the largest class of emissions, those to air, are very large (50% to 150%).

- 6) Variability in emissions to water among databases is even higher, over 1,000%. In general, the absolute value of chemical emissions to water, from a refinery, were reported to be very low compared to those for air.
- 7) Variability for the sum of all classes of solid waste from refineries was on the order of 30%.
- 8) The variability in emissions may be related to the different LCI database assumptions, and techniques for aggregating primary data collected at refineries, rather than variability of primary refinery data.
- 9) Using the physical chemistry and the analytical procedures for chemical species in wastewater, it was determined that total dissolved solids, total organic carbon, chemical oxygen demand, and oils appeared to be nonsensical results. Such apparently erroneous results can erode the credibility of LCI investigations.
- 10) In general the transparency of petroleum refinery LCI data, as a central component of larger life cycle studies, is at a relatively low level.
- 11) The variability of energy use and emissions of actual refineries is probably lower than that reported in LCI databases. This argues strongly that for a critical LCI module such as the refinery, an international effort is needed to clarify and prepare a more representative LCI of refineries. Much of this variability may only exist because of non transparency. Achieving a more representative refinery LCI ought to be a goal of the petroleum industry as the center of needed expertise. This might best follow the actual use of processes (Furuholt, 1995).

12) Finally, variability and technically impossible data are factors in establishing the credibility of the life cycle field and hence influence the large amount of life cycle concepts now emerging.

5.7. References

- Amoco, Project Summary of Amoco-USEPA Pollution Prevention Project at Yorktown, VA. Amoco Environment, Health, and Safety. Chicago, IL, 1995, 126p.
- Furuholt, E. Resources, Conservation and Recycling, 1995, (14) 251-263,
- Clark, G. and B. de Leeuw. How to Improve Adoption of LCA. Int. J. of LCA 1999 4(4), 184-187.
- Boustead. I., Eco-Profiles of the European Plastics Industry. Report 2. Olefin Feedstock Sources. A Report for the European Center for Plastics in the Environment (PWMI), May 1993, 10-13.
- PIRA International. PEMS Version 4.4. Randall Road. Leatherhead. Surrey. England, 1998, computer software version 4.4.
- PRé Consultants, SIMAPRO Version 4.0, B.V. Plotterweg 12 3821 BB Amersfoort the Netherlands, 1998, computer software version 4.0.
- Franke, M., et. al. European LCI for Detergent Surfactant Production. A Life-Cycle Inventory for the Production of Petrochemical Intermediates in Europe. Tenside Surf. Det. 1995, 32(5), 384-396,
- Frischknecht R., Hofstetter P., Knoepfel I., Done R., Zollinger E., et al.; ESU-ETHZ, 1994: Ökoinventare für Energiesysteme, Laboratorium für Energiesysteme, Gruppe Energie-Stoffe-Umwelt, ETH Zürich/PSI Villingen, 1994, ESU-Reihe 1/94.

EMPA, Swiss Federal Laboratories for Materials Testing and Research. ECORPO 1.5,
Lerchenfeldstr. 5, CH-9014, St. Gallen, 1996, computer software version 1.5.

Boustead, I., Naphtha Life Cycle Inventory Information, Boustead I. Ed. June of 1999, 1-7.

APHA-AWWA-WPCF Ed. Standard Methods for the Examination of Water and
Wastewater. 15 Ed., 1980, 93-94.

Table 5.1. LCI Refinery Data sets compared.

Data Set Label	Product	Partition of Energy	Partition of gas emissions	Partition of water emissions	Partition of solid waste	Classification of solid waste	Methodology for allocation	Includes transport	Source	Primary source
PWMI South European	Average refinery products for South Europe	E, F	no	no	no	yes	mass	yes	Boustead 1993	Industry
PEMS South European	Average refinery products for South Europe	no	no	no	no	no	n.c.	n.c.	PIRA 1998	PWMI Report 2
PWMI Average European	Average refinery products for North Europe	E, F	no	no	no	yes	mass	yes	Boustead 1993	industry
PEMS Average European	Average refinery products for North Europe	no	no	no	no	no	n.c.	n.c.	PIRA 1998	PWMI Report 2
EMPA Naphtha	Naphtha, Average Europe	no	P, F, T	no	n.r.	n.r.	n.c.	yes	Frichknecht 1994	EMPA
ECOPRO Naphtha	Naphtha, Average Europe	E, F, T	F, P, T, E	F, P, T, E	F, P, T, E	yes	n.c.	yes	EMPA 1996	BUWAL 250
SIMAPRO Naphtha BUWAL 250	Naphtha, Average Northern Europe	no	no	no	no	yes	n.c.	n.c.	PRE 1998	BUWAL 250
SIMAPRO Naphtha Average Europe	Average refinery products for Europe	no	no	no	no	no	n.c.	n.c.	PRE 1998	PWMI Report 2
PEMS Naphtha, Average Europe	Naphtha, Average Europe	no	no	no	n.r.	n.r.	n.c.	n.c.	PIRA 1998	ETH-ENET 30179 Oko-inventar
Boustead Naphtha, Average Europe	Naphtha for Italy, Netherlands, Austria and UK	E, F	F, P, T	F, P	F, P	yes	mass	yes	Boustead 1999	industry
SIMAPRO Diesel	Diesel, average Europe	no	no	no	no	no	n.c.	n.c.	PRE 1998	PWMI Report 2
PEMS Diesel	Diesel, average Europe	no	no	no	n.r.	n.r.	n.c.	n.c.	PIRA 1998	ETH-ENET 30179 Oko-inventar
EMPA Diesel	Diesel, average Europe	no	P, F, T	no	n.r.	n.r.	n.c.	yes	Frichknecht 1994	EMPA
ECOPRO Diesel	Diesel, average Europe	no	no	no	n.r.	n.r.	n.c.	n.c.	EMPA 1996	n.c.
FRANKLIN Average European	Average refinery products for Europe	** F, T	no**	no**	no**	no**	n.c.*	yes	Franke 1995	n.c.**

Notes

* Probably mass fraction, according to cross-checking of information presented as cited in a secondary source. ** As cited in a secondary source. n.r.- Not reported. E.- Electricity. F.- Fuel. T.- Transport. P.- Process. n.c. Not clear as presented in database. mass.- mass fraction.

Table 5.2. SIMAPRO-Naphtha Energy Data.

Energy	MJ/kg refinery products
Oil (non-feedstock)	1.41
Coal	0.15
Gas	3.34
Hydro Power	0.01
Nuclear	0.01

Table 5.3. LCI data ($F_{i,DATABASE}$), for generation of 1 MJ of electricity from power grid, and for comparison one source in which electricity is generated at the refinery.

	BOUSTEAD, at refinery (Boustead, 1993)	PEMS, Europe (PIRA, 1998)	SIMAPRO, Europe (PRE, 1998)	ECOPRO, Europe (EMPA, 1996)
Fuel				
coal (MJ)	0.01	1.25745	1.00293	0.9393
Oil (MJ)	1.22	0.3488	0.36225	0.39105
Gas (MJ)	1.61	0.291	0.27105	0.22971
Hydro (MJ)	0.01	0.209	0.198	0.220
Nuclear (MJ)	0.01	0.976		
Raw Materials				
Barite (mg)		48	49	
Bauxite (mg)		19	18	
Bentonite (mg)		38	51	
Ferro manganese (mg)		1	0.4	
Iron ore (mg)		940	366	
Lignite (mg)		34700	43100	217
Limestone (mg)		1420		
Sodium Chloride (mg)		25	23	
water (mg)	44000	6310000	6240000	
Zeolite (mg)		1	0.5	
Emissions to air				
dust (mg)	130		209	142
benzene (mg)			0.1	0.1
CxHy aromatic (mg)				1
methane (mg)		359	303	282
Hydrocarbons (mg)	2000			
non-methane VOC's (mg)		61	63	74
CO ₂ (mg)	168000	138000	133000	119000
CO (mg)	70	26	25	21
HF (mg)		3	2.3	2.8
N ₂ O (mg)		1	1	1
HCl (mg)		25	21	19

Table 5.3 (continued)

	BOUSTEAD, at refinery	PEMS, SIMAPRO, Europe	ECOPRO, Europe	Europe
SOx (as SO ₂ , mg)	1600	663	661	627
NOx (as NO ₂ , mg)	1600	304	283	0.256
Metals (mg)	1			6
Emissions to water				
BOD (mg)	1			
COD (mg)	1	1		
TSS (mg)	1	261	38	38.8
phenols (mg)	1			
Hydrocarbons (mg)	10		9.8	
nitrate (mg)		2	1.5	1.5
Total N (mg)		1	1.1	0.5
Cl (mg)		633	558	555
phosphate (mg)		4	3	3
TDS (mg)		28	175	456
Al (mg)		67	53.6	50
Ba (mg)		6	5	5
Cr (mg)		1		
Fe (mg)		76	85	67
Zn (mg)		1		
Solid emissions				
mineral waste(mg)	20			
slags & ash (mg)	5			
Mixed industrial (mg)	110			
Unspecified (mg)			17900	

Table 5.4 LCI data for burning fuel for thermal energy production. (F_{ij}) (Pre, 1998)

	F_{ij}	F_{ij}	F_{ij}
	Coal	Gas	Oil
	1kg	1 kg	1 kg
Heat value (MJ/kg)	30.3	54.3	45
Resources			
lignite (mg)	35,200	39,541	54,600
natural gas (m3)	0.021	1.56	0.0636
coal (mg)	1,660,000	29,656	41,100
crude oil (mg)	26,900	10,136	1,130,000
uranium ore (mg)	2.39	2.69	3.71
wood (mg)	15900	291	403
Energy hydropower (MJ)	0.154	0.173	0.239
Emissions to air			
dust (mg)	2,100	171	2,480
benzene (mg)	15.1	20.7	12.1
PAHs (mg)	0.0118	0.518	0.0476
CxHy aromatic (mg)	7.39	11.48	29.9
methane (mg)	11,700	8,994	4,710
non-methane VOC's (mg)	555	749	8,990
CO ₂ (mg)	2,840,000	3,188,339	3,760,000
CO (mg)	3,140	1,350	1,300
ammonia (mg)	1.56	0.317	444
HF (mg)	54.8	2.102	8.92
N ₂ O (mg)	34.8	34.4	76.3
HCl (mg)	1,490	19.9	87.6
SO _x (as SO ₂ , mg)	16,300	1,796	52,100
NO _x (as NO ₂ , mg)	6,990	9,520	9,520
Pb (mg)	2.4	0.023	2.43
Mn (mg)	0.613	0.001	0.014
Ni (mg)	1.79	0.138	28.4
Hg (mg)	0.092	0.015	0.015

Table 5.4 (continued)

	F_{ij}	F_{ij}	F_{ij}
	Coal (1kg)	Gas (1 kg)	Oil (1 kg)
Zn (mg)	1.91	0.048	2.65
Metals (mg)	636	6.01	169
Emissions to water			
BOD (mg)	0.0791	0.155	2.49
COD (mg)	2.76	2.088	48.5
AOX (mg)	0.005	0.001	0.196
TSS (mg)	115	1,573	2,340
phenols (mg)	0.208	0.323	8.13
toluene (mg)	0.106	0.312	6.7
PAH's (mg)	0.001	0.006	0.738
CxHy aromatic (mg)	1.15	3.23	48.2
oil (mg)	35.8	74.2	1500
TOC (mg)	16.6	1545	448
NH ₄ ⁺ (mg)	4.21	1.129	57.8
nitrate (mg)	2.47	1.462	37.4
Total N (mg)	1.66	0.090	56
As (mg)	5.28	0.097	0.177
Cl (mg)	13,900	608	30,500
phosphate (mg)	158	2.87	4.52
sulphate (mg)	12,000	544	1,530
TDS (mg)	8,590	1,045	22,100
Al (mg)	2,640	48.2	66.9
Ba (mg)	215	5.05	147
Pb (mg)	13.3	0.284	0.457
Cd (mg)	0.134	0.003	0.0644
Cr (mg)	26.5	0.633	1.14
Fe (mg)	851	78	116
Cu (mg)	13.2	0.238	0.43
Ni (mg)	13.3	0.242	0.49
Zn (mg)	26.6	0.486	1.16
Metals (mg)	279	8.159	353
Solid waste (mg)	Not reported	Not reported	Not reported

Table 5.5. Oil required as Feedstock (MJ) as reported in the data sets.

Database	Feedstock, MJ
PWMI South European	45.0
PEMS South European	45.0
PWMI Average European	45.0
PEMS Average European	45.0
EMPA Naphtha	52.7
ECOPRO Naphtha	45.9
SIMAPRO Naphtha-BUWAL 250	45.9
SIMAPRO Naphtha, Average Europe	45.0
PEMS Naphtha, Average Europe	45.0
Boustead Naphtha, Average Europe	45.2
SIMAPRO Diesel	45.0
PEMS Diesel	42.8
EMPA Diesel	48.2
ECOPRO Diesel	45.6
FRANKLIN Average European	47.4
Average	45.9
Median	45.0
Standard Deviation	2.2

Table 5.6. NOx emission distribution for the databases analyzed.

	Total value (mg NOx/kg refinery product)	Average from electricity	Average from heat	Average from processes	Distribution: calculated (c) or given (g)
PWMI	3,000	0.53%	15.85%	83.62%	c
South European					
PEMS	3,000	0.17%	15.98%	83.85%	c
South European					
PWMI	2,900	2.76%	17.57%	79.67%	c
Average European					
PEMS	2,900	0.08%	18.22%	81.70%	c
Average European					
EMPA Naphtha	<u>2,665</u>	<u>4.15%</u>	<u>94.53%</u>	<u>1.32%</u>	g
ECOPRO Naphtha	2,900	0.44%	18.67%	80.89%	g
SIMAPRO	2,900	0.42%	18.22%	80.89%	c
Naphtha-BUWAL 250					
SIMAPRO Naphtha,	2,900	0.42%	16.58%	83.00%	c
Average Europe					
PEMS Naphtha,	2,888	4.06%	65.93%	30.01%	c
Average Europe					
Boustead Naphtha,	<u>2,900</u>	<u>7.17%</u>	<u>92.82%</u>	<u>0.00%</u>	g
Average Europe					
SIMAPRO Diesel	2,900	0.09%	17.99%	81.92%	c
PEMS Diesel	2,864	3.66%	54.00%	42.34%	c
EMPA Diesel	<u>2,001</u>	<u>3.55%</u>	<u>94.85%</u>	<u>1.60%</u>	g
ECOPRO Diesel	2,660	2.30%	37.59%	60.11%	c
FRANKLIN Average	3,987	0.48%	14.39%	85.13%	c
European					
Average	2892	2.02%	39.55%	58.43%	
Median	2900	1.42%	18.45%	80.28%	
Standard Deviation	376	2.14%	32.07%	33.96%	
Average of underlined data		4.96%	94.07%	0.97%	

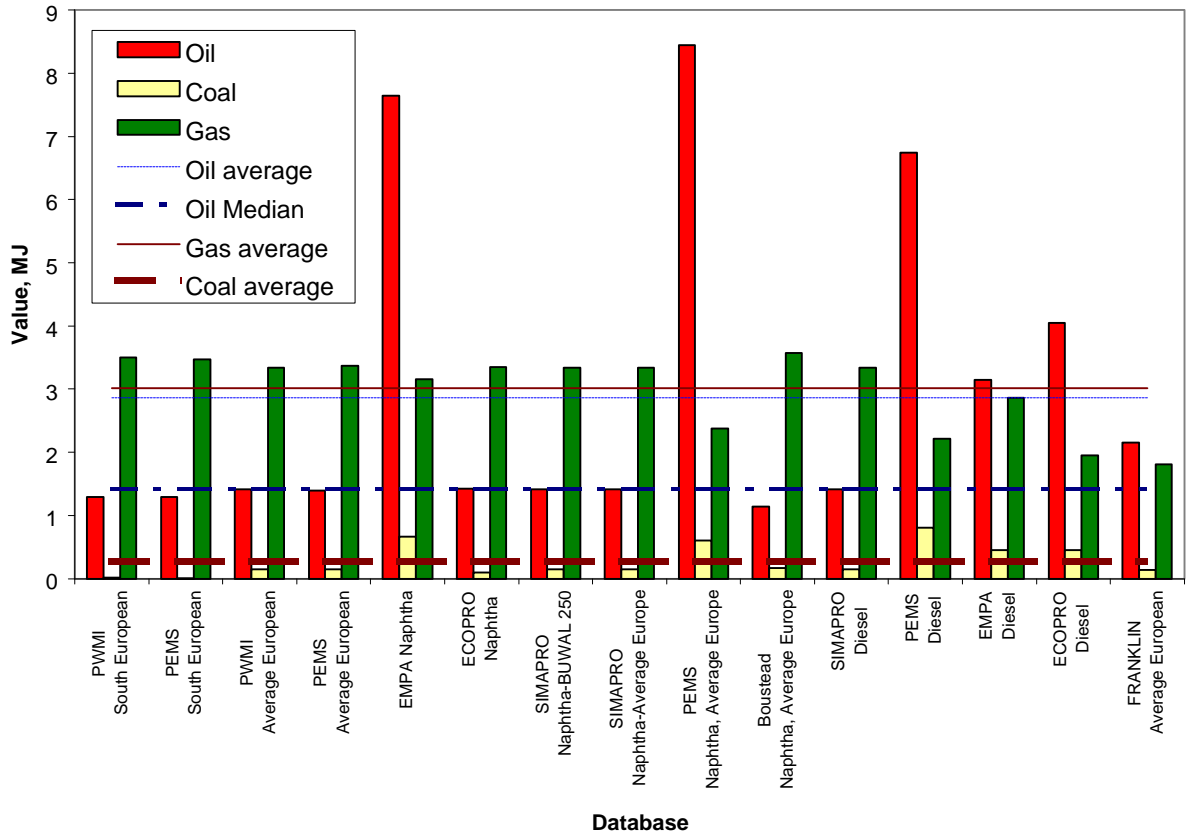


Figure 5.1. Comparison of Refinery Use of Oil, Natural Gas and Coal per kg of refinery product reported in the data sets analyzed (Feedstock energy value not included).

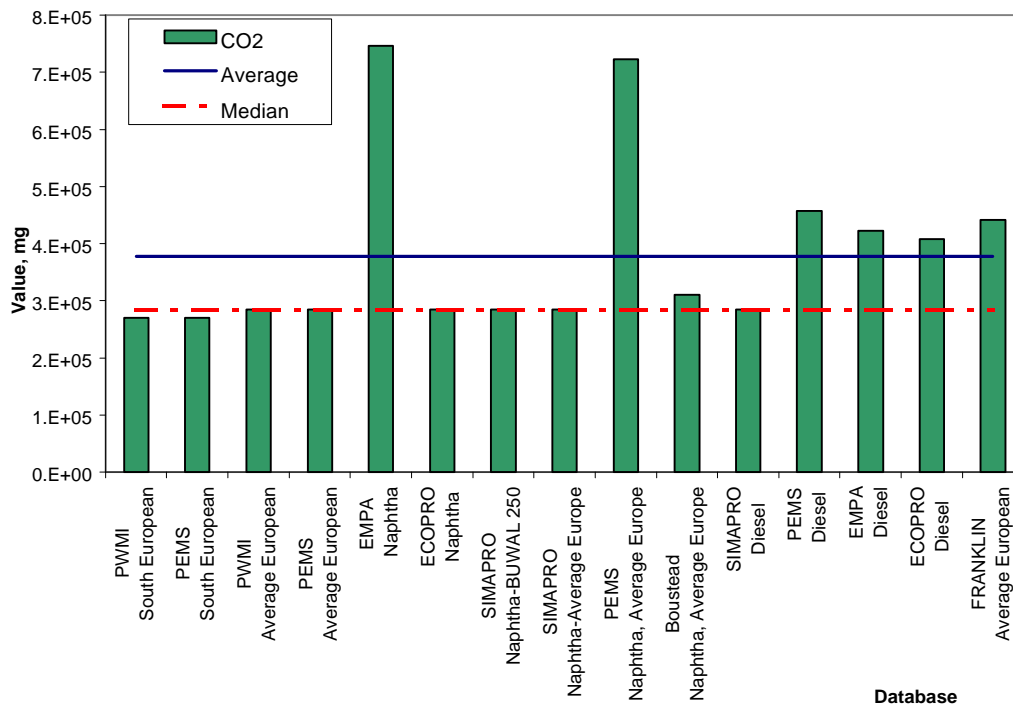


Figure 5.2. Comparison of the total carbon dioxide emissions per kg of refinery product reported in the data sets analyzed.

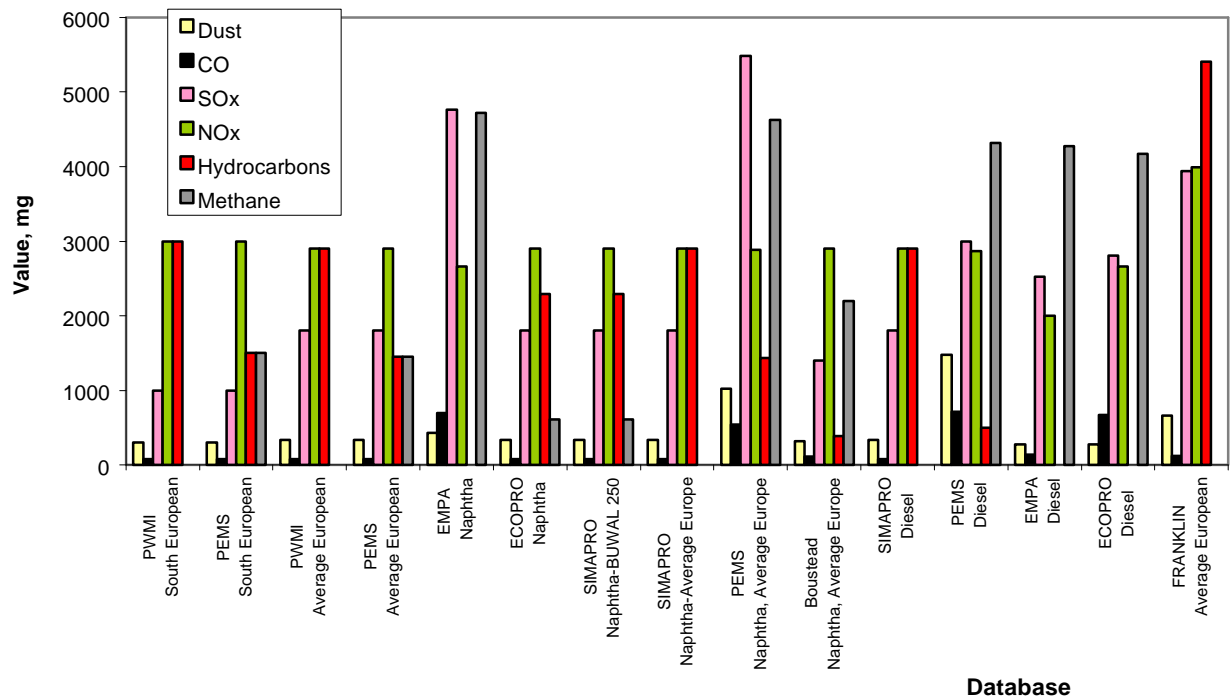


Figure 5.3. Comparison of the total air emissions (mg/kg of refinery product) of dust, carbon monoxide, hydrocarbons, methane, sulfur oxides and nitrogen oxides reported in the data sets analyzed.

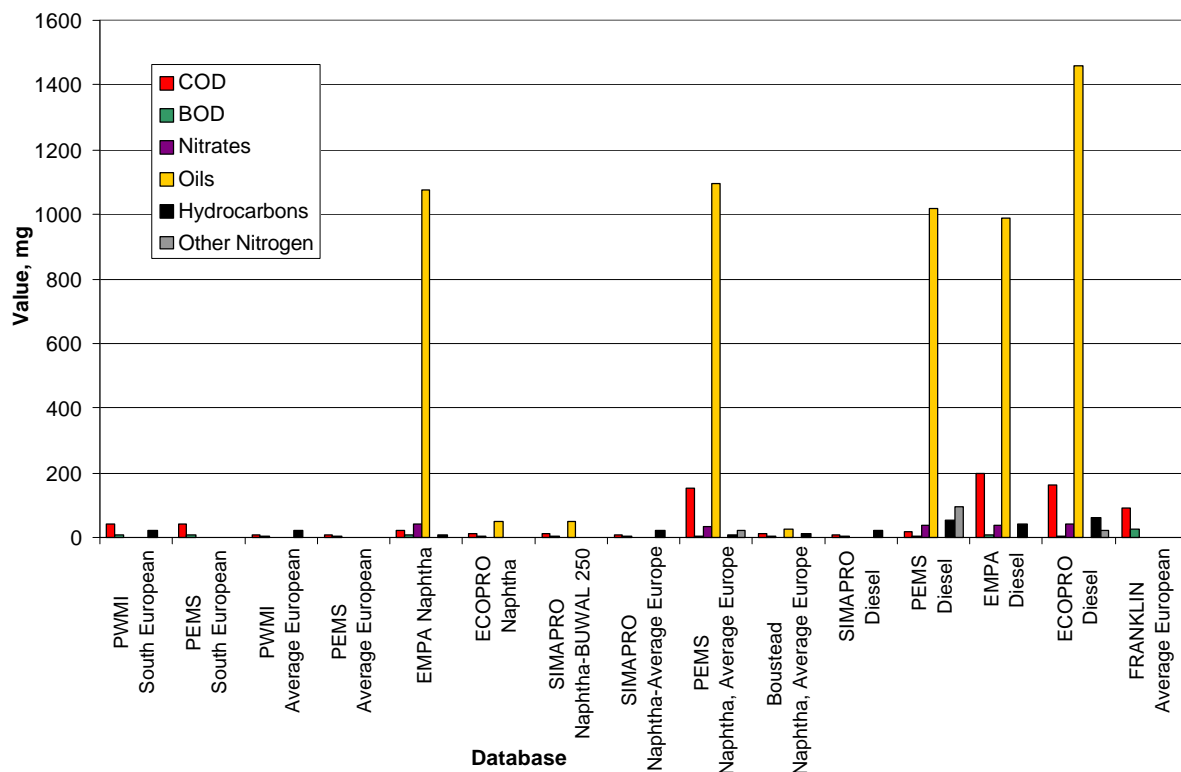


Figure 5.4. Comparison of some water borne emissions (mg/kg refinery product) reported in the data sets analyzed.

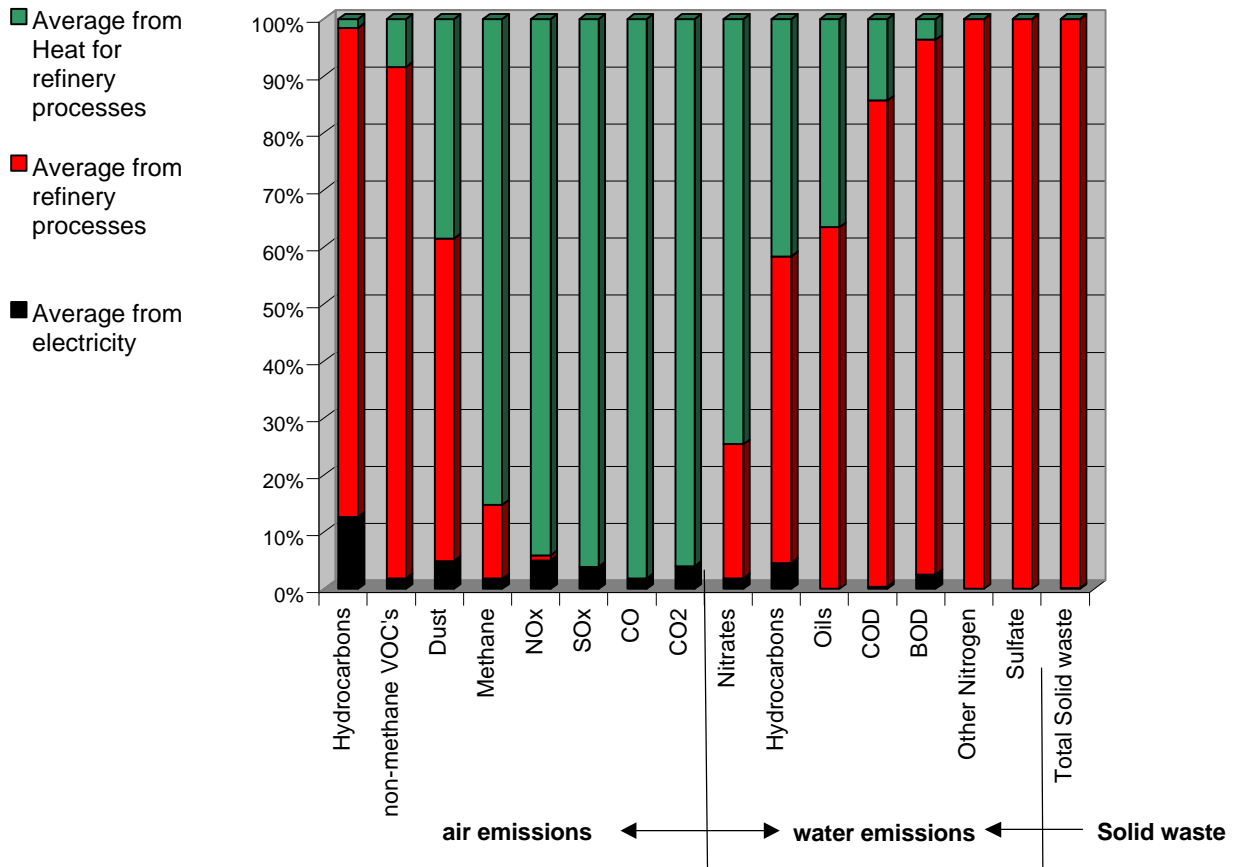


Figure 5.5. Comparison of the contribution to air and water emissions.

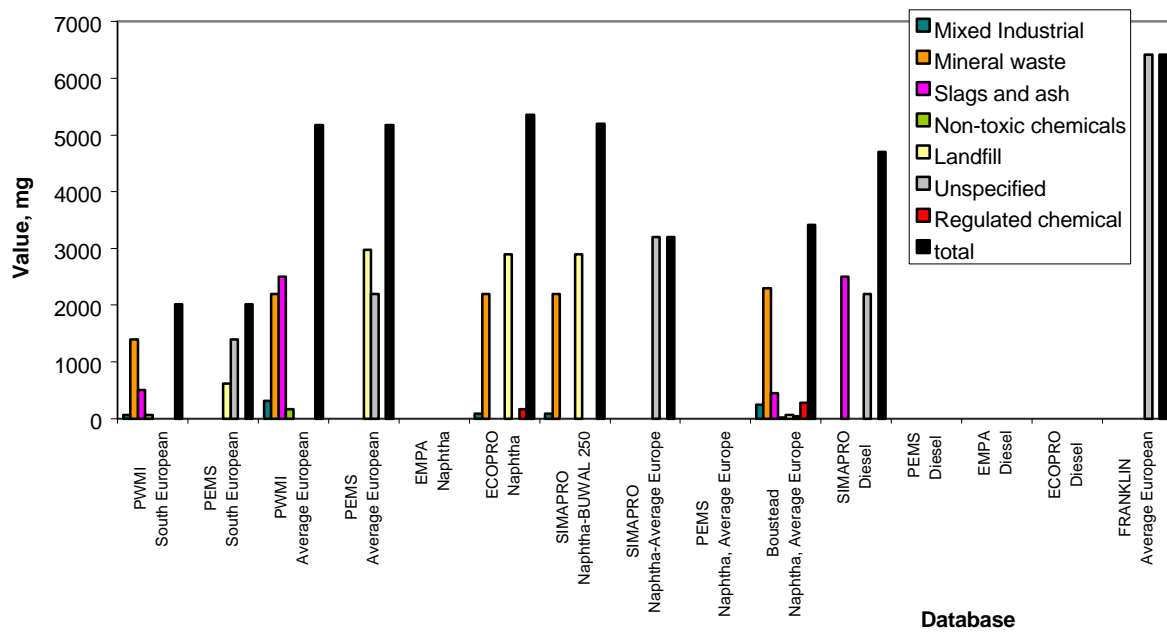


Figure 5.6. Comparison of the solid waste (mg/kg of refinery product) reported in the data sets analyzed.

6. TREATMENT MODULES - A PARTIAL LIFE CYCLE INVENTORY

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6. TREATMENT MODULES - A PARTIAL LIFE CYCLE INVENTORY

Abstract

When performing a Life Cycle Inventory (LCI) sometimes the data available in the literature or estimated by the practitioner only include pretreatment or manufacturing information. In those cases, there is a need to use a model for waste treatment to estimate the post-treatment data. In other cases, it is desirable to back calculate pre-treatment information from final environmental emissions.

In the present chapter, treatment modules for LCI were developed based in design equations and average literature data. The modules developed were for Wastewater Treatment Plant (WWTP), Solvent Incinerator, and Solvent Recovery.

For the WWTP module, biodegradation of organic matter and removal of Total Dissolved Solids (TDS) were considered the key treatment parameters. The results obtained were then compared with data collected directly from wastewater treatment facilities.

For the solvent incinerator module, the total average carbon content in kg per kg of chemical was used as a basis for the calculations, since the feed is normally a mixture of different organic compounds. A general basis for the estimation of emissions and energy recovered is provided to simplify the calculations in such a manner that computations for every single organic compound entering the incinerator are avoided.

Finally, for the solvent recovery module, computer simulations of solvent recovery via distillation of 12 common solvents were performed. The assumptions made for the simulations and the results obtained are shown.

The modules developed will serve in the generation of post-treatment gate-to-gate life cycle information. It is anticipated to be particularly useful in the instances when process

design techniques are employed for the estimation of LCI data, especially in chemical, biochemical and pharmaceutical industries.

Keywords: LCI post-waste treatment data, VOC emissions, thermal oxidizer, solvent incinerator, gate-to-gate LCI, wastewater treatment, life cycle inventory, wastewater treatment design, Chemical Oxygen Demand, Total Organic Carbon, Biochemical Oxygen Demand.

6.1 The Wastewater Treatment Plant Module

To develop the Wastewater Treatment Plant (WWTP) Module, calculations of life cycle information based in design equations and average data were developed and compared with data obtained by independent calculations and directly from two wastewater treatment facilities. The system is given in Figure 6.1.

6.1.1 COD Model

6.1.1.1 Calculation of Life Cycle Information using design equations and average data.

First, design equations were used to calculate the inputs and outputs of a conventional biological wastewater treatment plant based on 1 kg the COD as input. A conventional biological wastewater treatment plant with the flow diagram shown in Figure 6.1 was used as system.

6.1.1.1.1 Calculations for Oxygen Requirements, Carbon Dioxide generated and Sludge Produced.

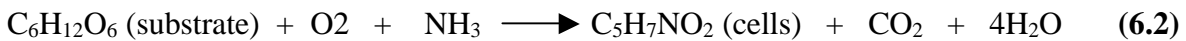
a) Equations used:

The following reactions describe the main mechanisms taking place in the activated sludge treatment (Rozich, 1992):

Cell Auto-oxidation:



Energy Generation and Cell Production:



The substrate are those organic chemicals generated from a manufacturing process that are liquid at 25°C and 1 atm., and that are suitable or likely to be discharged to a wastewater treatment plant. The substrate in (2) is one example, but all organic chemicals can be characterized by calculating the theoretical oxygen demand (ThOD) or the TOC. The organic substrate is thus the link between a chemical processing LCI module and the wastewater treatment module that yields emissions to the environment.

Eckenfelder (Eckenfelder, 1989, 1995) developed engineering design methods based in the equations (6.1) and (6.2), but generalizing for a wide variety of substrates and microbial colonies. The main design equations to estimate the required oxygen and the net biosolid production are as follow:

$$\text{O}_2 = a'S_0 + b'X_{\text{ML}} \quad (6.3)$$

$$X_{\text{p}} = aS_{\text{r}} - bX_{\text{ML}} \quad (6.4)$$

Where:

O_2 = Oxygen required, kg

X_p = Net Biosolid production, as kg VSS

a' = kg oxygen consumed / kg COD in feed

b' = kg oxygen consumed / kg of total cells, as volatile suspended solids (VSS)

S_0 = Substrate entering the treatment, as kg of COD

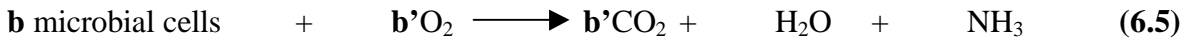
X_{ML} = Mass of total cells in the mixed liquor, as kg VSS

a = kg of cells produced, as VSS/kg of COD reduced (COD_r)

b = kg of cells undergoing auto-oxidation/kg total cells, as VSS

S_r =Substrate reduced in the treatment, as kg of COD reduced (COD_r)

As an illustration for Eckenfelder design, equations (6.1) and (6.2) can be written:



Since the production of CO₂ is the same as the requirements of oxygen, when expressed in molar basis, then:

$$CO_2 = 1.375 O_2 \quad (6.7)$$

Where CO₂ is the carbon dioxide produced in kg, and 1.375 is the ratio of molecular weights. Also, normally only data about b are available and then b' can be calculated using the stoichiometric relationship in reaction (6.1), giving:

$$b' = 1.42b \quad (6.8)$$

X_{ML} can be estimated from the substrate concentration by the relationship F/M (food/microorganisms), expressed as kg BOD/kg MLVSS.

b) Data:

The average data were taken from literature to perform the calculations using design equations, in Table 6.1. The values of a and a' represent average data that cover most of the wastewater substrates, and that are backed up by the results of different research works.

The ratio F/M is the average of the design data reported from 8 WWTP in the US, with a standard deviation in the sample of 0.09 (ASCE, 1983).

The factor b represents the average for chemical and petrochemical wastewater as reported in the reference (Ramalho, 1983).

The value for the COD/TOC ratio is the average data of wastewater from selected chemical industries, as presented in Table 2.2 of the reference. The values for the COD/BOD ratio and reduction of COD are the average from selected chemical industries taken from Table 4.1 of the reference, including only the following industry sectors: chemical intermediates, pharmaceutical, diversified chemical industry, custom pharmaceutical manufacture, complex organic, combined industrial, and organic chemicals.

c) Calculations:

Basis: 1 kg COD in the feed

$$X_{ML} = \frac{1 \text{ kg COD}}{1.89 \text{ kg COD}} \left| \frac{1 \text{ kg BOD}}{0.51 \text{ kg BOD}} \right| \frac{\text{kg MLVSS}}{\text{kg MLVSS}} = 1.04 \text{ kg MLVSS}$$

$$b' = 1.42b = 1.42(0.12) = 0.17$$

Oxygen required:

$$O_2 = a'S_0 + b'X_{ML} \quad (6.3)$$

$$= 0.45 \frac{\text{kg oxygen}}{\text{kg COD}} (1 \text{ kg COD}) + 0.17 \frac{\text{kg oxygen}}{\text{kg MLVSS}} (1.04 \text{ kg MLVSS}) = \underline{\underline{0.63 \frac{\text{kg O}_2}{\text{kg COD}}}}$$

Carbon Dioxide Liberated:

$$CO_2 = 1.375 O_2 = 1.375 \frac{\text{kg CO}_2}{\text{kg O}_2} (0.63 \text{ kg O}_2 / \text{kg COD}) = \underline{\underline{0.87 \frac{\text{kg CO}_2}{\text{kg COD}}}}$$

Biosolids produced

$$X_p = aS_r - bX_{ML} \quad (6.4)$$

$$= 0.55 \frac{\text{kg VSS}}{\text{kg COD}_r} (0.86 \text{ kg COD}_r) - 0.12 \frac{\text{kg VSS}}{\text{kg MLVSS}} (1.04 \text{ kg MLVSS}) = \underline{\underline{0.35 \frac{\text{kg VSS}}{\text{kg COD}}}}$$

The latter quantity was calculated in a dry-weight base. Since the average solid concentration in untreated biosolids from a WWTP is 5% (Metcalf & Eddy, 1980), the water going out with the sludge is:

$$\frac{0.35 \text{ kg VSS}}{\text{kg COD}} \bigg| \frac{0.95 \text{ kg water}}{0.05 \text{ kg VSS}} = \underline{\underline{6.65 \frac{\text{kg water in biosolids}}{\text{kg COD}}}}$$

6.1.1.1.2 Energy Requirements.

The major energy consumers in wastewater collection and treatment systems are the pumps and blowers used to move wastewater, sludge and air through the system. The average distribution of electricity usage in a WWTP is 47% for aeration, 19% for anaerobic treatment of biosolids, 13% for pumping, 2% lighting, and 19% for miscellaneous uses, including production and transmission losses (O'Brien, 1986).

Therefore, by estimating the energy required for aeration, it is possible to obtain an estimation of the total energy. The data for aeration electricity consumption taken from the literature (Shell, 1986; Gray, 1990) are given in Table 6.2, and the results of the electricity requirements per kg of COD in the feed, using the oxygen intake calculated before are shown in Table 6.3.

6.1.2 Comparison between these results and other data.

In Table 6.4, a summary of the data obtained is presented, contrasting it with the data obtained anonymously from two industrial WWTP, and the data given by the City of Raleigh, EM Johnson WWTP (Garland, 1998). The results are presented on a basis of 1 kg COD to be treated.

6.1.3 Ancillary Substances

During wastewater treatment some substances are used as additives, such as polymers, NaOH, ammonia etc., which are normally added to the wastewater in small amounts (each one of them a contribution of 6% or less of incoming BOD₅, CSWRCB, 1984), Table 6.5. Besides, the WWTP has requirements of gasoline for the vehicles and oil for machinery maintenance.

Furthermore, as a rule of thumb, to ensure adequate nitrogen and phosphorous for BOD removal, it is necessary to provide a nutrient mass ratio of 100:5:1 (BOD:N:P, Eckenfelder, 1995). Since industrial wastewater normally lack these nutrients, these are added as ammonia and some soluble orthophosphate. The estimated amount of ammonia and o-phosphate (as phosphoric acid) and the information on the additional substances used in the Raleigh WWTP per kg of COD in the influent is given in Table 6.5.

From the ancillary substances, the polymers, ammonia, and phosphorous are assumed to remain principally in the biosolid mixture after treatment; meanwhile the sodium hydroxide used mainly in the WWTP scrubbers will remain in the effluent of treated wastewater

6.1.4 Inorganic Salts

To model the amount of total dissolved solids that remain in the effluent after activated sludge treatment, it is assumed that heavy metals are adsorbed with typically 60-90% removal, and most of the water soluble salts go directly to the effluent and will not be adsorbed. Therefore, a 75% of adsorption for heavy metal salts and 10% for non-heavy metals salts was assumed, leaving the remaining 25% and 90%, respectively as effluent.

If the characteristics of the dissolved solids are not known, and these are expressed as total dissolved solids (TDS), then the assumption is that 30% of inorganic salts are retained in the sludge, with the remaining 70% of TDS leaving in the effluent with the treated water. The figure of 30% is derived from an average reduction percentage of TDS after the activated sludge treatment, Table 6.6 (CSWRCB, 1984; Eckenfelder, 1978).

For heavy metals, the inorganic removal percentages are greater than those for TDS. Of the TDS in municipal influent about 75% is accounted for as Ca^{++} , Mg^+ , K^+ , Na^+ , SO_4^- , Cl^- . Thus 30% removal reflects principally these major ions. For heavy metals (Zn, Se, Pb, Ni, Mo, Hg, Cu, Cr, Cd and As), the sum of the median concentration in municipal influent is about 2 mg/L (Chang, 1983) and thus is a very small fraction of TDS.

Using the sum of the same heavy metals in secondary effluent (Chang, 1983a) the removal is 93% (and thus appearing in the biosolids stream). Therefore, a first estimate

model uses a 30% removal (70% in effluent) for TDS and a 93% removal (7% in effluent) for heavy metals

6.1.5 Specific Organic Compounds

Since manufacturing processes generate specific organic compounds, it might be desirable to count with an estimate of the effluent concentration of each individual organic compound to perform further assessments. Therefore, an estimated removal percentage was sought. One estimate would be 86%, found earlier for TOC/COD removal, Table 6.4, but this includes in the effluent the biological products generated in the aerobic treatment.

Data of organic compounds biodegradation in WWTP were also taken from different sources (USEPA, 1979; Lankfor, 1990; CSWRCB, 1984; Eckenfelder, 1978). These showed a median degradation percentage of the organic compound in activated sludge systems of 95% with a standard deviation of 17%. These data include 70 entries of organic compounds, including haloalkanes, benzene, haloalkanes, phenol, halophenoles, phthalates, naphthalenes, and pyrenes.

To account for the effects of volatilization, the WWTP mechanisms of removal of a wide range of individual organic compounds was modeled using the EPA software Water8 (USEPA, 1995). The results of computer modeling show a median degradation percentage of 98%, with 1.2% volatilized for compounds with boiling point less than 140 C, 0.07% for compounds with boiling point greater than 140 C and the rest in the effluent.

Therefore, from the literature data and the modeling, it was estimated that for the WWTP module 96% (weight) of individual organic compounds was biologically transformed in an activated sludge plant (arithmetic average from literature and modeling results). About

1% is volatilized for compounds with a boiling point of less than 140 C. The remaining 3% is released in the effluent (4% for high-boiling-point compounds).

Nevertheless, if the effects of volatilization as a removal mechanism are not accounted for; not big difference is expected, since the low percentage of volatilization estimated.

6.1.6 Summary of LCI for WWTP Module

Table 6.7 presents the summary of the LCI data for the WWTP module, showing the results both for a basis of 1 kg of TOC in the influent, and 1 kg of COD in the influent.

For inorganic salts not containing heavy metals, 90% will remain in the effluent and the other 10% will be adsorbed in the biosolids. For the inorganic salts containing heavy metals, 25% remain in the effluent and the rest in the biosolids (see point 6.1.4.). As an example, Table 6.8 shows the summary of LCI for a wastewater containing 1.9 kg inorganic salts/kg TOC (0.66 kg TDS/kg COD), typical of an untreated municipal wastewater of medium concentration (CSWRCB, 1984). It was assumed that 10% of the salts contained heavy metals (~0.2 kg/kg TOC, ~0.06 kg/kg COD), but the conditions will vary from case to case.

For a LCI application, it is assumed that the biosolids are sent to stabilization and landfill, as described in section 6.4.

6.1.7. Limitations of the Model

Even though the results of the module are considered to have enough accuracy for the purposes of the broad LCI study, the model contains the following limitations:

The main emphasis on the model is the biodegradation of the organic matter sent to the WWTP and thus provides only an approximation for trace metals or trace toxic elements or compounds.

This model does not account for ammonia emissions from the WWTP that occur mainly in municipal plants, since for industrial applications, there is normally a deficit of ammonia, resulting in the need to add this compound to the wastewater (Table 6.5).

The estimation of energy requirements tends to be general, but changes should be made if the energy requirement distribution varies significantly from the one presented here.

6.2 Solvent Incinerator (Thermal Oxidizer) Module

Modeling a solvent incinerator (or thermal oxidizer) for life cycle studies, it is assumed that spent organic solvent (either liquid or gas) is fed to the incinerator. Air is used for the combustion. Water vapor, carbon dioxide and trace of organic compounds leave the incinerator, and part of the energy released by the combustion reaction is recovered from this hot stream (Figure 6.2).

Both gas and liquid solvent process emissions can be treated in the thermal oxidizer, and the feed is normally a mixture of different organic compounds. Since the combustion reaction is well-known, a model was developed directly using some rules of thumb for incineration technology.

Since the solvent incinerator module will be linked to gate-to-gate life cycle information modules; a general basis for the estimation of emissions and energy recovered is needed to simplify the calculations in such a manner that individual computations for every single organic compound entering the incinerator are avoided.

6.2.1 Methodology

A solvent incinerator operating with 99.99% efficiency (Curzons, 2000) and a combustion temperature of 900 C was assumed. Both gas and liquids can be potentially fed into the incinerator, depending of the arrangements of the feed stream. Water outputs are not considered as chemical emissions in the analysis from a Life Cycle perspective.

Since the carbon dioxide emitted is dependent of the formula of the compound combusted, total mass of volatile organic compounds (VOC's) is therefore not an appropriate basis in order to obtain a generalized model. Assuming complete combustion, the amount of carbon dioxide produced can be calculated directly using stoichiometric relations, the efficiency of the incinerator (99.99%), and the mass of carbon entering the oxidizer are shown in equation (6.9).

$$\text{CO}_2 \text{ emission} = m_c \frac{44 \text{ kg CO}_2}{12 \text{ kg C}} h \quad (6.9)$$

where m_c is the mass of carbon contained in the solvent stream, and h is the efficiency of the incinerator. If significant sulfur and nitrogen are present, then a direct conversion to SOx and NOx can be calculated.

Therefore, the mass of carbon contained in the stream was considered to be adequate for the estimation of emissions at the level of accuracy required. The total amount of solvent leaving the incinerator without being converted is calculated with equation (6.10)

$$\text{Solvent emission} = \text{VOC's} = m_{\text{solvent feed}} (1 - h) \quad (6.10)$$

where $m_{\text{solvent feed}}$ is the amount of solvent sent to the incinerator.

The theoretical heat of combustion was first calculated for the gas and liquid feed scenario at 900 C. The heat of combustion at 900 C is calculated with equation (6.11)

$$\Delta H_c(900\text{ C}) = \Delta H_c^o + (900 - 25) \left(\sum_{\text{products}} n_i C_{p_i} - \sum_{\text{reactants}} n_i C_{p_i} \right) + \Delta H_{v,\text{products}} - \Delta H_{v,\text{reactants}} \quad (6.11)$$

where ΔH_c^o is the standard heat of combustion at 25 C, $\Delta H_c(900\text{ C})$ is the heat of combustion at 900 C, n_i is the stoichiometric coefficient in the combustion equation for either product or reactant i , C_{p_i} is the mean specific heat capacity at constant pressure for either product or reactant i , and ΔH_v is the latent heat of vaporization of products or reactants that undergo phase change between 900 and 25 C.

Once the heat of combustion at 900 C is calculated, the total released energy is estimated with the theoretical Q (heat of reaction plus sensible heat, plus latent heat) according to equation (6.12):

$$Q = \Delta H_c(900\text{ C}) + \sum_{\text{reactants}} n_i C_{p_i} \Delta T_i + \Delta H_{v,\text{reactants}} \quad (6.12)$$

where ΔT_i is the difference in temperature between inlet liquid or gas and 900 C.

To develop a general model, the released heat (Q) of nine common solvents was first expressed on the basis of the carbon content of the solvent, Table 6.9. The solvent was fed to the incinerator as a liquid at 25 C, and with air supply in stoichiometric proportions.

The average of the values of released heat (Q) was used as an estimate of the total energy released by the reaction. For an incinerator operating at 900 C, it was assumed that 75% of the energy released was recovered for steam production (avoided emissions), according to the rules of thumb of heat recovering systems efficiency reported by Branan, 1994. Therefore, the total energy recovered is calculated as shown in equation (6.13):

$$\text{Energy recovered} = 0.75h m_C (\bar{Q})_{\text{carbon base}} \quad (6.13)$$

where $(\bar{Q})_{\text{carbon base}}$ is the average heat released expressed as MJ/ kg of carbon contained in the solvent. From Table 6.9 one can see that heat release (MJ/kg of carbon) has less variability and can be used more widely to estimate incinerator LCI behavior.

6.2.2 Results

To verify the assumption that the same energy recovered can be used for either gas or liquids fed to the thermal oxidizer, the calculations of total energy recovered were performed for ethanol, using two scenarios:

- a) ethanol is fed as a liquid at 25 C
- b) ethanol is fed as a gas just above the boiling point (b.p.= 79 C)

For ethanol, the combustion reaction is shown in equation (6.14):



The heat of combustion at standard conditions is: $\Delta H_c^o = -1.367 \text{ MJ/gmol}$. The specific heat capacities for ethanol, carbon dioxide, water and oxygen are 112.4, 55.0, 75.3 and 35.0 J/gmol-K, respectively. In the ΔH_c calculations at 900 C, one molecule of ethanol reactant condenses (-42.3 KJ/gmol of ethanol) and three molecules of water product vaporize (+43.99 KJ/gmol of water). Therefore, applying equation (3) heat of combustion at 900 C is $\Delta H_c(900 \text{ C}) = -1.174 \text{ MJ/gmol}$.

If we consider a feed stream of gaseous ethanol at 80 C and the stoichiometric requirements of air at 25 C (8.94kg air/kg ethanol), then the sensible heat to raise the ethanol from 80 C to 900 is 92.16 kJ/gmol., and to heat the air from 25 to 900 is 437.5 kJ/gmol. Therefore, the total heat released according to equation (4) is $Q = -1.174 + 0.0921 + 0.4375 = 0.644 \text{ MJ/gmol}$ of ethanol. In all these cases, no incremental

supplemental fuel is needed for combusting the ethanol, although such fuel might be needed for other materials being combusted in parallel.

If we consider a feed stream of liquid ethanol at 25 C and the stoichiometric requirements of air, then the sensible heat for the ethanol from 25 C to 900 is 98.35 kJ/gmol, and to heat the air from 25 to 900 is 437.5 kJ/gmol. Therefore, the total heat released according to equation (4) is $Q = -1.174 + 0.0983 + 0.4375 = 0.638$ MJ/gmol of ethanol (as compared to 0.644 MJ/gmol for ethanol as a gas at 80 C).

The average theoretical heat released in the combustion reaction (Q), when a liquid stream is fed at 25 C is thus assumed to be a good estimate of the total energy released in the oxidation reaction, both for the scenario of a gas feed and a liquid feed. With the results, we can conclude that it is also a safe assumption to use the same energy result whether gas or liquids are fed to the thermal oxidizer.

The calculations for other eight solvents were performed then using the conditions of the scenario A (liquid fed at 25 C). Table 6.9 and 6.10 summarize the calculations and the results for the module, respectively.

6.2.3 Limitations of the Model

Even though the results of the module are considered to have enough accuracy for the purposes of the study, the model presents the following limitations:

Since complete combustion is assumed, ashes, carbon monoxide and nitrogen oxides emissions are not considered. Should field information about those emissions become available, it is advisable to include these in the model. A sensitivity analysis might be useful to estimate the trade-off of including other emissions.

This model considers that no extra fuel is required, and the released energy is recovered in 75% to produce steam. This is the assumption that the incinerator is operated with a large amount of organic material with an overall heat value sufficient to sustain combustion. Thus, for any specific set of process emissions, to be managed by a thermal oxidizer or incinerator, only the incremental emissions and energy are applicable. This transparent module allows modifications on a site-specific basis.

6.3. Solvent Recovery Module

Distillation is most commonly used for purifying solvents. Solvents with different vapor pressures can be separated from one another by fractional distillation. Azeotropic mixtures can be separated by extractive or azeotropic distillation (e.g., addition of benzene to a water – ethanol mixture), by chemical reaction of a component (e.g., addition of acetic anhydride to an ethanol – ethyl acetate mixture), or by altering the pressure during distillation (Ullmann, 1985).

For modeling the solvent recovery module, a model of a traditional distillation column was used, as shown in Figure 6.3. In this system the spent solvent is fed into the column and distilled. Purified solvent is recovered and the remaining spent stream is sent either to the thermal oxidizer or to the wastewater treatment plant, depending on the water content of the stream.

6.3.1. Methodology

For the Solvent recovery module, computer simulations of solvent recovery of 13 common solvents were performed using CHEMSEP software (Kooijman and Taylor, 1992).

The main objective of this simulation is to obtain an estimate of the energy required in the recovery unit, the cooling requirements of the solvent recovery modules, and an estimation of the potential heat recovery from the solvent recovery module.

The solvents of interest are shown in Table 6.11. These solvents were chosen based on common solvents for pharmaceutical application. Chloroform, as indicated in Table 6.11, is used as an approximation for the recovery of methylene chloride, a solvent widely used in pharmaceutical industries.

For the simulations, simple distillation with a total condenser (liquid overheads) was assumed. Since the composition of the spent solvent will vary, a distillation of a mixture of 90% mass of solvent with 10% mass of water was used as an approximation for the recovery system.

The columns were assumed to have 10 trays operated at constant atmospheric pressure, with a reflux ratio of 1.3 (Mix, 1978). The feed stream was assumed at 25 C, being fed in the 5th tray. Raoult's Law for K and Antoine's Vapor Pressure equation were used as equilibrium models.

To estimate the amount of heat that can be recovered from the heat released at the condenser (condenser duty) the rules of thumb for heat recovery systems efficiency were used (Branan, 1994). The heuristic rules associate the temperature of the stream to be cooled (overheads) with a potential recovery percentage (shown in Table 6.11). The potential heat recovery is calculated as a percentage of the condenser duty.

6.3.2. Results

The information given by the simulation includes mass and energy balance, as well as component and temperature profile for the column. Table 6.11 shows a summary of the results for this module using the assumptions described in the methodology.

In order to couple this module to a given LCI, it is necessary to link each solvent for which recycling is an option (in kg of solvent to be treated) to the given outputs of the module. These outputs are condenser duty (cooling requirements, MJ/kg solvent treated), reboiler duty (steam requirements, MJ/kg of solvent treated) and potential energy recovery (MJ/kg of solvent treated). For LCI applications, the sub-modules for energy generation may be used for the LCI data of the cooling tower and steam generation. Also, it could be assumed that the heat recovered is used for steam production, as avoided emissions (Jiménez-González and Overcash, 2000).

6.3.3. Limitations of the Model

Even though the results of the module are considered to have enough accuracy for the purposes of the study, the model presents the following limitations:

In this model, the mixture of pure solvents and water at ideal conditions are being considered as an approximation of the distillation energy to recover solvents. In the practice, those solvents are found mixed with organic and inorganic compounds that will surely change the conditions of equilibrium and thermodynamic properties of the system. Due to the variability of the concentration and composition in the spent solvent stream, and the unavailability of specific data regarding concentrations and properties of the substances, this ideal water-solvent mixture was used as an approximation.

Since ideal behavior is assumed in the models, the results do not take into account the azeotropic behavior in the systems described (e.g. ethanol, isopropyl alcohol). When the Gamma-Phi K model, the Extended Antoine Vapor pressure and the Peng-Robinson Equation of State are used to take the azeotropic behavior into account in the ethanol and isopropanol system, the differences found between the ideal behavior and the latter modeling ranked from 7.3 to 16.9% (Table 6.12). This is not seen as a major discrepancy, since again, the ideal water-solvent system is taken as an approximation system to estimate the distillation energy for solvent recovery, therefore, the ideal case is used for all solvents.

Nevertheless these limitations, when the compositions and concentrations of the spent solvent streams are known, altogether with the properties of the substances present with the solvent, the modeling can be run again to give a more accurate result regarding the energy required for the recovery. Also, the recovery or purity goals can be changed and new solvents can be added to the list at any time.

6.4. Waste to Landfill

For the organic material being sent to landfill (e.g. biosolids from the wastewater treatment plant), the data developed by Kim and Overcash was used (Kim and Overcash, 1998). For this system, a process consisting in anaerobic digestion, dewatering and landfilling is proposed. The data utilized were taken directly from the literature (Kim and Overcash, 1998) and converted to dry-basis for standard utilization. The raw data and the dry-basis calculations are presented in Table 6.13.

To account for the landfill of inorganic products, the data developed by Barlaz was used (Barlaz, 1998; Table 6.14). For this system, the energy necessary for the operation of

the landfill and the TDS present in the leachates are considered. Amounts reported for metals are just present at the trace level and are considered negligible.

6.5 References

- ASCE. Activated Sludge: A comparison of Oxygen and Air System. American Societe of Civil Engineers, 1983
- Barlaz, Landfill process model presentation, personal communication, 1998
- Branan, C. R., Rules of Thumb for Chemical Engineers. Gulf Publishing Company, Houston, TX, 1994.
- Chang A. C., and Page, A. L., Soil deposition of trace metals during groundwater recharge using surface spreading. In: (T. Asano, ed.) Artificial Recharge of Groundwater. Ann Arbor Publishers, Inc. 1983
- Chang, A. C., and Page, A.L., Fate of Trace Metals During Land Treatment of Municipal Wastewater. Proceedings of the Workshop on Utilization of Municipal Wastewater and sludge on Land., University of California, Riverside, CA., 1983
- Cheremisinoff, P.L. and Young R.A., Air pollution control and design handbook part I, Marcel Dekker, Inc., 1977.
- Cooper, C.D. and Alley, F.C., Air pollution control: A design approach, Waveland press Inc., 1994.
- CSWRCB. Irrigation with Reclaimed Municipal Wastewater, A Guidance Manual. California State Water Resources Control Board. Report Number 84-1 wr., 1984
- Curzons, Alan. Personal communication. 2000.
- E. Roberts Alley & Associates, Inc., Air quality control handbook, McGraw-Hill, 1998.

Eckenfelder, W., Industrial Water Pollution Control, McGraw Hill, 1989

Eckenfelder, W., Activated Sludge Treatment of Industrial Wastewater, Technomic Pub. Co., 1995

Eckenfelder, WW Jr., Water Quality Eng. For Practicing Eng. 1978

Garland John. Data of E.M. Johnson WTP, City of Raleigh. Facsimile communications. July 29, and Sept. 8, 1998.

Gray, N. F., Activated Sludge, Theory and Practice. Oxford Science Publications, 1990

Heinsohn, R.J. and Kabel, R.L., Sources and control of air pollution, Prentice Hall, 1999.

Jiménez-González, C., and Overcash, M. , Energy Sub-Modules Applied in Life-cycle Inventory of Processes. Clean Products and Processes, in press, 2000.

Katari, V.S., Vataavuk, W.M., and Wehe, A.H, Incineration techniques for control of volatile organic compound emissions Part I. Fundamentals and process design consideration, JAPCA, 37, 1, 91, 1987.

Kim, S., and Overcash, M., Environmental Benefits of Biosolids. Du Pont Project Report, NCSU, Department of Chemical Engineering. December 1998.

Kooijman, H., and Taylor, R., CHEMSEP version 2.0, computer software. CACHE Corporation, Austin, TX, 1992

Lankfor P.W. and Eckenfelder WW Jr. Toxicity Reduction in Industrial Effluents. 1990

Mallard W.G. and Linstrom P.J., Eds., NIST Chemistry WebBook, NIST Standard Reference. Database Number 69, November 1998, National Institute of Standards and Technology, Gaithersburg. MD, 20899 (<http://webbook.nist.gov>).

Metcalf and Eddy Inc., Wastewater Engineering: Treatment, Disposal, Reuse. McGraw Hill, 198

- Mix, T.J.; Dweck, J.S.; Weinberg, M. CEP, [49-55], 1978
- Nevers, N, Air pollution control engineering, McGraw-Hill, 1995.
- O'Brien, J. K. Alternative Methods of Financing Energy Conservation projects for Activated Sludge Systems. Article in Treatment Efficiency and Energy Use in Activated Sludge Process Control, Robert M. Arthur, Ed., 1986
- Ramalho, R. S., Introduction to Wastewater Treatment Processes, Academic Press, 1983
- Rozich, A. F. Design and Operation of Activated Sludge Processes Using Respirometry, Lewis Publishers, 1992
- Shell, G. L., Field Determination of Oxygen Transfer for Maximum Energy Conservation. Article in Treatment Efficiency and Energy Use in Activated Sludge Process Control, Robert M. Arthur, Ed., 1986
- Smith, J.M. Van Ness H.C.. Introduction to chemical engineering thermodynamics. New York: McGraw-Hill, c1987. 4th ed.
- Ullmann, F. (1985): Ullmann's Encyclopedia of Industrial Chemistry, 5th ed., John Wiley & Sons.
- USEPA, Fate of Priority Pollutants in Publicly Owned Treatment Works. Pilot Study. EPA-440/1-79-300, 1979
- USEPA, Water8 Computer Model, Air Emission Program, Wastewater Treatment, Version 4.0, May 1st., USEPA, Research Triangle Park, NC, 1995.

Table 6.1. Average Data for WWTP design.

Parameter	Value	Reference
a(COD basis)	0.55	[Eckenfelder, 1995]
a'(COD basis)	0.45	[Eckenfelder, 1995]
b	0.12	[Meltcalt, 1980]
F/M (kg BOD/kg MLVSS)	0.51	[Ramalho, 1983]
COD reduction (%), COD _r	86	[ASCE, 1983]
COD/BOD ratio	1.89	[ASCE, 1983]
COD/TOC ratio	2.86	[ASCE, 1983]

Table 6.2. Oxygen delivery of different aeration systems.

Aeration System	Given Range	Range Average	Units	Reference	Average
Low speed	1.52-2.12	1.82	kg O ₂ /kWh	[Gray, 1990]	1.84
	1.2-2.4	1.80	kg O ₂ /kWh	[O'Brien, 1996]	
	1.5-2.3	1.90	kg O ₂ /kWh	[Industrial]	
High speed	1.06-1.37	1.22	kg O ₂ /kWh	[Gray, 1990]	1.11
	0.8-1.2	1.00	kg O ₂ /kWh	[Industrial]	

Table 6.3. Electricity Requirements.

Aeration System	Electricity for aeration	Estimated total electricity for the WWTP	Units
Low speed	0.34	0.72	kWh/kg COD
High speed	0.57	1.21	kWh /kg COD

Table 6.4. Comparison of Life Cycle Information for the WWTP module, Organic Matter Model.

	Industrial (A)	Industrial (B)	City of Raleigh	Proposed Model
COD _{in} , kg	1.00	1	1	1
TOC _{in} , kg	0.35	0.40	0.35	0.35
BOD _{in} , kg	0.54	0.16	0.48	0.53
COD/BOD	1.84	6.00	2.08	1.89
BOD/TOC	1.55	0.4	1.38	1.51
COD/TOC	2.86	2.5	2.86	2.86
COD Removed, %	86	85	98.7	86
Oxygen uptake, kg	0.53	0.52	---	0.63
CO2 emissions, kg	0.73	0.68	0.49	0.87
Sludge, kg (dry)	0.20	0.28	0.52	0.35
Sludge, kg (wet)	----	----	-----	7.00
Electricity (kWh)	0.33	1.14	1.58	Low- 0.72 High-1.21 Value used- 1.1

Table 6.5. Average Data for WWTP design. COD/BOD=2.08

Substance	g/ kg BOD _{in}	g/kg TOC _{in}	g/ kg COD _{in}	Final Fate of the direct substances
Sodium Hydroxide	25.8	38.9	13.6	Effluent
Polymers	2.4	3.7	1.3	Biosolids
Ammonia	60	93.3	32.6	Biosolids
Phosphoric acid	31.6	47.7	16.7	Biosolids
Total direct	119.8	183.6	64.2	
Gasoline	7.3	11.0	3.8	
Oil	2.7	4.1	1.4	
Total indirect	10	15.1	5.2	

Table 6.6. Reduction data for TDS (organic and inorganic) after the activated sludge treatment.

Influent (mg/L)	Effluent (mg/L)	% reduction	Source
1404	867	38.2%	[CSWRCB, 1984]
1125	827	26.5%	[CSWRCB, 1984]
930	570	38.7%	[CSWRCB, 1984]
----	----	<30.0%	[Eckenfelder, 1978]
Average of 3 municipal plants	Average of 7 activated sludge plants*	33.0%	[USEPA, 1979]
	Average	<33%	
	Value used	30%	

* Influent and Effluent plants are not the same

Table 6.7. Summary of LCI data for the WWTP. TOC and COD basis (no TDS included). Numbers do not balance because the oxygen intake and the water produced are not included.

Inputs, TOC Basis		Inputs, COD Basis	
<i>TOC_{in}, kg</i>	1	<i>COD_{in}, kg</i>	1
<i>Ancillary Substances, kg</i>	0.18 direct 0.01 fuel & oil	<i>Ancillary Substances, kg</i>	0.06 direct 0.005 fuel & oil
<i>Electricity (kWh)</i>	3.1	<i>Electricity (kWh)</i>	1.1
Outputs, TOC Basis		Outputs, COD Basis	
<i>TOC_{effluent}, kg</i>	0.14	<i>COD_{effluent}, kg</i>	0.14
<i>Ancillary Substances in the effluent (NaOH), kg</i>	0.038	<i>Ancillary Substances in the effluent, (NaOH) kg</i>	0.013
<i>CO2 emissions, kg</i>	2.49	<i>CO2 emissions, kg</i>	0.87
<i>Biosolids, kg (dry)</i>	1 organic 0.142 ancillary	<i>Biosolids, kg (dry)</i>	0.35 organic 0.047 ancillary
Total Outputs, kg	3.81	Total Outputs, kg	1.42

Additional Ratios	
TOC Removed, %	86
COD Removed, %	86
Adsorption to biosolids of Inorganic salts with heavy metals, %	75
Adsorption to biosolids of Inorganic salts without heavy metals, %	10
Inorganic TDS in effluent, % of TDS _{in}	70
Individual organic compound volatilized (bp < 140 C), % of initial mass	1
Individual organic compound in the effluent (bp < 140 C), % of initial mass	3
Individual organic compound volatilized (bp > 140 C), % of initial mass	0
Individual organic compound in the effluent (bp > 140 C), % of initial mass	4
COD/BOD	1.89
BOD/TOC	1.51
COD/TOC	2.86

Table 6.8. Example of LCI data for the WWTP with TDS in the influent. TOC basis. Numbers do not balance because the oxygen intake and the water produced are not included.

Inputs, TOC Basis	
<i>TOC_{in}, kg</i>	1
<i>Inorganic TDS_{in}, kg</i>	1.9- total 0.2 (heavy metal salts) 1.7 (non-heavy metal salts)
<i>Ancillary Substances, kg</i>	0.18 direct 0.01 fuel & oil
<i>Electricity (kWh)</i>	3.1
Outputs, TOC Basis	
<i>TOC_{effluent}, kg</i>	0.14
<i>Inorganic TDS_{effluent}, kg</i>	1.58-total 0.05 (heavy metal salts) 1.53 (non-heavy metal salts)
<i>Ancillary Substances in the effluent (NaOH), kg</i>	0.038
<i>CO2 emissions, kg</i>	2.49
<i>Biosolids, kg (dry)</i>	1 organic 0.142 ancillary 0.32-total inorg. salts (0.15 heavy metal salts, and 0.17 non-heavy metal salts)
Inputs, COD Basis	
<i>COD_{in}, kg</i>	1
<i>Inorganic TDS_{in}, kg</i>	0.66- total 0.06 (heavy metal salts) 0.60 (non-heavy metal salts)
<i>Ancillary Substances, kg</i>	0.06 direct 0.005 fuel & oil
<i>Electricity (kWh)</i>	1.1
Outputs, COD Basis	
<i>COD_{effluent}, kg</i>	0.14
<i>Inorganic TDS_{effluent}, kg</i>	0.555-total 0.015 (heavy metal salts) 0.54 (non-heavy metal salts)
<i>Ancillary Substances in the effluent (NaOH), kg</i>	0.013
<i>CO2 emissions, kg</i>	0.87 substrate
<i>Biosolids, kg (dry)</i>	0.35 organic 0.047 ancillary 0.105 total inorg. Salts (0.045 heavy metal salts and 0.06 non-heavy metal salts)

Table 6.9. Results from the Incineration Model for 10 common substances.

Solvent	Formula	MW	boiling point	Heat of vaporization (kJ/gmol)	Stoic. Coefficient for O ₂	Stoic. Coefficient for CO ₂	Stoic. Coefficient for H ₂ O	Cp (kJ/gmol-K)	Heat of combustion (kJ/gmol solvent)	Cool reactants at 25 C (kJ/gmol solvent)	Heat products at 900 C (kJ/gmol solvent)	Heat of combustion at 900 C (kJ/gmol solvent)	Sensible heat for solvent and air (25 to 900 C, kJ/gmol)	Total heat released at 900 C (KJ/gmol)	Total heat released (MJ/kg solvent)	Carbon content (kgC/kg solvent)
Ethyl acetate	C4H8O2	88.11	77	35.69	5	4	4	0.17	2238.54	-337.57	632.26	-1943.85	877.92	-1065.93	12.10	0.54
ethanol	C2H6O	46.07	79	42.3	3	2	3	0.1124	1367.60	-232.53	426.07	-1174.06	535.85	-638.21	13.85	0.52
methanol	CH4O	32.04	64	35.2	1.5	1	2	0.08	725.71	-151.14	268.00	-608.85	288.75	-320.10	9.99	0.37
toluene	C7H8	92.14	110	35.65	9	7	4	0.155	3910.90	-446.90	776.63	-3581.17	1448.13	-2133.05	23.15	0.91
thf	C4H8O	72.11	65.9	29.81	5.5	4	4	0.124	2533.20	-306.75	632.26	-2207.69	910.58	-1297.11	17.99	0.67
acetic acid	C2H4O2	60.05	118	23.7	2	2	2	0.123	875.16	-192.58	316.13	-751.61	399.29	-352.32	5.87	0.40
hexane	C6H14	86.18	69	28.85	9.5	6	7	0.195	4163.20	-490.41	1058.32	-3595.29	1556.04	-2039.25	23.66	0.84
ether	C4H10O	74.12	35	28.52	6	4	5	0.17	2732.00	-359.02	742.19	-2348.83	1023.75	-1325.08	17.88	0.65
isopropyl alcohol	C3H8O	60.1	83	39.85	4.5	3	4	0.162	2006.00	-319.41	584.13	-1741.28	798.00	-943.28	15.70	0.60
	Average	67.88							2283.59						15.58	0.61
	Std. Dev.	20.22							1213.12						5.86	0.18

Table 6.10. Summary of the Incinerator Module.

1)	Assuming an average heat of combustion and heat released at 900C															
2)	Assuming only significant emission is CO ₂															
3)	Assuming 75% efficiency in heat recovery for a temperature of 900 C (Branan, 1994)															
4)	Assuming the energy produced is used for steam production															
	Ave. heat value															
	Basis:															
	Total CO ₂ formed															
	Voc's emissions															
	Energy released															
	Energy recovered															

Table 6.11. Summary of the Solvent Recycling Module. Results of the modeling using Chemsep Software: Assumptions: simple distillation, 10 stages and feed at the 5th. Stage, Raoult's Law for K model, Antoine's Equation for Vapor Pressure, Ideal Equation of State, Reflux ratio of 1.3, column operated at constant atmospheric pressure, feed at 25 C, feed is a 90:10 mixture of solvent and water, 100% heat transfer efficiency, and recovery goal is 75%

Solvent	Formula	MW	% recovered	% purity of recovered solvent	Condenser duty (MJ/kg of solvent treated)	Reboiler duty (MJ/kg of solvent treated)	Condenser Temperature (C)	Boiling point (C)	Reboiler Temperature (C)	% potential heat recovery	Potential Heat Recovery (MJ/kg spent solvent treated)
Ethyl acetate	C4H8O2	88.1	75.21%	98.66%	-0.678	0.814	79.2	77.0	93.2	25%	-0.170
ethanol	C2H6O	46.1	75.34%	98.95%	-1.485	1.666	78.7	79.0	89.0	25%	-0.371
methanol	CH4O	32	75.82%	99.90%	-1.926	2.079	64.7	64.0	78.6	25%	-0.482
toluene	C7H8	92.1	75.31%	92.19%	-0.493	0.671	103.4	110.0	106.5	25%	-0.123
Tetrahydrofuran	C4H8O	72.1	75.74%	99.83%	-0.733	0.835	66.1	65.9	88.3	25%	-0.183
acetic acid	C2H4O2	60.1	75.41%	96.78%	-0.549	0.661	105.8	118.0	116.0	25%	-0.137
hexane	C6H14	86.2	74.98%	99.70%	-0.588	0.723	69.2	69.0	90.6	25%	-0.147
dichlorobenzene -1,2	C6H4Cl2	147	74.97%	99.99%	-0.643	0.839	104.2	180.7	180.4	25%	-0.161
ethyl ether	C4H10O	74.1	75.59%	99.99%	-0.635	0.688	34.7	35.0	69.5	0%	0
isopropyl alcohol	C3H8O	60.1	75.52%	98.08%	-1.193	1.390	83.0	83.0	92.1	25%	-0.298
dimethylformamide	C3H7NO	73.1	75.28%	99.99%	-0.730	1.010	107.0	153.2	152.7	25%	-0.182
acetone	C3H6O	58.1	75.15%	99.98%	-0.881	0.974	56.1	56.2	80.2	25%	-0.220
chloroform (i)	CHCl3	119	74.79%	99.92%	-0.429	0.492	61.3	61.3	89.6	25%	-0.107
Ave.			75.32%	98.77%	-0.843	0.988					-0.199

As an approximation for methylene chloride

Table 6.12. Summary of the Solvent Recycling Module. Results of the modeling using Chemsep Software: Assumptions: simple distillation, 10 stages and feed at the 5th. Stage, Gamma-Phi for K model, Extended Antoine's Equation for Vapor Pressure, Peng-Robinson Equation of State, Reflux ratio of 1.3, column operated at constant atmospheric pressure, feed at 25 C, and recovery goal is 75%

	Solvent	% water in feed	% recovered	% purity of recovered solvent	% purity of known azeotrope	Condenser duty (MJ)	Reboiler duty (MJ)	Condenser Temperature (C)	Boiling point (C)	Reboiler Temperature (C)	% potential heat recovery	Potential Heat Recovery (MJ)
1	ethanol	10	75.34%	98.95%	95.00%	-1.485	1.666	78.7	79.0	89.0	25%	-0.371
	ethanol (azeotrope)	10	75.30%	93.42%	95.00%	-1.625	1.798	78.3	-	79.4	25%	-0.406
	% difference					8.62%	7.34%					8.62%
2	IPA	15	75.50%	96.55%	91.00%	-1.236	1.440	83.6	83.0	94.7	25%	-0.309
	IPA (azeotrope)	15	75.44%	87.98%	91.00%	-1.487	1.673	80.5	-	81.0	25%	-0.372
	% difference					16.88%	13.93%					16.88%

Table 6.13. Summary of the data for landfilling organic matter, including Anaerobic Digester, Dewatering and Landfill. Numbers in bold denote the data taken from the literature

	per kg wet biosolids	per kg dry biosolids
Anaerobic Digester (thermophilic, heat and electricity recovery)		
Electricity, MJ	4.89E-02	2.45E+00
Electricity, KWh	1.36E-02	6.79E-01
CO2 emissions, g	9.26E+00	4.63E+02
Dewatering		
Electricity, MJ		7.20E-02
Electricity, KWh		2.00E-02
Landfilling		
Electricity, MJ	4.09E-03	1.86E-02
Electricity, KWh	1.14E-03	5.17E-03
Diesel, MJ	8.00E-02	3.64E-01
Diesel, kg	1.76E-03	8.01E-03
Methane emissions, g	3.33E+01	1.51E+02
CO2 emissions, g	1.32E+02	6.00E+02
ammonia emissions, g	7.82E+00	3.55E+01
COD, g	7.72E-02	3.51E-01
metals to soil, g	5.01E-01	2.28E+00

Table 6.14. Summary of the data for landfilling inorganic compounds

Parameter	per kg dry inorganics
Electricity, MJ	1.86E-02
Electricity, KWh	5.17E-03
Diesel, MJ	3.64E-01
Diesel, kg	8.01E-03
leachate, L	3.97E-02
TDS, kg	5.95E-05

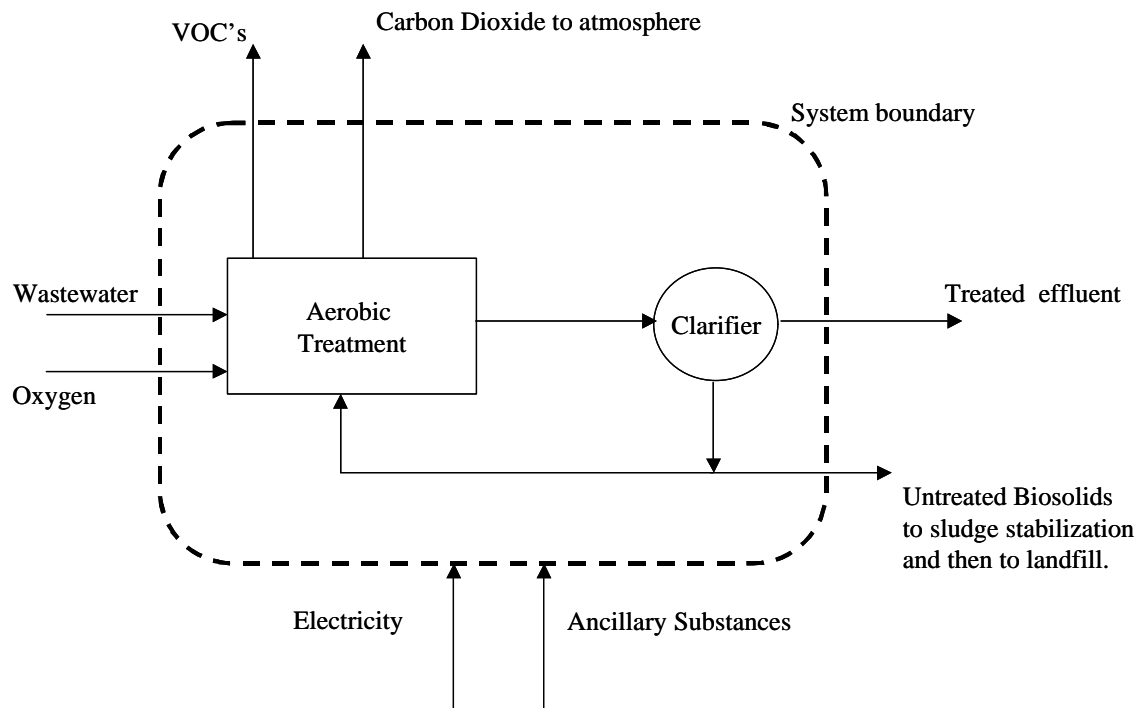


Figure 6.1. Flow diagram and system boundary of the WWTP module under study.

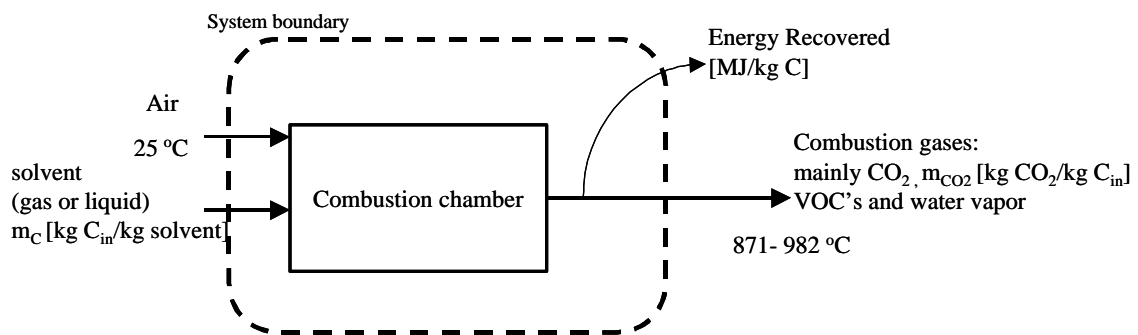


Figure 6.2. Schematic of the Solvent Incinerator Module.

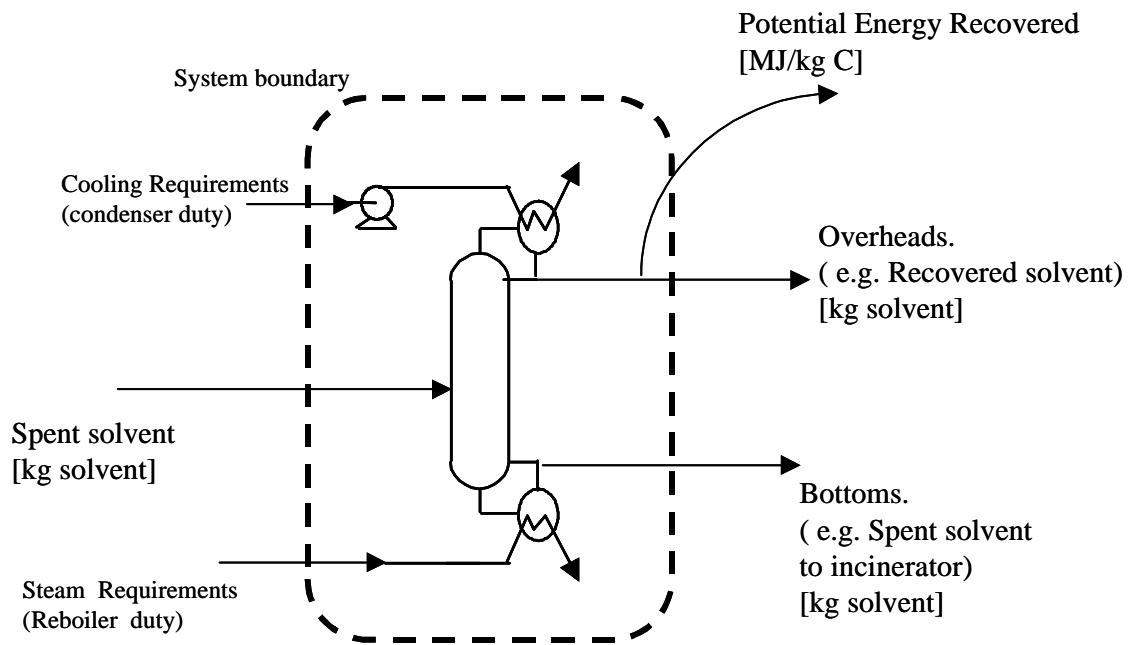


Figure 6.3. Schematic of the Solvent Recovery Module.

**7. ENERGY OPTIMIZATION DURING EARLY DRUG
DEVELOPMENT AND THE RELATIONSHIP WITH
ENVIRONMENTAL BURDENS.**

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7. ENERGY OPTIMIZATION DURING EARLY DRUG DEVELOPMENT AND THE RELATIONSHIP WITH ENVIRONMENTAL BURDENS.

Abstract

In the pharmaceutical industry, changes in the formulation of a product are likely to be very difficult due to the testing required to ensure that the reformulation has the same quality as the original drug. Although changes in the process do occur as part of continuous improvement, it is preferred to make as many improvements as possible before approval to reduce the cost associated with changing procedures.

Therefore, there is the need to introduce environmental factors as an integral part of the decision-making process at the Research and Development (R&D) stages of design for drug manufacturing.

In the present work, energy life cycle information is developed to provide environmental input into process selection and development within the pharmaceutical industry. The evaluation and comparison of energy requirements and total energy-related emissions at various stages of the development process for a pharmaceutical product were conducted.

It was found that the main optimization in energy usage for this specific system took place during the pilot scale stage of the process development (about 60% energy reduction from lab to pilot). The reductions in energy usage are translated in even higher reduction of total energy-related emissions (for the full-scale processes, around 76%).

It could be clearly seen that energy optimization in the early stages of process design translates into a lower level of life cycle emissions.

Keywords: Pharmaceutical industry, pharmaceutical process development, life cycle energy optimization, analysis, pharmaceutical synthesis.

7.1 Introduction:

What organizations learn during the initial drug development phase clearly has an effect on learning during production. Each process development project not only creates new production capabilities, but also adds to the company's know-how. Thus, a successful initial process development project can be visualized as improving the starting point of the process development curve (Pisano, 1997, Overcash, 1988). The better initial conditions are leading to the shorter time to achieve a determined level of efficiency with a new drug.

Process development for bulk pharmaceuticals is oriented to several key objectives. The first priority is to design a process that can synthesize an extremely high quality final product with reproducibility. Another priority is to improve process efficiency in order to reduce the capital expense required to achieve the first priority (Forman, 1994). This leads to priorities for the availability of raw materials, while cost and energy are only a secondary consideration.

Changes to a synthetic route late in the development cycle can require a great deal of rework, as optimization conditions and new solutions are developed. The same concept applies to changes due to environmental factors. Including overall environmental criteria as inherent factors of process development and optimization is an essential part of anticipating and attempting to solve problems that might arise in actual production, as well as an intrinsic characteristic of environmentally conscious manufacturing (USEPA, 1991).

Introducing the environmental life cycle information at an early stage would represent a powerful tool to face the potential global environmental challenges before the manufacturing phase. This allows the company to rapidly cycle through multiple routes early in the development process, while leaving sufficient time to optimize and refine the process.

As a case study, a life cycle is being conducted in collaboration with Pfizer, Inc on a chiral pharmaceutical product, sertraline. The present work is focused on the results obtained in the first stage of this case study regarding the role that early research and changes in the production processes play in overall energy optimization, and the effect of those early changes on the environmental impact.

7.2 Chiral Pharmaceuticals. A Case Study

The chosen pharmaceutical product, sertraline, is marketed as a pure enantiomer (Sheldon, 1990). From all possible isomers tested for activity, the required high selectivity resided in the cis(+) isomer of sertraline.

At an industrial level, the main raw material in the synthesis of sertraline is known as Regulatory Starting Material (RSM) and in this case is purchased as a racemate. The process currently performed is the conversion from racemic RSM to sertraline. This synthesis is processed in batches throughout four steps.

For this synthesis there are three alternate processes reported (Welch et. al., 1984; Pfizer, 1985; Pfizer, 1999) which use different solvents in the first three steps of the conversion. These variations were labeled as TOL, THF and EtOH processes after the solvent used in the first step in each alternative.

Besides the use of a different solvent in the first step, the EtOH process has the particularity of being a non-isolation process during the first three steps of the synthesis.

This means that there are no isolation of intermediates throughout the first three steps of the route, and thus no need to evaporate and separate the solvent (EtOH) until the third step is completed. On the other hand, for the THF and TOL processes, the intermediates are isolated and purified (crystallized) in each step.

These alternatives were generated by the normal course of process development and optimization, which in this case had diverse motivations, including efficiency and environmental concerns. The alternatives were developed in the following order: TOL (1984), THF (1985) and EtOH (1999). The process development of these alternatives required three stages: laboratory, pilot, and full scale.

The present work is focussed on the role that early changes in the production process play for the energy requirements for the TOL, THF and EtOH processes for sertraline. Another area of interest is the effect of early energy optimization over the total emissions generated in energy production.

7.3. Methodology

As pointed out before, the present work belongs to a broader life cycle inventory analysis of sertraline. Specifically, it is part of the collection of energy data within the two alternate manufacturing processes for producing sertraline. For this purpose, the methodology was designed as follows:

1. The three production processes for sertraline production (TOL, THF and EtOH), were identified and targeted as the system under study. This first step required close collaboration with the researchers and process development team at the company.

2. Process development was then divided in three stages for the purposes of this study: laboratory scale (grams of final product), pilot scale (~20 kg of final product), and full scale (> 500 kg of final product).
3. For all the processes, data regarding typical mass and process variables (e.g. temperature, and pressure) were collected throughout the three stages of development for each process. A mass balance was performed for each process at each scale. At the laboratory scale, the data were collected from patents, literature, and company's records. At pilot and full scale, the information was obtained exclusively from company records. At this stage, also close collaboration with the company was required to ensure that the results were representative.
4. Cooling, heating and mechanical energy requirements were estimated for each process at each scale. The energy requirements considered sensible heat, heat of reaction, energy for separation units, pumping, and agitation. When possible, direct numbers from the company's research and production were used. If direct data were not available, then equations and data from literature were used to calculate the energy requirements.
5. Once the energy requirements were calculated for both processes, the energy sources and sinks were defined. Steam at 345 and 931 kPa (50 and 135 psig), cooling water, refrigeration cycle, and electricity generated by coal burning were defined as the sources or sinks of energy. The cooling water was used for streams that needed to be cooled to at least 25 C, and the refrigeration cycle was assumed for streams that needed to be cooled below that temperature.
6. For each source or sink, energy sub-modules were developed. Each energy sub-module provides the information of the emissions released per energy unit produced and

dissipated. The detailed methodology and calculations of the energy sub-modules were given in Chapter 4 and Jiménez-González and Overcash, 2000.

7. Once the energy sub-modules were developed, the energy related emissions corresponding to the energy requirements were estimated for each process at all the scales.

The sources of the data employed, the equations used, and assumptions made are presented as follows:

7.3.1 Sensible Heat.

For calculating the energy required to increase and decrease the temperature, equation (7.1) was used:

$$Q=mC_p(T_f-T_i) \quad (7.1)$$

The mass, final and initial temperatures were provided directly by the company. Because none of the heat capacities of sertraline intermediates were available, the average heat capacity of the rest of the mixture was used (Domalski and Hearing, 1998). The fact that more than 90% of the mixtures is generally solvent supports this assumption. Heat losses of 15% for full and pilot scales and 25% for laboratory scale were considered in the calculations (Curzons, A., personal communication).

7.3.2 Heat of reaction.

Up to this date, there is not available information about the enthalpies of reaction for three of the four steps in the synthesis. Nevertheless, the estimation was made using the theory of group contribution (Reid et. al, 1977). The heat of formation and heat capacities for the reactant species were either taken from literature (Domalski and Hearing, 1998; Holdman, 1978) or estimated by the group contribution theory (Reid et. al, 1977).

Comparing the estimations of heat of reaction calculated with the group contribution theory, the experimental datum for the first step in the synthesis, the estimated difference is less than 5%.

7.3.3. Heating or cooling a vessel at a constant temperature.

The heat added to the vessels for maintaining a certain temperature for a period of time was calculated using equation (7.2).

$$Q=UA(T_w-T)t \quad (7.2)$$

It was assumed an approach of 20 K when the system was cooled with water, and 10 K when the system was cooled with refrigerant (Walas, 1987). The area was assumed in an average of 75% of vessel capacity, taking into consideration the areas of cylinders for full and pilot scales and a sphere for laboratory scale. The average contact areas were 15.9m² for full scale, 4.5 for pilot scale and 0.09 for laboratory scale.

The global coefficient of heat transfer (U) was estimated with the following the equation widely known in literature (Bird et. al., 1987; Sandler et. al., 1987). The values of fouling factors were taken from empirical data from the literature (Perry, 1987). All the physical properties required were taken from or estimated accordingly the methods describe in the literature (Perry, 1987; Reid. et. al., 1977). The U values calculated were 40.3 BTU/hr-ft²-F (5.8 J/s-m²-C) for full scale, 41.8 BTU/hr-ft²-F (6.0 J/s-m²-C) for pilot scale and 33.8 BTU/hr-ft²-F (4.9 J/s-m²-C) for laboratory scale.

7.3.4. Electricity

The data of energy required by agitators and pumps were provided directly from Pfizer. In the cases when filtration time was not provided, it was estimated with the following typical filtration velocities from the literature (Perry, 1987).

TiO₂ filtration, step 1:

- Slow filtration
- Filtration velocity 0.01-0.02 gal/min/ft²
- Filter area: 5 m²

Crystal filtration

- Medium filtration
- Filtration velocity 0.2-5 gal/min/ft²
- Filter area: 4 and 5 m²

The filtration energy requirement was calculated with the horsepower curve for filters (Dickey et. al., 1961; Dickey, 1991; Warring, 1981). The electricity-related emissions were taken from data in the literature (Boustead, 1993; Oliver, 1999; Chalmers Industriteknik, 1994; EMPA, 1996).

7.3.5. Cooling Tower

The total energy requirements for cooling tower, as well as the flow of make-up water were provided by Pfizer. Ion exchange pretreatment for make up water was considered. A total hardness of 100 mg/L of Ca²⁺ and 155 mg/L of Mg²⁺ was assumed in the water to be pretreated (Hill, 1990). A 10% solids in the pretreatment sludge was also used in the calculations (Fountain, 1982). The blowdown was considered as a 5% of the make-up water (McKelvey, 1959). The details of the methodology and calculations for the cooling tower were given in Chapter 4 and Jiménez-González and Overcash, 2000.

7.3.6. Refrigeration Cycle

A typical saturated refrigerant cycle with ammonia was assumed, with a vaporization pressure of 167 kPa (at -23 °C) and condensing pressure of 615.3 kPa (at 20 °C) (Lemmon et.

al., 1998). An compressor efficiency of 50% was used in the calculations (Dossat, 1997; Olivo, 1990).

The refrigerant losses were calculated assuming an average make-up of 10% mass of refrigerant per year, and the maintenance wastes regarding oil and filter change for the compressor were estimated to average 0.54 kg/kW of compressor (0.4 kg/HP of compressor, Chacón, M. A., 1998).

The pumping requirements for the refrigerant and the condensing liquid were calculated with the general equation presented by Perry, 1987. A total pressure head of 7.93 m of H₂O (26 ft of H₂O) for the refrigerant pump and 4.27 m of H₂O (14 ft H₂O) for the condensing liquid pump were used in the calculations (Dossat, 1997). The detailed methodology and calculations for the refrigeration cycle were given in Chapter 4 and Jiménez-González and Overcash, 2000.

7.3.7. Steam

Steam at 345 and 931 kPa (50 and 135 psig) of pressure is needed in a proportion of 55% to 45%, respectively. For estimating steam requirements, it is assumed that during heating the vapour enters as saturated steam and leaves as saturated liquid. Water entering the boiler is assumed to be at 71 C. In steam generation four kind of wastes were considered:

- a) combustion gases
- b) blowdown
- c) water pretreatment
- d) electrical consumption related wastes

Two fuels for combustion are used in Pfizer for the production of sertraline: natural gas and fuel oil No. 2 (See Chapter 5), in a 80-20 proportion, respectively. Combustion

gases were calculated with material balance (Cohen-Hubal, 1992, Perry, 1987). Blowdown was estimated as 5% of boiler capacity and electricity requirements of $1.4\text{E-}02$ MJ/kg of vapour generated (62% for water pumping and the rest for fuel pumping, Cohen-Hubal, 1992) The detailed methodology and calculations for steam production were given in Chapter 4 and Jiménez-González and Overcash, 2000.

7.4. Results and Discussion

7.4.1. Energy requirements

The calculations for energy requirements were performed as described in the methodology. For purposes of analysis, the energy requirements were divided into cooling, heating, and mechanical energy (Figure 7.1).

Laboratory scale processes are operated completely using electrically operated equipment for cooling, heating, stirring, and filtering. Laboratory scale routes exhibit in general longer hours of agitation, heating, and cooling, yielding therefore the greatest consumption of energy per unit of product, with large mechanical energy requirements

In contrast, at full scale the requirements of mechanical energy are much smaller compared with the requirements of energy for cooling and heating. From the energy calculations it can be deduced that during process development at pilot scale the main process improvement for this specific design is the optimization of energy requirements, especially regarding the mechanical energy.

The reduction of total energy requirements at pilot scale compared to the laboratory scale was of 60% for the TOL process, of 66% for the THF process, and of 55% for the EtOH process.

Since there is no significant difference between the total energy requirements at full and pilot scale for the TOL and THF processes, there was no improvement in the total energy requirements of any of these processes.

In contrast, the EtOH process exhibits a large improvement (around 62% reduction) from pilot to full. This can be explained in part by the fact that the EtOH process is carried out with no isolation of the intermediates during the first three steps of the production. Nevertheless, the reduction of total energy requirements at full scale compared to the laboratory scale was of 70% for the TOL process, of 71% for the THF process, and of 86% for the EtOH process.

However, there is a marked reduction regarding mechanical energy from lab to pilot and pilot to full. The reduction of mechanical energy from laboratory scale to pilot scale is 78% for the EtOH process, 80% for THF process and 84% for TOL process. Meanwhile the reduction of mechanical energy from pilot scale to full scale is 75% for the EtOH process, 86% for THF process and 61% for TOL process. This presents a fairly uniform reduction in mechanical energy requirements per stage (average of 81% of reduction from lab to pilot, and 74% from pilot to full). This improvement can partly be attributed to a better utilization of resources because of the mass production of the chemical.

On the other hand, the heating requirements seem to remain in the same range, with no apparent tendency, with the exception of TOL process at laboratory scale and EtOH at full scale. These two exceptions can be explained in the light of the mass needed to be distilled (heat of vaporization contribution), since for TOL-lab process, more distillations are required than the rest of the processes, and fewer for the EtOH-full. The TOL-lab process requires more distillations due to the several changes of solvent performed in the purification

(washing) of the intermediates in the laboratory synthesis. The EtOH process at full scale, however, does not isolate the intermediates in the first three steps.

The cooling requirements appear to increase at full scale for the TOL and THF processes, mainly because of lower temperatures achieved in the full scale operation of this two alternatives, in comparison to pilot scale. Those low temperatures are due mainly to crystallization units. Again, the EtOH process shows a constant reduction of the cooling requirements from pilot to full, in contrast to the other two, mainly due to higher operation temperatures and to the non-isolation synthesis alternatives (EtOH lowest temperature: -5 C, TOL lowest temperature: -10 C, THF lowest temperature -15 C).

There is also no significant difference between the total energy requirements of the THF and TOL processes at the same scale. This is explained mainly by the fact that the steps for the sertraline synthesis remain the same, but with the utilization of a different solvent. The differences in the heating and cooling requirements are explain by the slight differences in process conditions (lower cooling temperatures, higher times of heating/cooling). For the EtOH processes, the differences are explained chiefly by the non-isolation character of the process.

The energy per reaction-separation step follows the same pattern as the energy requirements, Figure 7.2. For TOL and THF processes at full-scale processes, however, the energy per step is slightly larger than for pilot scale, which shows a lower efficiency of energy usage for those processes. The latter also support the earlier statement that the EtOH process is more energy-efficient due to the non-isolation nature of the process, which explain the contrasting differences between EtOH and TOL/THF processes. For all the processes,

the energy required per step at laboratory scale is about three times as much as for full or pilot scales.

7.4.2. Energy Sub-modules

As pointed out before, the emissions related to electricity usage were taken from data in the literature. The electricity grid used is an average of the data found for the USA and the UK, Table 7.1. This average was chosen looking for a generalization of electricity production, since the plant has production sites in both places. No major variation is expected due to the usage of this average value, since no major differences between the UK and USA grid were observed in the data reported in the literature.

Energy sub-modules for heating with steam, cooling water, and refrigeration were developed according to the methodology section. A more detailed description of the methodology, calculations and results was given earlier in Chapter 4 and Jiménez-González and Overcash, 2000. The emission data for the extraction and purification of the fuels used for heating were taken from the literature (EMPA, 1996; CIT, 1992; Boustead, 1993; PIRA, 1998; BUWAL, 1991, Jiménez-González and Overcash, 1999). The results of the energy sub-modules were shown in detail in Chapter 4 and Jiménez-González and Overcash, 2000; however, a summary of the sub-modules is shown here in Tables 7.2 to 7.4:

7.4.3. Energy-related Emissions

The emissions generated in energy production were calculated using the aforementioned energy sub-modules, and then adding the corresponding emissions for fuel extraction and production.

As pointed out before, at laboratory scale all the energy requirements are satisfied by electricity-operated equipment, meanwhile in the pilot and full scales, only the mechanical energy (e.g. agitation, filtration, pumping) is provided by electricity.

Therefore, two scenarios were evaluated. Scenario A calculates the energy emissions for laboratory scale, taking into consideration that all energy requirements are satisfied by electricity (the actual case). Scenario B, estimates the energy related emissions at laboratory level using the sub-modules of heating and cooling the same way these are used at full and pilot scales.

Figure 7.3 shows the total normalized cradle-to-gate energy-related emissions for scenario A, and likewise Figure 7.4 shows the emissions for scenario B. The scenario B approach is a more useful for the sake of comparison, showing in a clearer way the improvements in energy usage during the development process.

From both scenarios, it can be concluded that there is no significant difference between the TOL and THF processes at full and pilot scales, but at laboratory scale it can be noted that a significantly larger requirements of electricity, translates in a proportionally larger overall emissions related to energy. On the other hand, for the EtOH process, there is a larger difference between scales, as discussed below.

As it can be noted in Figure 7.5, the total energy-related emissions for the TOL process were reduced throughout the R&D process optimization. At pilot scale the energy – related emissions were reduced about 66% and the full scale these were reduced an extra 12%. Meanwhile, for the THF process at the plot scale, the emissions were reduced 69% from the laboratory scale, and at full scale the emissions decreased an extra 8%. Although this seems to differ with the net increment of total energy requirements, it is explained by the

change of the distribution between cooling, heating and mechanical for pilot and full scales, especially the large diminishing of mechanical energy, which provides the largest amount of emissions per kJ.

Furthermore, the difference of energy-related emissions for TOL and THF processes at full-scale is only about 8%. This fact may suggest that the energy usage at full scale for this series of synthesis steps is tending to an optimum level for the given conditions.

On the other hand, for the EtOH process, the energy-related emissions were reduced 62% from lab to pilot, and an additional 65% from pilot to full scale, Figure 7.5. The amount of energy-related emissions of the EtOH process at full scale is 60% of the total emissions for the TOL process at full scale and 56% of the total emissions for the THF process at full scale.

At this point, it is important to mention that the TOL process was the first to be developed for this system, the THF process development started afterwards to substitute toluene from the processes due to fire and explosion concerns. Also, the THF process has a slightly higher yield for the reaction (30% vs. 28% of the TOL process). The EtOH process is the latest to be developed, and as pointed out before, the EtOH process is carried out with non-isolation of the intermediates during the first 3 steps of the synthesis, in contrast with the THF and TOL processes, which require isolation of the intermediates in each step.

If the energy related-emissions from a source outside the pharmaceutical plant are compared with the total energy-related emissions, it is clear that at laboratory scale, the contributions of energy-related emissions come mostly from external sources (fuel extraction, fuel burning, electricity generation), as it is shown in Figure 7.6. The internal energy-related emissions are from heating and cooling (excluding refrigeration). Meanwhile, for pilot scale, the contribution of emissions from external sources decreases, and finally at

full scale, the energy-related emissions from external sources is less than half of the total energy-related emissions.

The behavior of the improvement rate in energy-related emissions in the R&D process (from lab to full scale) was compared in a time scale using as basis the year of the first reference in the literature for the process. It was found that the improvement rate from lab to full scale increases almost linearly with time, as seen in figure 7.7.

These results show that the improvements during R&D of this pharmaceutical product, that are normally driven by yield improvements, had a proportional effect in energy usage and energy related emissions. Furthermore, it supports the hypothesis that what is learned in previous process improvements facilitates reaching the desired conditions when designing a new process.

On the other hand, the total energy requirements and the total energy-related emissions, instead of a constant reduction with time, show an increase in the second point (THF process, Figure 7.8). Although this increase is not highly significant, as pointed out before, it might be an indication of the trade off between the safety considerations taken to switch from toluene to THF, and the slight yield increase of the process, which are not necessarily directly proportional to each other.

7.5. Data Quality

The reliability and thus the applicability of the results of a life cycle assessment are dependent on the quality of the original data providing the background for the assessment. Since the results presented in this paper constitute a part of a life cycle project, data management should therefore be included as an integrated part of the analysis.

Data quality is the specific characteristic of data as expressed through information about the data (metadata). The data quality indicators used were: reliability (R), completeness (C), geographical correlation (G), temporal correlation (t), and technological correlation (T). A 1 to 5 scale for each indicator is used, 1 being the most accurate and 5 the least accurate, following the guidelines in literature (Pedersen and Suhr, 1996). Table 5 shows a summary of the data quality indicators for this work.

7.6. Conclusions

The improvements carried out in earlier stages of development have a positive impact not only in the overall cost of the product, but in the energy required for production, and the overall emissions related to energy production. The present work is a clear example of the case in which the improvements made throughout the process development have positive environmental consequences, in this particular case, regarding energy usage and energy-related emissions.

The main optimization in energy usage for this specific system has taken place during the pilot scale stage in process development. The reductions of energy usage per unit of final product in this stage are significant (60% for the TOL process and 66% for the THF process and 55% for the EtOH).

Since the contributions for energy-related emissions are significantly larger for electricity and heating than for cooling, the efforts directed to optimizing electricity and heating requirements will be more efficient in rendering a better environmental output regarding the emissions generated in energy production. As shown in the results of the energy sub-modules, energy optimization in the production processes translates into a lower level of emissions derived from the production of energy.

Energy is an important player in any life cycle study. The quantification of energy requirements is a crucial part in assessing the environmental burdens of a process. Analyzing the behavior of energy requirements in the stages of process development provides a background understanding for the future synthesis design that takes the environmental factor into consideration.

In a future perspective, this research project is intended to coordinate with route selection and design in the pharmaceutical industry. Furthermore, the evaluation of the different effects and environmental impacts due to the emissions analyzed, are part of ongoing research, and are yet to be addressed. The rapid development of computer-aid synthesis, stricter environmental regulations, and the need for environmentally conscious manufacturing are the driving forces for future utilization.

The relevance of this kind of research is proved by the fact that the progress in cleaner process design is directly proportional to the understanding we have of the system and the many interrelated factors involved.

7.7. Acknowledgments

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7.8. References

Bird, R.B., Stewart, W.E., Lightfoot, E. N. Fenómenos de Transporte. Ed. Repla. (1987).

- Boustead, I., Eco-Profiles of the European Plastics Industry. Report 2. Olefin Feedstock Sources. A Report for the European Center for Plastics in the Environment (PWMI), May 1993, 10-13.
- BUWAL. Ecobalance of Packaging Materials, State of 1990. Environmental Series No. 132. BUWAL, Berne Switzerland, 1991.
- Chacon, Miguel Angel. Personal communication, October 15, 1997.
- Chalmers Industriteknik. LCA Inventory Tool version 3.0. Chalmers Industriteknik, Goteborg, Sweden, (1994)
- CIT, Life of fuels, Ecotraffic AB, Stockholm, Sweden, 1992
- Cohen-Hubal, E.A. Net Waste Reduction Analysis Applied to Air Pollution Control Technologies and Zero Water Discharge Systems. NCSU MSc Thesis. (1992)
- Curzons, Alan. Personal communication, September 26, 1997.
- Dickey, G.D. Filtration. Reinhold Publishing Co. 353p. (1991).
- Dickey, G.D., Bryden, C.L., Theory and Practice of Filtration, Reinhold Pub. Corp., 346p. (1961).
- Domalski, E.S. and Hearing, E. D. Condensed Phase Heat Capacity Data. in NIST Standard Reference Database Number 69. Eds. W.G. Mallard and P. J. Linstrom. National Institute of Standards and Technology, Gaithersburg MD, 20899 . (<http://webbook.nist.gov>). November (1998).
- Dossat, R. J. Principles of Refrigeration. 4th. Ed. Prentice Hall. 512p. (1997).
- EMPA (Swiss Federal Laboratories for Materials Testing and Research), ECOPRO 1.5, Life Cycle Analysis Software. St. Gallen (1996).

- Forman et al, Environmentally Proactive Pharmaceutical Process Development. Pollution prevention Via Process Modifications, Halwagi and Petrides, Ed. (1994) 36-45.
- Fountain. R.L., Water Treatment Plant Operation, Chemistry for Operators. Ann Arbor Science, Vol. 4, (1982).
- Hill, G.B. Cooling Towers, Principles and Practice. 3rd. Ed. Butterworth-Heinemann, 191p. (1990).
- Holdman, C. D., Handbook of Chemistry and Physics. West, R. C. and Selby, S. M. Ed. (1978).
- Jimenez Gonzalez, C. Life Cycle Analysis in Pharmaceutical Applications, Ph.D. Preliminary Oral Examination, NCSU, (1997).
- Jiménez-González, C. and Overcahs, M. R. Energy sub-modules applied in life-cycle inventory of processes. Clean Products and Processes, V. 2, in press, 2000.
- Jiménez-González, C. and Overcash, M. R. LCI of Refinery Products: Review and Comparison of Commercially Available Databases. 1999 AIChE Annual Meeting. Dallas, TX, Oct. 31-Nov. 5, 1999.
- Lemmon, E. W., McLinden, M.O., Friend, D.G. Thermophysical Properties of Fluid Systems. NIST Standard Reference Database Number 69. Eds. WG Mallard and P J Linston. National Institute of Standards and Technology. (<http://webbook.nist.gov>). November (1998).
- McKelvey, K. K. The Industrial Cooling Tower, with a special reference to the design, construction, operation, and maintenance of water cooling towers,. Elsevier Publishing Company. 429p. (1959).

- Oliver, M., The viability of Solar Photovoltaics with Specific Reference to Building Integrated Photovoltaics Cladding systems. Ph.D. Dissertation. Centre for Environmental Strategy, University of Surrey, United Kingdom, (1999).
- Olivo, C. T. Principles of Refrigeration. 3rd. Ed. Delmar. 556p. (1990).
- Overcash, M. Hazardous Waste Reduction- Measurement of Progress. Haz. Wastes and Haz. Materials. Vol. 5, No. 3, (1988).
- Pedersen, B. W. and Suhr, M. W. Data quality management for life cycle inventories-- an example of using data quality indicators. Journal of Cleaner Production, Vol. 4, No. 3-4 (1996) 167-174.
- Perry, R. H., Chilton, C.H.. Manual del Ingeniero Químico. Chapter 10. McGraw Hill, 5a. Ed. (1987).
- Pfizer Inc., US Patent 4,536,518. Aug. 20, (1985).
- Pfizer Inc., World Patent WO 9936394A1. Jul. 22, (1999).
- PIRA International. PEMS Version 4.4. Randall Road. Leatherhead. Surrey. England, 1998, computer software version 4.4.
- Pisano, G. P., The Development Factory. Lessons from Pharmaceuticals and Biotechnology. Harvard Business School Press. 343p. (1997).
- Reid, R. C., Praunitz, J. M., Sherwood, T. K. The Properties of Gases and Liquids. 3rd. Edition, 687p. (1977).
- Sandler, H.J., Luckiewics, E.T. Practical Process Engineering. A Working Approach to Plant Design. Chapter 16. McGraw Hill. 638p. (1987).
- Sandler, H.J., Luckiewics, E.T. Practical Process Engineering. A Working Approach to Plant Design. Chapter 14. McGraw Hill. 638p. (1987).

- Sheldon, R. A. The Industrial Synthesis of Pure Enantiomers. *Drug Information Journal*.
Vol. 24 (1990) 129-139.
- U.S. Environmental Protection Agency. *Guides to Pollution Prevention in the
Pharmaceutical Industry*. 74p. (1991).
- Walas, S. M. Rules of Thumb. *Chemical Engineering*, March 16, 75-80 (1987).
- Warring, R.H. *Filters and Filtration Handbook*. Gulf Publishing Co., 432p. (1981).
- Welch, W. M., et al. Nontricyclic Antidepressant Agents Derived from cis- and trans-1-
Amino-4-aryltetralins. *J. of Med. Chem.*, Vol 27 (1984) 1508-1515.

Table 7.1. Emission factors used as energy sub-module for electricity generation (cradle-to-gate LCI information for electricity)

Average of USA and UK Grid for Electricity Production.	%*
Coal	48.0
Natural Gas	18.0
Oil	4.0
Nuclear	25.0
Hydro	5.0
Other solid fuel	2.0
Emissions	Emission Factor (kg/kWh electr)
Atmospheric Emissions	
Nitrogen Oxides	1.26E-03
CH ₄	2.09E-03
Sulfur oxides	1.76E-03
Carbon Monoxide	1.62E-04
CO ₂	5.94E-01
VOC's	1.37E-04
Solid waste (ash)	2.70E-02
Waterborne Emissions	
Total Dissolved Solids (TDS)	1.51E-03
BOD ₅	7.20E-05
COD	1.80E-03

* May not add up to 100 due to rounding.

Table 7.2. Results for the energy sub-module for heating a process stream with steam produced using natural gas as fuel.

Steam pressure	Fuel Required (m ³ /MJ)	NO _x (kg/MJ heated)	CO ₂ (kg/MJ heated)	Blowdown (kg/MJ heated)	Pretreatment (kg/MJ heated)	Electricity (kWh/MJ heated)
931 kPa (135 psi)	0.04	3.70E-4	0.08	0.024	2.97E-3	1.93E-3
345 kPa (50 psi)	0.03	3.43E-4	0.07	0.023	2.80E-3	1.81E-3

Table 7.3. Results for the energy sub-module for heating a process stream with steam produced using Oil No. 2 as fuel.

Steam pressure	Fuel required (kg/MJ)	SOx (kg/MJ heated)	NOx (kg/MJ heated)	CO2 (kg/MJ heated)	Blowdown (kg/MJ heated)	Pretreatment (kg/MJ heated)	Electricity (kWh/MJ heated)
931 kPa (135 psi)	0.032	1.99E-4	8.99E-5	1.03E-1	2.47E-2	2.97E-3	1.92E-3
345 kPa (50 psi)	0.029	1.84E-4	8.33E-5	9.52E-2	2.33E-2	2.80E-3	1.81E-3

Table 7.4. Results for the energy sub-module for cooling a process stream.

Cooling method	Blowdown (kg/MJ cooled)	Pretreatment waste: sludge with 10% of CaCl ₂ /MgCl ₂ (kg/MJ cooled)	Heat required to remove using a cooling tower (MJ/MJref)	Spent Oil (kg/MJ cooled)	Refrigerant Losses (kg/MJ cooled)	Electricity (kWh/MJ cooled)
Cooling Tower	4.67E-2	4.60E-3				1.18E-2
Refrigeration			1.16	1.33E-5	1.60E-7	9.02E-2

Table 7.5. Data quality indicators for sertraline Case Study
Energy-related calculations

Factor evaluated	R	C	G	t	T
Mechanical Energy Requirements	1	2	1	1	1
Heating and Cooling Requirements	2	2	1	1	1
Emissions Related to Mechanical Energy Requirements	2	1	2	1	2
Emissions Related to Heating Requirements	2	1	1	1	2
Emissions Related to Cooling Requirements	2	1	1	1	2

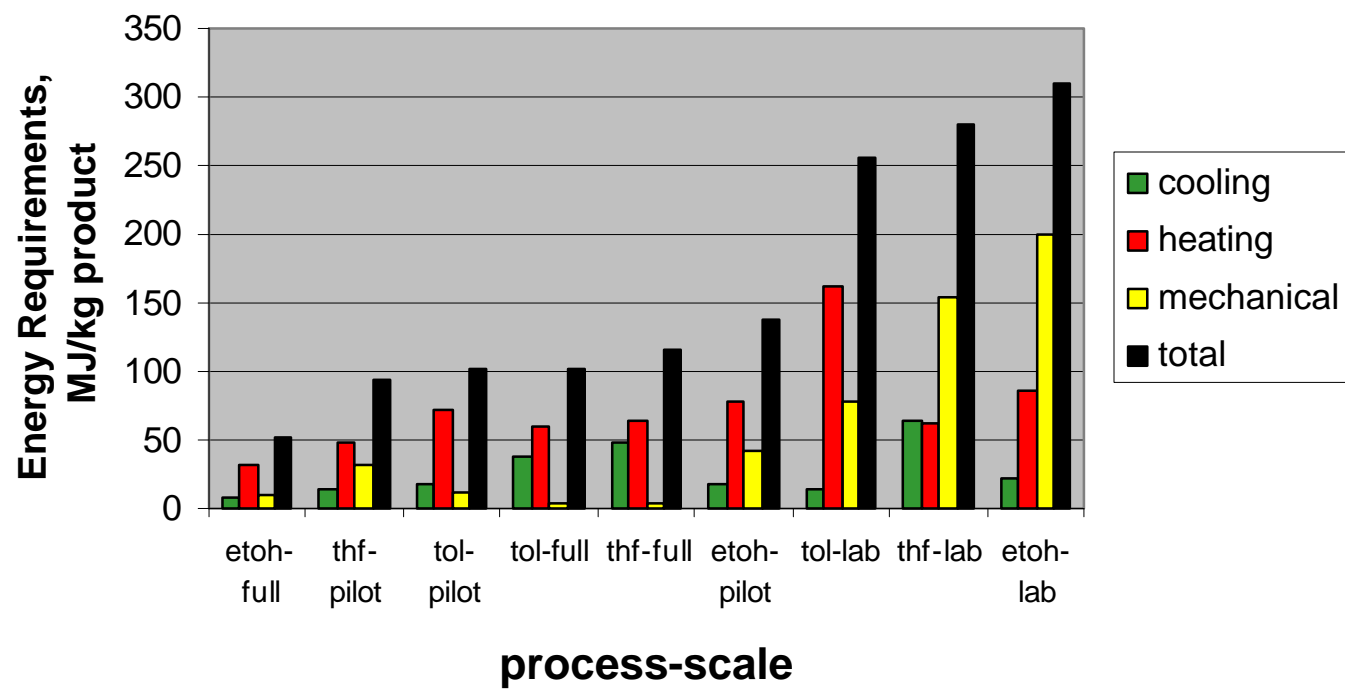


Figure 7.1. Energy Requirements for the EtOH, THF and TOL process at full, pilot and laboratory scales.

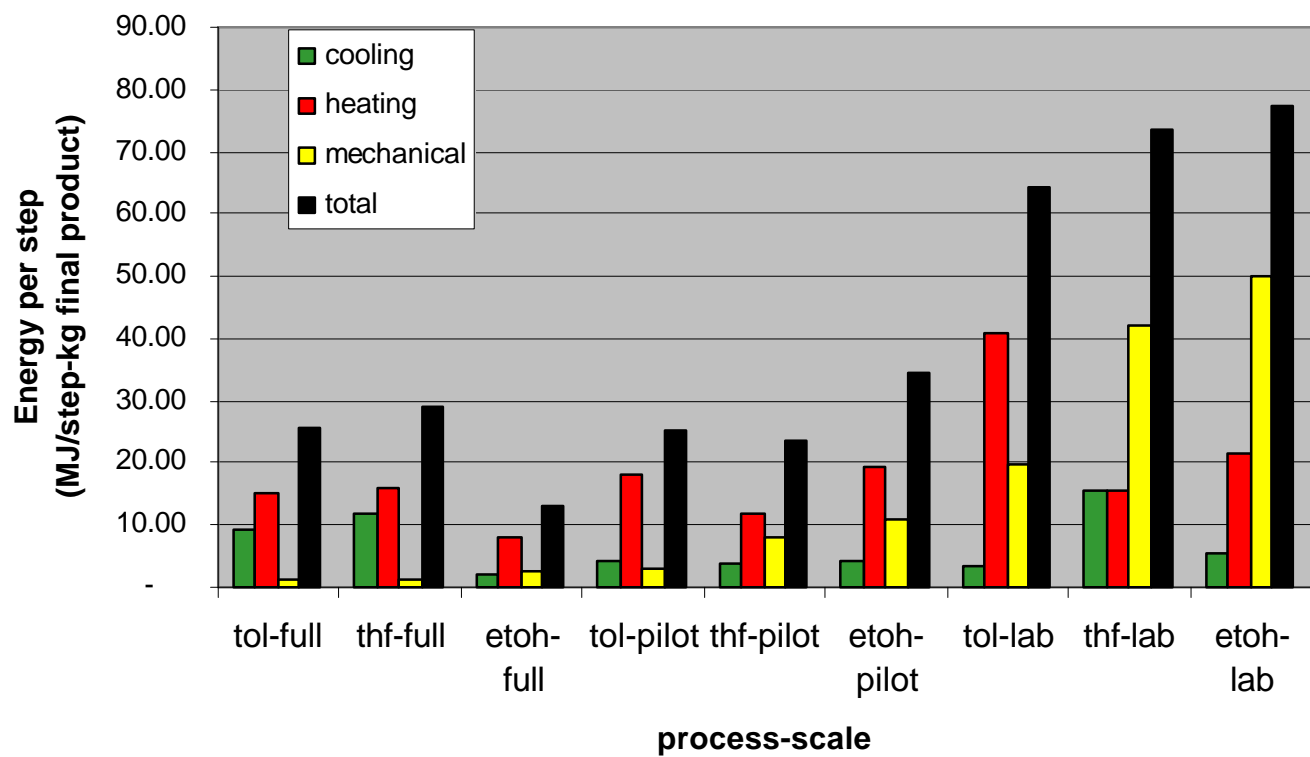


Figure 7.2. Comparative energy per reaction-separation step for this process.

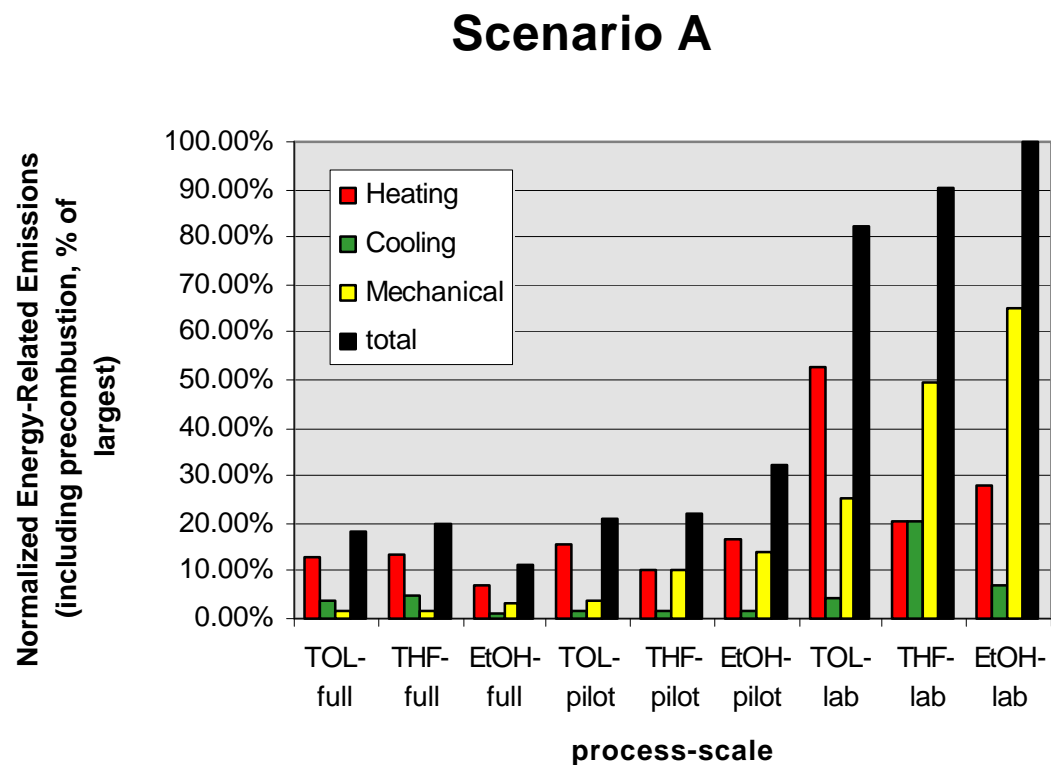


Figure 7.3. Normalized comparison of total energy-related emissions for the EtOH, THF and TOL process at full, pilot and laboratory scales, including all emissions back to natural resources. Scenario A (lab. Scale assuming only electricity usage).

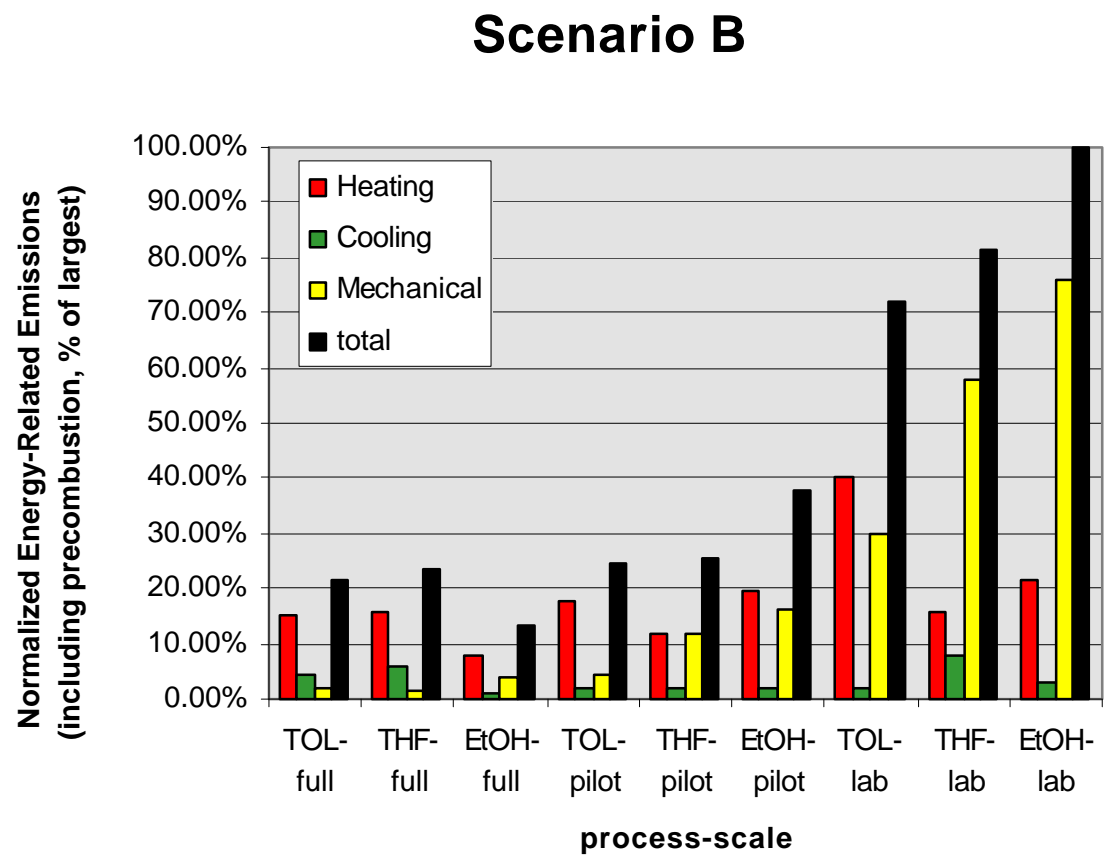


Figure 7.4. Normalized comparison of energy-related emissions for the EtOH, THF and TOL process at full, pilot and laboratory scales, including the emissions related to extraction and purification of fuels. Scenario B (lab. Scale assuming usage of steam and cooling tower sub-modules).

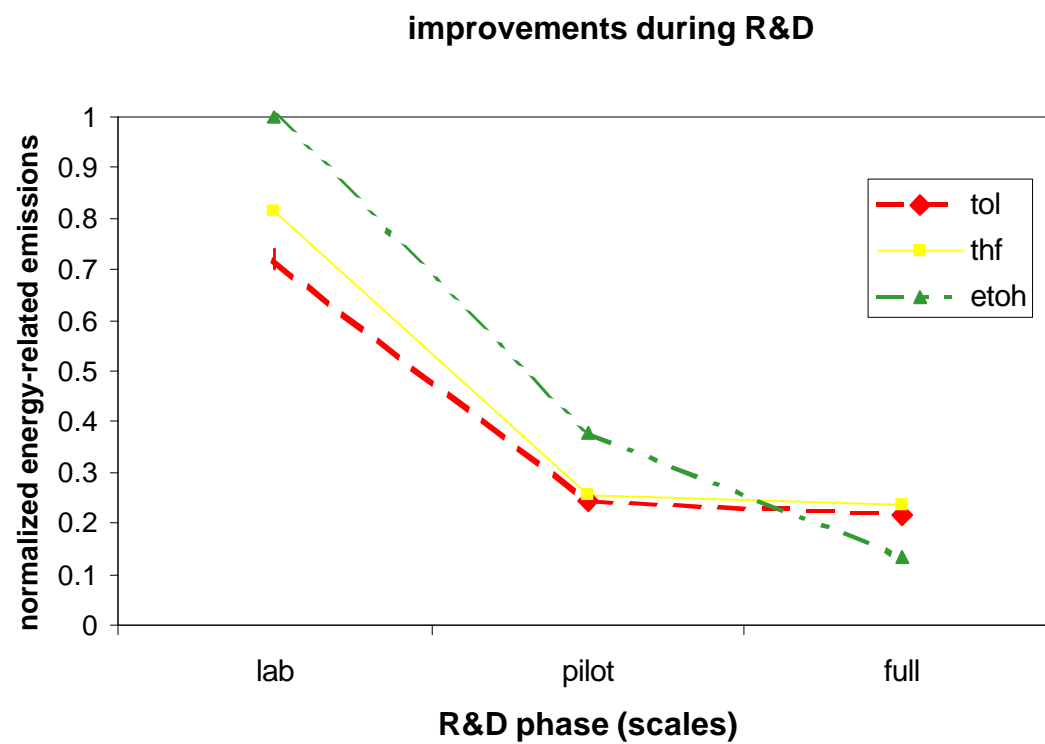


Figure 7.5. Graph of the normalized total energy related emissions throughout the R&D process for THF, TOL and EtOH.

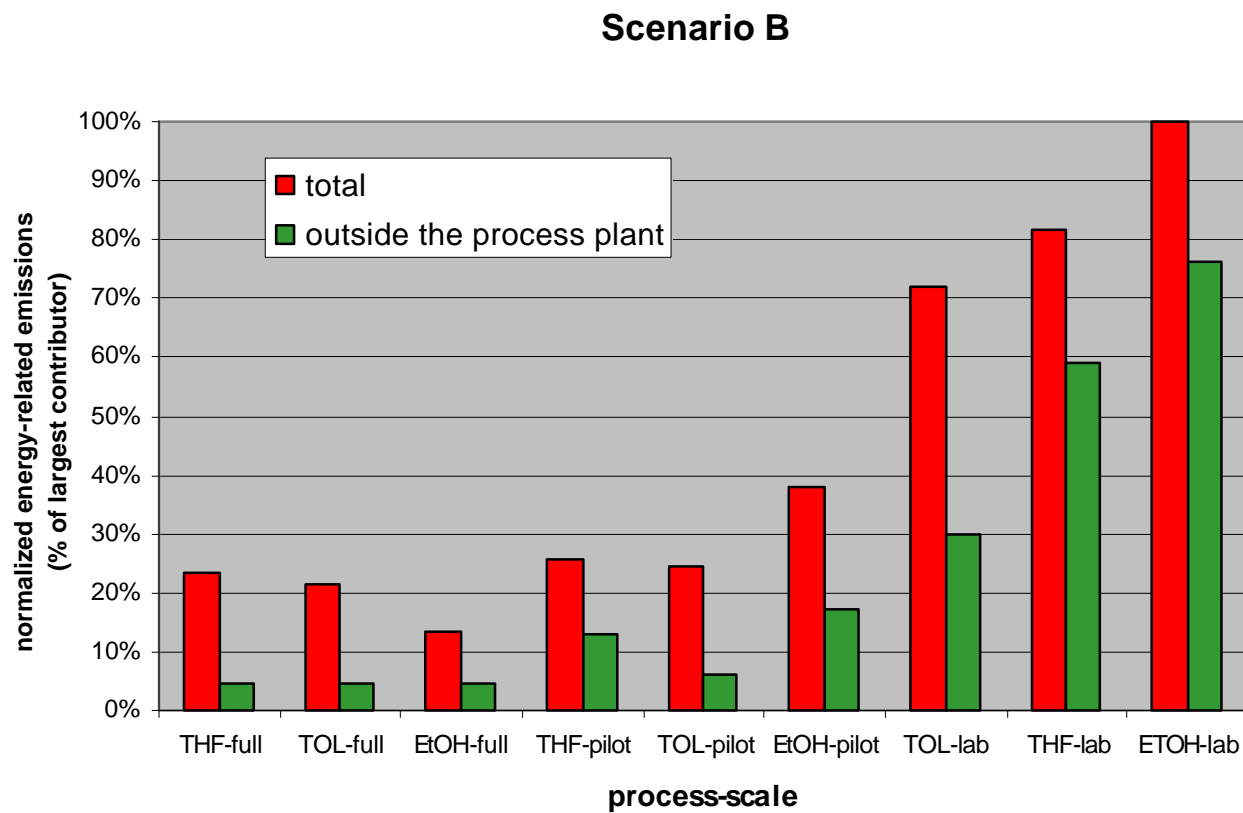


Figure 7.6. Normalized comparison of energy-related emissions for the THF and TOL process at full, pilot and laboratory scales, including the emissions related to extraction and purification of fuels, and comparing the total energy-related emissions and the produced outside the process plant.

Scenario B (lab. Scale assuming usage of steam and cooling tower sub-modules).

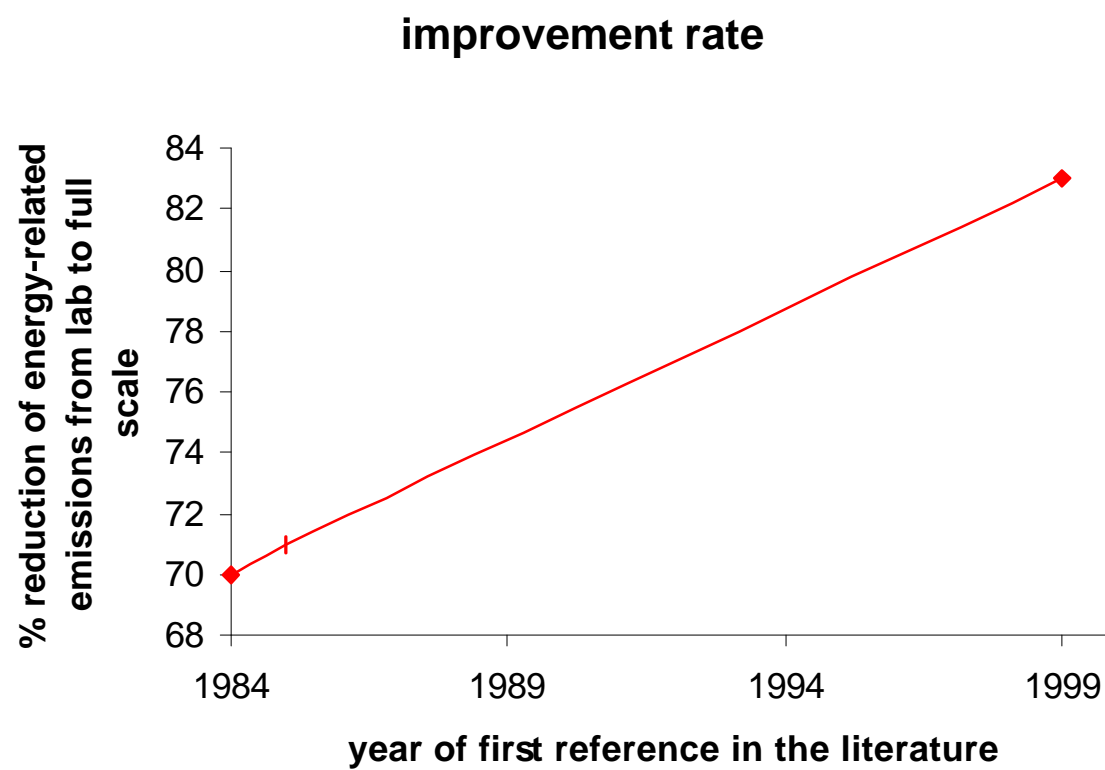


Figure 7.7. Percentage of reduction of total energy-related emissions from laboratory to full scale vs. time. TOL, THF and EtOH processes.

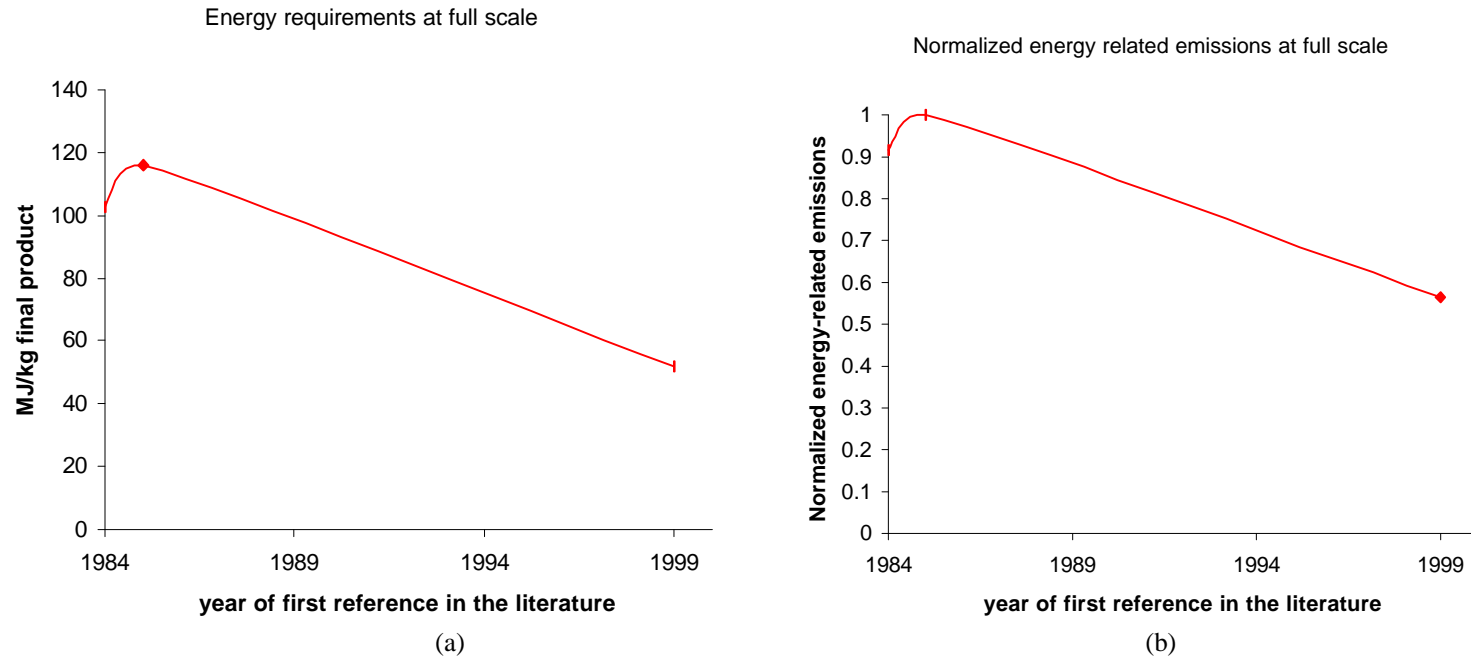


Figure 7.8. Energy requirements vs. time (a) and normalized energy-related emissions vis. time (b).

8. TARGETED ANALYSIS: THE LIFE CYCLE APPROACH

Abstract

Two examples of analysis that can be made using a life cycle approach are discussed. The comparison between improvements in yield versus improvements in solvent usage and the analysis of effects of solvent recovery on total wastes is presented.

Keywords: life cycle, pharmaceuticals, solvent recovery, solvent usage.

8.1. Introduction

Life cycle can be used to analyze, in a different light, aspects of process and product design. In this chapter, two examples of the uses of life cycle in decision-making processes inside the pharmaceutical industry are presented.

One application is to perform the equivalent of an environmental sensitivity analysis when evaluating different options of improvement. As it was shown before, solvent usage plays a big role in the environmental performance of a pharmaceutical process, but normally the yield is one of the decisive factors when looking for a new synthetic route. How can we compare those two factors and decide when it is convenient to invest resources to improve one or the other? The first example is the improvement in reaction yield when compared to the improvement in solvent usage with a life cycle viewpoint.

Another important issue is the way solvent recovery is perceived inside of a company. In some cases it is seen as a scheduling problem, or an issue for which costs do not justify investing time and money. The second example presents a life cycle approach that can provide a wider view regarding solvent recovery.

8.2. Total yield versus solvent usage

Total yield can be seen as how efficiently the carbon back-bone of a molecule is being formed. The classical evaluation of the effectiveness and efficiency of a synthesis is yield, however, yield does not take into account other factors, such as the amount of solvent or catalyst that are used to carry out the reaction. It is possible to have a synthetic route with 100% yield that generates waste that is far larger in mass and volume than that of the desired product. This issue has been dealt formerly in concepts like atom economy (Freitas Dos Santos, 1999; Anastas and Williamson, 1996; Anastas and Williamson, 1998; Anastas, 1998, Curzons et. al., 2000).

On the other hand, there are several ways in which a solvent can influence the environmental performance of a synthesis, such as the effect of a solvent in the efficiency of the reaction, the ability of being regenerated, the level of solvent toxicity, and the need of extra separation steps to purify the reaction product. In most pharmaceutical applications, the solvent does not get incorporated into the final product (therefore, it is 0% atom-economical), but it is used to improve the efficiency of the reaction. The goal is to achieve the highest efficiency with the least amount of solvent that has the least toxic characteristics

One of the uses of the life cycle approach is to compare the relative benefits of investing resources in improving solvent usage versus improving reaction yield per se. In this example, solvent usage is analyzed without taking into consideration solvent recovery, but this could be included

From the Sertraline case study (Chapter 2), we recall that Sertraline is produced from tetralone as a regulatory starting material, therefore the synthesis of sertraline from tetralone is done 'inside' the company, while the synthesis of tetralone (and all the tetralone

intermediates) is done ‘outside’ the company. For this example, two ways of producing Sertraline have been compared:

1. Sertraline via THF process, with tetralone produced via route 4
2. Sertraline via THF process, with tetralone produced via route 3.

Two scenarios of improvements are proposed, the first is to improve the yield of the reaction in 10%, and the second is to reduce the solvent usage by 10%. For these scenarios no solvent recovery is included, and therefore all solvent outputs are considered waste to be treated (which occurs frequently). The post-treatment results of the two scenarios are shown in Figures 8.1 and 8.2.

It can be seen in Figure 8.1 that the effect of increasing the overall yield of the reaction by 10% in the total waste is minimal inside the manufacturing (97 versus 96 kg/kg sertraline), since most of the waste produced in the synthesis is solvent related (slightly more than 90%). Nevertheless, for the two routes shown, when that 10% improvement is translated into the overall mass of waste that is reduced, we have an improvement of about 3000-fold for route 3 and 300-fold for route 4 (ratio of reduction in outside waste to inside waste reduction).

When solvent usage is reduced by 10%, the reduction of total mass of waste produced ‘inside’ is considerably higher than the reduction with yield improvement (about 8%, inside waste reduction from 97 to 89 kg/kg sertraline). When this is translated to the whole production chain, the reduction is the result of not producing the amount THF reduced in the pharmaceutical process (about 600 kg), thus the ratio of outside improvement to inside improvement is about 75:1.

One interesting issue about this comparison is that the figure of 600 kg of waste not-produced by reducing solvent usage is about 5 times smaller than the waste saved by improving the yield of route 3 in 10%, but has an effect 2 times larger than improving the yield of route 4 by 10%.

For the routes evaluated in the Sertraline case study, the behavior in this comparison is as in route 3, with the said exception of route 4. There are two possible explanations of this phenomenon, which might even occur at the same time. The first of these is that route 4 has achieved an already high level of efficiency that might be close to the maximum yield, in which case issues such as how efficiently solvent is utilized become more important. The second explanation might be more obvious, since route 4, as can be clearly seen in Figure 8.3, is a simpler route, with fewer synthetic steps, which involves less complexity and for which raw materials come from efficient processes, such as the refinery production of the naphthol required for the synthesis (Figure 8.3)

8.3. Solvent recovery

Solvent usage plays an important role in the production of pharmaceutical products (Curzons et al, 2000). As stated before, it is common practice inside pharmaceutical companies to treat solvent as another waste to dispose or treat.

Internal solvent recovery has traditionally implied a series of challenges for the pharmaceutical industries. It requires a more sophisticated organization and careful operation than the average industrial solvent recovery. This is related to the strict regulations governing this kind of production processes and a traditional need to operate with large volumes of solvent in order to make the recovery economics favorable, which brings

scheduling and storage problems. Still nowadays, in-situ solvent separation and recovery is an option that requires further exploration, but nevertheless, external solvent recovery for uses in other industries is also an alternative for the cases in which internal solvent recovery is not feasible.

One of the paradigms that solvent recovery faces, is that the perception of the environmental advantage for recycling the solvent is limited to the plant boundaries, focused on cost accounting, environmental regulations and in-plant total waste.

The life cycle approach is useful to evaluate the net environmental benefits of recovering solvent. For this example, the case scenario of the recovery of 1 kg of tetrahydrofuran (THF) as solvent is employed. In this case, the question to be answered is: what is the environmental advantage of recovering 1 kg of THF by distillation over incinerating 1kg of THF?

Bar 1 in Figure 8.4 shows the total material waste produced in the distillation of 1 kg of THF (0.368 kg) and bar 2 shows the total material waste produced in the incineration of 1 kg of THF (0.573 kg). The traditional analysis taking as boundary of the analysis the manufacturing plant will assess a credit as the difference between distilling and incinerating the solvent, that is $0.573 - 0.368 = 0.205$ kg of waste/kg of THF recovered.

However, when recovering 1 kg of THF, emissions are being avoided because there is also no need to produce that kilogram of solvent, and not only in the THF production plant, but all the intermediate processes required for the THF production, depicted in the chemical tree of Figure 8.5. When introducing the life cycle approach those avoided emissions are also included. Therefore, the environmental advantage (or credit) for recovering 1 kg of THF is 78 kg in avoided emissions from manufacturing, plus the avoided emissions of

incineration, minus the emissions for distillation, as shown in Figure 8.4. This is a 380-fold greater environmental credit than just examining the in-plant benefit.

This different perspective of solvent recovery might also help to justify the investment related to solvent recovery infrastructure, since while the market cost of solvents is quite cheap nowadays, the broader total costs (e.g. resource depletion, societal) are not. Further, an environmental credit should be given for such a beneficial decision.

8.4. Conclusions

The life cycle approach provides not only a mean to evaluate different alternatives, but also to identify points of improvement and compare the impacts on the overall environmental performance of a process or activity.

In the examples given above, life cycle provided a comparison between investing resources for the improvement in two different areas (e.g. yield versus solvent usage) and also provided a tool to estimate the overall environmental ‘credit’ of recycling a specific solvent (in this case THF). This kind of analysis can be extended to other areas or more case scenarios, and used for decision-making processes.

8.5. References

- Anastas, P. T. and Williamson T. C., Green Chemistry: Frontiers in Benign Chemical Synthesis and Processes. Paul Anastas and Tracy Williamson Eds., Oxford, New York, oxford University Press, 1998
- Anastas, P. T., Green Chemistry: Theory and Practice, Oxford, New York, oxford University Press, 1998

Anastas, P.T., Green Chemistry: Designing Chemistry for the Environment, Washington DC, American Chemical Society, 1996

Curzons, A. D.; Constable, D. J.; Mortimer, D. N. and Cunningham, V. L., So you think your process is green, how do you know? Using Principles of Sustainability to determine what is green, a Corporate Perspective of SmithKline Beecham. SmithKline Beecham report. Worthing, UK, 2000.

Freitas Dos Santos, L., Green Chemistry: Practical Considerations, Version 1., SmithKline Beecham, ERL, Harlow, UK, March 1999

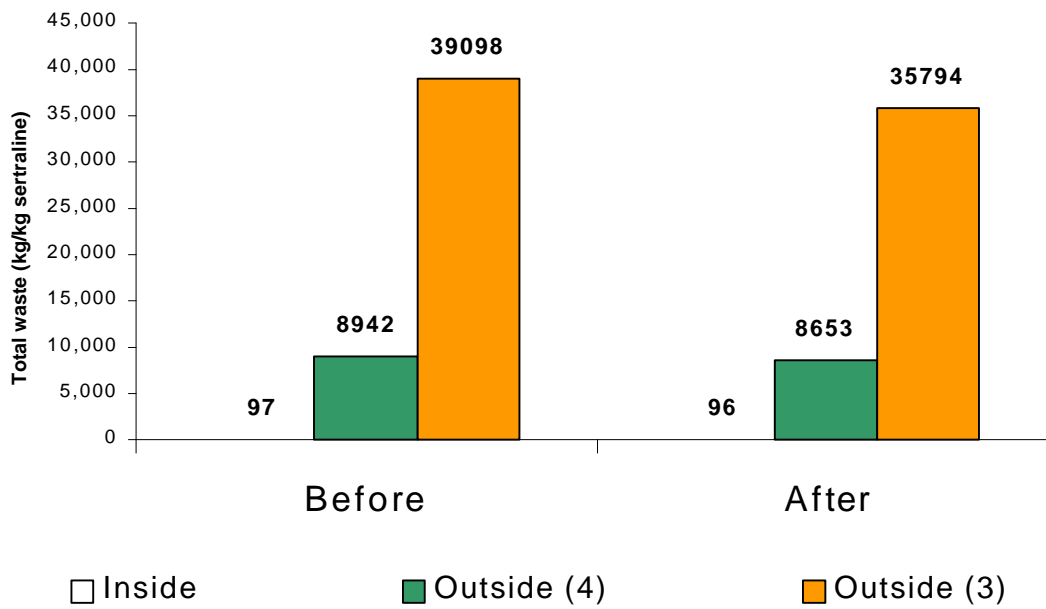


Figure 8.1. Total chemical losses for sertraline (with routes 3 and 4) before and after a 10% of total yield improvement

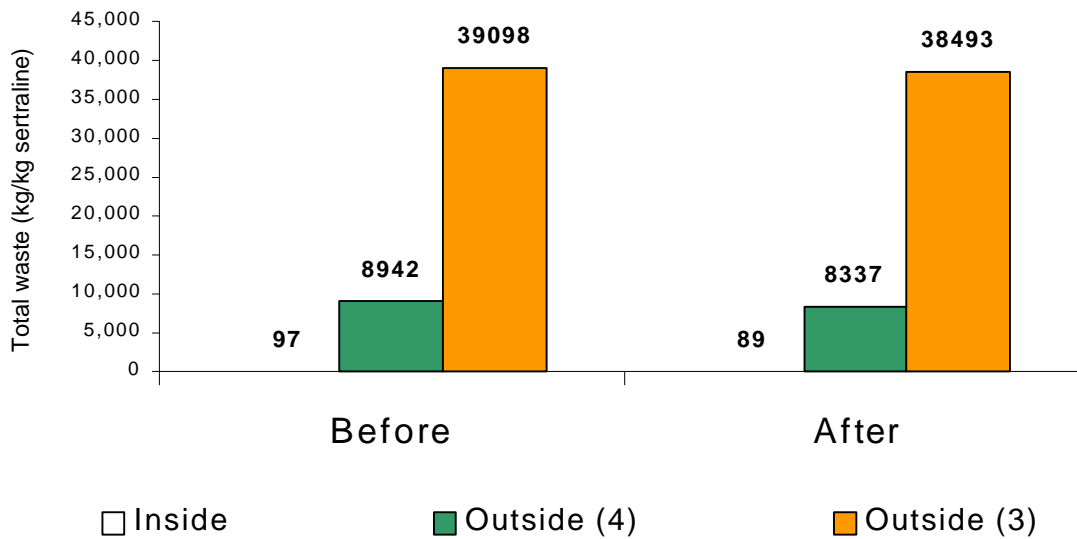


Figure 8.2. Total chemical losses for sertraline (with routes 3 and 4) before and after a 10% of solvent usage reduction

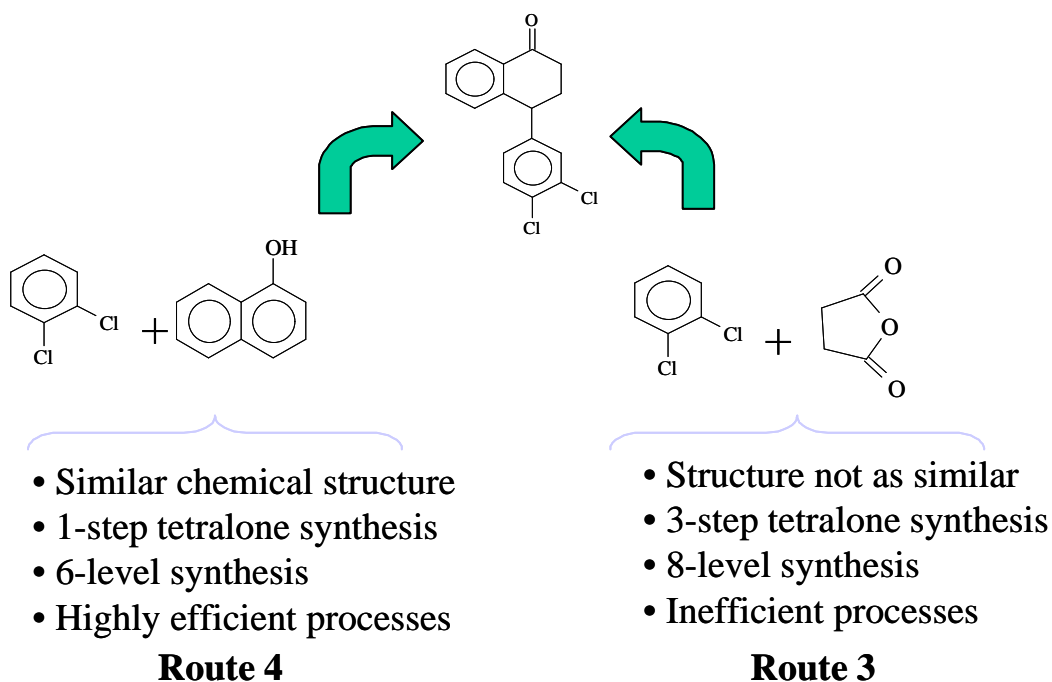


Figure 8.3. Schematic comparison of main characteristics of route 4 and route 3 for tetralone production

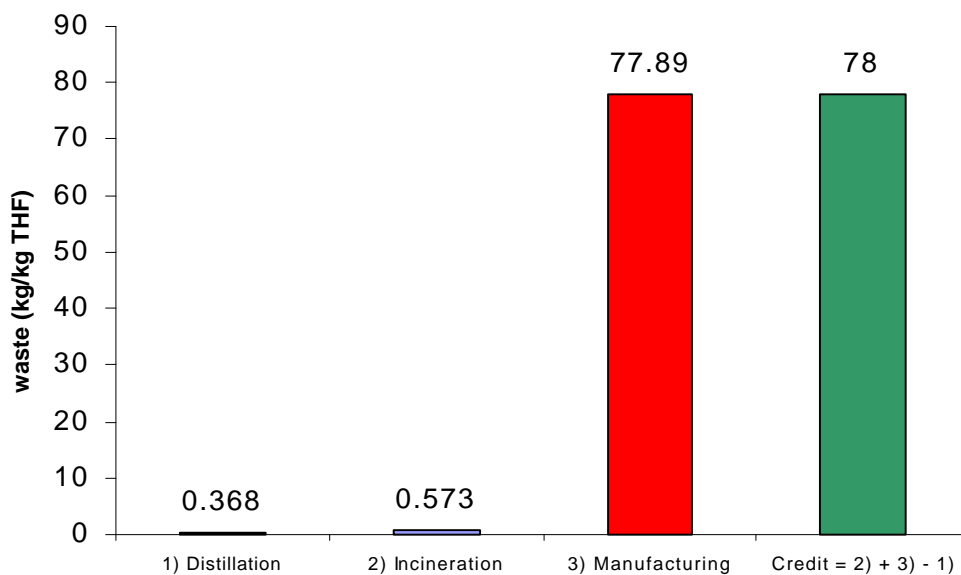


Figure 8.4. Total chemical losses saved by recovering 1 kg of THF

Tetrahydrofuran, C ₄ H ₈ O	Hydrogen, H ₂	Natural Gas											
	Furan, C ₄ H ₄ O	Furfural, C ₅ H ₄ O ₂						Corncobs					
								Water, H ₂ O					
								Sulfuric acid, H ₂ SO ₄	Sulfur trioxide, SO ₃	Sulfur, S	Naphtha Refinery	Petroleum Reserve	
		Calcium acetate monohydrate, Ca(C ₂ H ₃ O ₂) ₂ ·H ₂ O						Calcium Hydroxide, Ca(OH) ₂	Limestone				
									Carbon Dioxide, CO ₂	Natural Gas			
										Air			
								Water, H ₂ O					
								Acetic Acid, C ₂ H ₄ O ₂	Carbon Monoxide, CO	Natural Gas			
										Water, H ₂ O			
									Carbon Dioxide, CO ₂	Natural Gas			
										Air			
								Methanol, CH ₃ OH	Natural Gas				
									Water, H ₂ O				
Water, H ₂ O													

Figure 8.5. Chemical tree for the production of THF (Tetrahydrofuran)

**9. HOW DO YOU SELECT THE ‘GREENEST’ TECHNOLOGY?
DEVELOPMENT OF GUIDANCE FOR THE PHARMACEUTICAL
INDUSTRY**

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9. HOW DO YOU SELECT THE 'GREENEST' TECHNOLOGY?

DEVELOPMENT OF GUIDANCE FOR THE PHARMACEUTICAL INDUSTRY

Abstract

Green processes will be developed more often if scientists take an integrated approach looking at both chemistry and technology. When considering technology selection it is vital to understand the associated environmental and safety, as well as operational, quality, and cost differences to meet the sustainability challenge. There is a clear need for guidance in this area.

This chapter proposes the concept of a 'Clean/Green Technology Guide' as an expert system that would provide the scientists with comparative environmental and safety performance information on available technologies for commonly performed unit operations in the pharmaceutical industry. At this stage, a framework has been developed using a metric set based on the concepts of sustainable development. This framework proposes to evaluate the alternatives on a case-scenario basis, and will compare traditional and emerging technologies. A life cycle approach is used in the evaluation of the alternatives. This chapter illustrates this approach by comparing batch, mini- and micro-reactors.

Keywords: clean technologies, pharmaceutical processes, process design, technological evaluation, microreactors.

9.1 Introduction

In previous work the sustainable development context carried out in programs for green chemistry and green technologies for some pharmaceutical companies has been described (Curzons et.al., 2000)

When considering environment and safety we need to ask the question: what might the typical bench and management level scientist or engineer require to assist in making the best possible technology decisions – those that are most ‘green’? Current thinking suggests that the best way to make a product ‘green’ is to consider what needs to be done during the design phase to ensure that there are as few adverse impacts as possible while maximizing the benefit it brings to society. This is one of the components in the philosophy of the ‘Design for the Environment’ approach.

If companies are to move forward ‘green’ processes then there is the need to consider two interrelated components: ‘green’ chemistry and ‘green’ technology. This chapter considers the ‘green’ technology component, but it is essential that both components (green chemistry and green technology) are developed in parallel in order to achieve a ‘green’ process and move towards more sustainable business practices.

Most chemists tend to focus on reactions rather than the technology around the reaction (the unit processes needed to manufacture a product). That is to say, in general, if a reaction does not ‘work’, chemists are more inclined to change the reaction rather than to investigate a different set of unit processes in which to perform the reaction. Issues of mass and energy (heat/cool) transfer, mixing, phase transfer, and general reactor design, etc., are generally not as rigorously pursued by the synthetic organic chemist as by the engineer. If these issues are not adequately considered, there may be larger inefficiencies during development. Given increased and ever increasing pressures to reduce time to market, and the diversity of products introduced to market, chemists must

continue to work with engineers in a collaborative manner to solve the problems associated with mass and energy inefficiency.

Scientists currently face a difficult task in the selection and evaluation of the most appropriate technology for each part of a series of reaction and separations steps during both the development and scale-up phases of new drugs. There are many aspects that need to be considered in the selection of technologies, including product quality, operability, efficiency, environmental and safety, and of course, economics.

The importance of considering environmental and safety aspects in the early stages of process design is widely recognized. To this extent, there are many efforts directed at using and developing more 'clean technologies' and 'green chemistries'. One of the main challenges of integrating new concepts into pharmaceutical process design, is the need to measure how 'clean' a technology is or how 'green' a specific set of reactions are, so scientists can identify and compare the alternatives.

A framework has been developed based on life-cycle principles, which will enable scientists to consider environmental and safety issues around alternative process technologies in the early stages of the process design. This will allow a more focussed decision and might also encourage scientists to consider alternative technologies if these have real benefits. This section presents the concept and the framework of the 'Clean Technologies' Guidance', which will eventually provide an expert system that gives scientists comparative information about the different technologies, emphasising but not being limited to environmental and safety aspects.

9.2. Methodology

It is considered important that clean technologies guidance in the pharmaceutical industry has the following characteristics, among others:

- Has strong scientific and technological basis, and at the same time be simple and user-friendly (simple but not simplistic).
- Be an easy-to-use, dynamic tool that allow scientists and engineers to compare alternative technologies
- Focuses in the most commonly used operations in pharmaceutical processes.
- Takes into consideration the scientists' needs.
- Ultimately the tool must be accessible to the users.
- The Process must be transparent

The methodology employed in the development of the Clean Technology Guidance can be described as follows (Figure 9.1):

1. Developing the Framework. This framework was designed to be target-oriented, so that technologies can be compared on the basis of the objective or goal of a specific process operation (e.g. concentration of mother liquors). The technological alternatives for each target were defined by discussion with external and internal scientists and by literature reviews (e.g. distillation, membrane processes, etc.). This is an ongoing process, which is being undertaken in a prioritised manner.

2. Metrics and Heuristics. Four metrics to be evaluated were selected: energy, environment, safety, and efficiency. In a later stage of the framework, it will be necessary to include the metrics around the economics. To evaluate those four metrics, comparison indicators were also chosen (e.g. energy requirements, mass intensity, production of CO₂, among others).

3. Case-Scenario Studies. One of the big challenges of any guidance is how to make the assessment generic for technologies whose performance may be process-specific. To begin to tackle this, we have chosen a case-scenario approach. The initial case-scenario was carefully chosen to be as relevant and representative as possible of the type of process occurring in the pharmaceutical industry. In subsequent development stages of the guidance, additional scenarios will be incorporated. It is considered vital that the information and the assessments are fully documented and cover general information such as operational considerations, limitations, etc.

4. Comparative ‘Ranking’ of the alternatives. The evaluation of the technology suite for a given scenario will result in comparative data around the selected metrics.

Technological development is a very dynamic process, as is the development of the Green Technology Guide. New process design targets and new technologies will emerge, and therefore new case scenarios will need to be studied in the future.

9.3. The Framework

Table 9.1 shows a representative sample of the framework for the Clean Technology Guide. The first column groups the process operational ‘targets’.

The second column indicates the characteristics of the separation, when applicable; this may be used to define the appropriate technological alternatives for the target.

The third column presents the technological alternatives for each selected process design target. Clearly the number of options may expand as new technologies are developed.

Finally, the metrics for the evaluation of environment, energy, safety and operational issues are presented. The framework ‘matrix’ will represent the ‘front-end’ tool and might be color-coded based on a heuristics set to be developed by team consensus to facilitate easy identification of key issues and opportunities. The following is proposed: green (for alternatives that have significant advantages), red (for alternatives that have significant disadvantages) and yellow (for alternatives that do not represent significant disadvantages or advantages).

However, the results of the assessment will be linked to a more detailed and transparent review and explanation of the technology, the heuristics, metrics, and case-scenarios aspects and data

9.4. The Indicators

A range of core and complementary indicators have been explored to develop the metrics. From these, five indicators that are thought to best define the characteristics necessary to compare the technologies have been then selected. Table 9.2 contains illustrative indicators.

A life cycle analysis approach has been used to ensure a more holistic view that will move closer to the concept of sustainability. Where possible and appropriate these indicators will include, as much as possible, cradle-to-gate environmental life-cycle inventories, which take into consideration the emissions for the extraction and transformation of raw materials, energy and even for waste treatment. This is especially important when considering energy. Different utilities (steam, electricity) have different associated emission profiles (e.g. greenhouse gases) and it is important to capture these to enable meaningful comparisons between technologies that may utilize different utility profiles. We have also considered the life cycle impact for differences in material usages.

The mass indicators define both the environmental impacts and raw materials utilization. The energy indicators simply evaluate the energy consumption of the alternatives, expressed in the utility requirements (steam, electricity, etc.).

Currently there is only a qualitative view for safety and operational considerations. It is desirable to develop a quantitative measurement for these two aspects.

9.5. Scenario Example

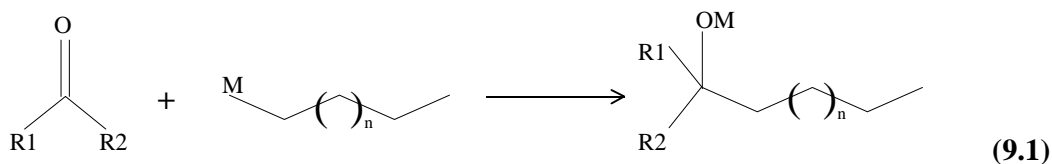
A case-study compares microreactors, minireactors and batch reactors. It is presented to illustrate the methodology, but it is considered just a starting point in the evaluation and discussion process.

Microfabrication techniques and scale-up replication have fuelled spectacular advances in the electronics industry, and these are now creating new opportunities for reaction engineering. The researchers studying and developing this emerging technology claim that it is possible to work with high-heat and high-mass transfer rates in microfluidic systems. This potentially will allow reactions to be performed under more aggressive conditions with higher yields than in conventional reactors. [Jensen, 1999; Krummradt, 2000]

The early trials of microreaction and intensified chemistry seem to suggest that these technologies work best with fast chemistry (reaction times of minutes, seconds or less). [Green, 1998; Srinivasan, 1997, Bender, 1998]. The case study that has been taken as a first approach to formulate this comparison was presented in the literature [Krummradt, 2000]. This reaction was chosen because the literature reports a comparison of the microreactor system with a lab-scale batch reactor, a production scale batch reactor

and a so-called minireactor. Nevertheless, some assumptions had to be made in the calculations presented here, and these are defined below.

The reaction is carried out between a carbonyl compound and an organo-metallic agent to produce a fine chemical, as shown in (9.1):



This reactive system proceeds in the liquid phase and it is exothermic (standard heat of reaction ca. -300 kJ/mole), the main reaction and most side reactions are fast (residence time < 10 s), some parallel and consecutive reactions can occur, and the compounds are sensitive to temperature.

The experimental results reported in the literature relate to processes carried out in micro- and minireactors compared to traditional batch reactors both at laboratory and full-scale operations (Table 9.3). The literature describes that the minireactor concept was developed after some problems with blockage in the initial microreactors experiments. The 'minireactor' had the same design as the microreactor, but with wider channels, small enough to keep the desired features of a microreactor and big enough to avoid blockage. The characteristics of the reactor systems evaluated are as follows:

Mass Indicators.

To estimate the mass indicators which compare the performance of the reactors, two main issues considered were:

- 1) Conversion Efficiency (e.g. percentage of unreacted precursor)
- 2) Formation of unwanted compounds (parallel or subsequent reactions)

Since there were not enough data in the article reviewed to estimate the relative usage of solvent, and there is no basis to sustain an assumption at the present time, the added solvent intensity indicator is not developed. Moreover, the mass intensity and residue intensity indicators exclude solvent usage.

The mass indicators presented in Table 9.4 are shown in a molar basis; normally it would be done in a mass (kg) basis, but in this case a molar basis was selected since no information regarding mass flows was available. It is assumed, that the reactants are fed into the system in equimolar ratio. The column 'theoretical minimum' allows a comparison of the alternatives assuming 100% efficiency.

Studies in the literature indicated little or no by-product formation using the micro- and minireactor systems. However for batch processes, the formation of unwanted products cannot be avoided in the aggressive reactor environment for a period of 5 hours under the reactor conditions prior to quenching. In this case, a time of 5 hr is needed to ensure complete heat dissipation and therefore minimize the risk of a violent reaction.

Unfortunately, the data found do not give the mechanism of formation of by-products (e. g. concurrent vs. subsequent reactions) or the efficiency of precursor consumption. Therefore it is not clear whether the reduction of by-product formation derives from side or concurrent reactions. The concept of less production of by-products is considered important, but because there is not sufficient information to establish a reasonable assumption, it is only treated qualitatively.

Energy Indicators

The reaction is exothermic and requires cooling. Comparisons consider the electricity required for cooling via refrigeration. This represents the major part of the overall energy. Although there are no heating requirements in this example, it is expected

that with endothermic reactions the relative characteristics of a microreactor would be similar.

The following formula was used to estimate the electricity required for refrigeration:

$$W = \frac{Q}{\eta} \left| \frac{T_1 - T_2}{T_1} \right| \quad (9.2)$$

Where:

W = work (electrical energy), MJ

Q = heat to be dissipated by the refrigeration system, MJ

T1 = outlet temperature of the system to be cooled, K

T2 = inlet temperature of the system to be cooled, K

η = efficiency of the system (common value = 50%)

It is expected that the major contribution to the refrigeration requirements is the dissipation of the reaction energy, so the standard heat of reaction is taken as an approximation of the total heat to be dissipated.

For each MJ of refrigeration needed, it is also necessary to dissipate around 1.2 MJ of heat (Jiménez-González and Overcash, 2000). Cooling through cooling water was assumed in the heat dissipation for the refrigeration system. An 85% of heat transfer efficiency is also assumed. Table 9.5 shows the results for the energy requirements.

Safety Considerations

The literature suggests that the small intrinsic volume of the system, combined with the efficient heat management in microreactors, significantly increase potential process safety.

Also, hazardous materials can be produced at the point-of-use, minimizing storage of hazardous substances (given that the downstream conditions are designed in such a way that no temporary storage is needed).

Operational Considerations for microreactors

The operational considerations for the microreactors as found in the literature [Ponton, 1998; Ehrfeld, 2000; Floyd, 2000] are as follows:

- Improved mass- and heat transfer
- Improved control of residence time and temperature distribution
- Possibility of higher selectivity, yield and quality
- Numbering-up instead of scaling-up (replicating the microreactors instead of designing in the macro-scale)
- Faster development of new processes or substances
- Continuous operation of traditional batch processes
- Potential problems regarding blockages.
- Need to equalize the further work-up with the reaction.

Traditionally, processes are scaled-up from the laboratory into pilot plant and then into production. This is a lengthy process and can have an associated failure risk (e.g. reduced yield, quality, unforeseen scale-up effects). For microreactors, the concept of

numbering-up implies similar conditions between the laboratory scale and production scale, and could eliminate most of the potential scale-up issues.

Life Cycle Approach

Table 9.6 shows the energy-related environmental burdens in a cradle-to-gate approach expressed in g of emissions per mole of product. Energy-related emissions were calculated with the data presented in the literature [Jiménez-González and Overcash, 2000]. Other factors that will eventually need to be considered are:

1. The waste produced due to differences in yield and waste treatment.
2. The emissions for productions of raw materials.

Comparative Ranking.

Table 9.7 shows the final comparative ranking given to the alternatives in the scenario evaluated.

9.6. Conclusions and future work

The proposed Clean Technology Guide will provide another component in the Design for the Environment Toolkit. It will provide scientists and engineers with comparative information for technologies that can be used for commonly performed operations in the pharmaceutical industry.

This expert system is presented here at the concept stage, together with work-in-progress. The main challenge will be to translate into general principles the findings from

specific scenarios, while keeping the transparency of the methodology. The authors recognize that this is a challenging and continuing process.

9.7. Acknowledgements

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9.8. References

- Bender, M. et. al., High-Temperature Micro Catalysis: a New Design for Comparative Reaction Studies in Technical and Model Systems, *Microreaction Technology, Proceedings of the 1st International Conference in Microreaction Technology*, W. Ehrfeld Ed., pages 54-61, Springer, 1998.
- Curzons, A. D., Constable, D. J., Mortimer, D. N, Cunningham, V. L., So you think your process is green, how do you know? Using Principles of Sustainability to determine what is green – A Corporate Perspective. Internal Document of SmithKline Beecham, Worthing, UK, 2000.
- Ehrfeld, W., et. al., Implementation of Microreaction Technology in Process Engineering. *Microreaction Technology: Industrial Prospects. IMRET 3: Proceedings of the 3rd International Conference in Microreaction Technology*, W. Ehrfeld Ed., Springer, 14-36, 2000.
- Floyd, T. M., et. al. Novel Liquid Phase Microreactors for Safe Production of Hazardous Speciality Chemicals. *Microreaction Technology: Industrial Prospects. IMRET*

- 3: Proceedings of the 3rd International Conference in Microreaction Technology, W. Ehrfeld Ed., Springer, 171-180, 2000.
- Green, A., Process Intensification: The key to survival in global markets? Chem. And Industry, March 1998, 68-72
- Jensen, K. F., Microchemical Systems: Status, Challenges, and Opportunities. AICHE Journal, Vol. 45, No. 10, 2051-2054, October 1999.
- Jiménez-González, C., M. Overcash, M. R. Energy sub-modules applied in life-cycle inventory of processes. Clean Products and Processes 2 (2000) 1, 57-66, 2000.
- Krummradt, H, et. al., Experiences with the use of microreactors in organic synthesis. Microreaction Technology: Industrial Prospects. IMRET 3: Proceedings of the 3rd International Conference in Microreaction Technology, W. Ehrfeld Ed., Springer, 181-186, 2000.
- Ponton, J. W., Observations on Hypothetical Miniaturised, Disposable Chemical Plant, Microreaction Technology, Proceedings of the 1st International Conference in Microreaction Technology, W. Ehrfeld Ed., pages 11-19, Springer, 1998.
- Srinivasan, R. et. al., Micromachined Reactor for Catalytic Partial Oxidation Reactions. AIChE Journal, November 1997, Vol 43, No. 11, 3059-3069

Table 9.1. Representative Sample of the Framework for the Clean Technology Guide.

TARGET	Type of separation	TECHNOLOGICAL OPTIONS	ENVIRONMENT	ENERGY	SAFETY	OPERATIONAL
Organic solvent removal	solid/liquid	Centrifugation				
		Atmospheric Distillation				
		Vacuum distillation				
		Evaporation				
		Filtration				
		Microfiltration				
		Nanofiltration				
		Reverse Osmosis				
	Liquid/liquid: miscible	Solid/liquid extraction				
		Ultrafiltration				
		Atmospheric Distillation				
		Vacuum distillation				
		Azeotropic distillation				
		Extractive distillation				
Phase Separation (during washes and work-ups)	Liquid/liquid: immiscible	Freeze concentration				
		Pervaporation				
Water Removal from Organic Solutions	Liquid/liquid	Centrifugation				
		Gravity separation				
		Atmospheric Distillation				
		Vacuum distillation				
		Extractive distillation				
		Azeotropic distillation				
Solvent Exchange (for forward processing and crystallization)	Liquid/liquid	Freeze concentration				
		Pervaporation				
		Desiccation with MgSO ₄				
		Atmospheric Distillation				
		Vacuum distillation				
Isolation of product from solution	solid/liquid	Put and take distillation				
		Extraction				
	Liquid/liquid: (oils)	Nanofiltration				
		Crystallisation				
Isolation of product from slurry	solid/liquid	High sheer mixer				
		atmospheric distillation				
Solid drying	solid/liquid	vacuum distillation				
		Centrifugation				
Reactions	---	Filtration				
		Spray dryer				
		Tray dryer				
		Batch reactors				
		In ionic fluid				
		In subcritical fluids				
		In supercritical fluids				
		Electrochemical				
Vortex mixers						
Catalytic systems	---	Minireactors				
		Microrreactors				
		Supported catalysts				
Equipment and reactor cleaning	---	Unsupported catalysts				
		Solution				
		High pressure cleaning				
		Traditional CIP				
		Spray ball				

Table 9.2. Comparative Indicators.

Mass indicators
Mass intensity (not including water), kg/kg usable product
Added Solvent intensity, kg added/kg usable product
Wastewater intensity, kg/kg usable product
Specific Compounds released, kg/kg usable product:
Efficiency (%)
Quality (% purity)
Energy Indicators
Heating MJ/kg usable product
Cooling, MJ /kg usable product
Electricity, M/kg usable product
Cooling (Refrigeration cycle), MJ refrigeration/kg usable product
Life Cycle Indicators
CO2 emissions (g/kg usable product)
Safety Considerations
Operational Considerations

Table 9.3. Description of the reactor options for the case-scenario

Reactor type	T (C)	Residence time	Yield (%)	Area / volume (m²/m³)	Dimensions
Flask	-40	0.5 h	88	80	0.5 L
Stirred vessel (Production)	-20	5 h	72	4	6000 L
Microreactor	-10	< 10 s	95	10,000	2 x 16 channels of w x h = 40 x 220 micrometers
Minireactor	-10	< 10 s	92	4,000	Capacity of 3 E-5 m ³ /s (volume about 300 ml)

Table 9.4. Mass Indicators for the Example Described.

Mass indicators	Flask 0.5 L	6000 L Vessel	Micro- reactor	Mini- reactor	Theoretical minimum
Mass intensity (does not include solvent usage) total moles in/moles product	2.27	2.78	2.10	2.17	2.00
Added Solvent intensity	----	----	----	----	----
Added water intensity	0	0	0	0	0
Residue intensity (does not include solvent), moles residue/moles product	0.27	0.78	0.10	0.17	0
Efficiency (yield, %)	88	72	95	92	100

Table 9.5. Energy Indicators for the Example described.

Energy Indicators	0.5 L Flask	6000 L vessel	Micro- reactor	Mini- reactor
Cooling (with cooling water)	0.42	0.42	0.42	0.42
Electricity (only refrigeration energy is included), MJ/mole product	0.167	0.107	0.080	0.080

Table 9.6. Energy-related emissions for the Example described.,

Parameter	Units	micro	mini	6000L	0.5 L
CO ₂	g/mol	1.34E+01	1.34E+01	1.79E+01	2.78E+01
CO	g/mol	3.66E-03	3.66E-03	4.88E-03	7.58E-03
CH ₄	g/mol	4.72E-02	4.72E-02	6.28E-02	9.76E-02
VOC	g/mol	3.09E-03	3.09E-03	4.12E-03	6.40E-03
NO _x	g/mol	2.85E-02	2.85E-02	3.79E-02	5.89E-02
SO _x	g/mol	3.99E-02	3.99E-02	5.31E-02	8.25E-02
COD	g/mol	4.07E-02	4.07E-02	0.00E+00	0.00E+00
BOD ₅	g/mol	1.63E-03	1.63E-03	0.00E+00	0.00E+00
TDS	g/mol	5.43E-02	5.43E-02	5.42E-02	8.42E-02
Solid waste	g/mol	6.10E-01	6.10E-01	2.17E-03	3.37E-03

Table 9.7. Green Technologies' Metrics for the Scenario Presented

Technological Alternative	Environment	Safety	Efficiency	Energy
Microreactors	Green	Green	Yellow	Green
Minireactors	Green	Green	Green	Green
6000 L batch reactor	Yellow	Yellow	Red	Yellow

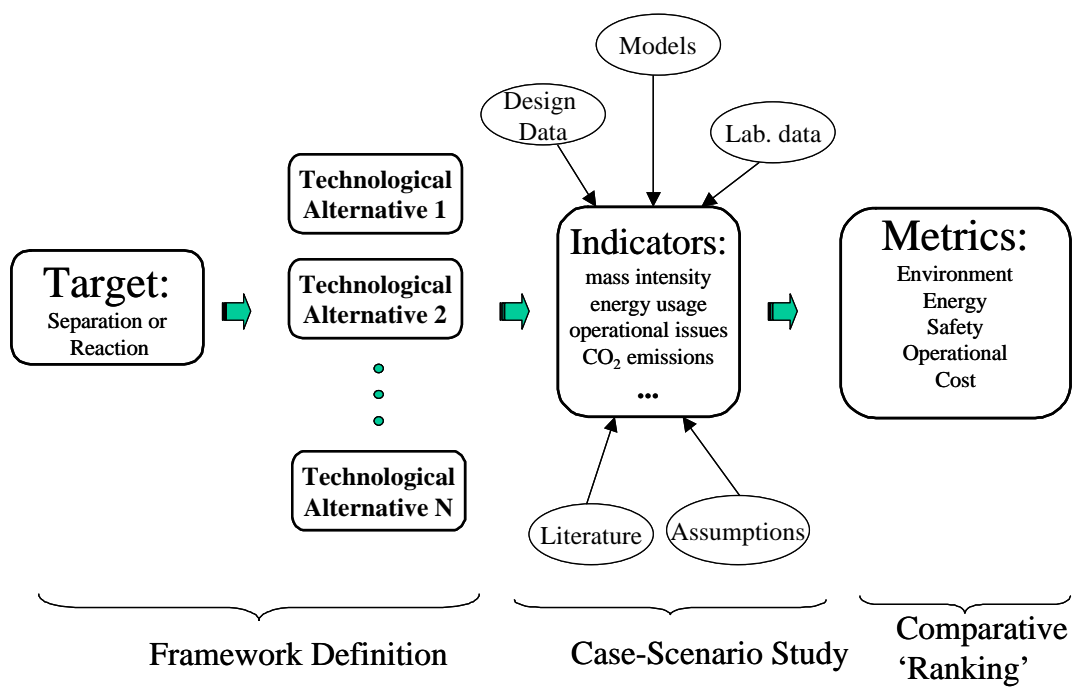


Figure 9.1. Methodology for the Development of the Clean Technology Guide.