

Bridging the Gap from Pilot Plant Experimental Records to Life Cycle Inventory

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Abstract

Conducting life cycle assessment (LCA) at pilot-scale can help chemical and pharmaceutical industries to generate environmental load data, identify environmental hotspots, and provide options for building sustainable manufacturing plants from the process design and development stage. However, collecting life cycle inventory (LCI) data is time intensive and may be arduous for process development. In this paper, a systematic methodology was developed to bridge quickly the gaps between pilot plant operation and LCI, and also scale up to predict LCI at industrial-scale. According to ISO 14040 series of standards for LCA, the methodology classifies various data-available scenarios and integrates experimental measurements with engineering and empirical calculations to provide suitable data for LCI. This methodology builds a reliable, convenient and easily following basis, which enables industrial process developers to gain a much clearer view of the environmental footprint at process design stage, thereby enabling earlier design changes to reduce impacts.

Keywords: Development of life cycle inventory (LCI), Experimental records, Pilot plant, Data gaps

Nomenclature

| | |
|--------------|---|
| A | Heat transfer area, m ² |
| BE | Bond energy, kJ/mol |
| C_{Conv} | Conversion rate of a material in a reaction, % |
| C_p | Heat capacity, kJ/kg/K |
| D | Datasets from the experimental records |
| D_a | Diameter of impeller, m |
| E | Energy, kWh |
| F_{Alloc} | Allocation factor for multiple outputs from one unit process |
| f_{Load} | Load factor of an equipment |
| f_n | Quantification factor of the n th unit process |
| f_{Stoi} | Stoichiometric coefficient of a reaction |
| g | 9.81 m/s ² |
| ΔH | Energy for condensation or vaporization, kJ/mol |
| ΔH^0 | Standard enthalpy of a chemical, kJ/mol |
| h | Convection heat transfer coefficient for fluid, W/m ² /K |
| k | Thermal conductivity, W/m/K |
| M | Mass, kg |
| m | Moles of material, mol |
| n | Rotational speed of agitator, rps |
| N_p | Power number of agitator |
| N_Q | Flow number of agitator |
| O | Multiple output from one unit process |
| ΔP | Pressure difference, Pa |
| Q | Flow rate of liquid or gas, kg/s |
| q | Volumetric flow rate, m ³ /s |
| T | Temperature, K |
| Δt | Time of operation, s |
| U | Heat transfer coefficient, W/m ² /K |
| UN_n | Datasets of the n th unit process |
| V | Volume, m ³ |
| x | Mass fraction, % |

Subscripts

| | |
|---------|---------------------------------|
| ASMat | Auxiliary and service materials |
| Bond | Bond |
| Charg | Charging |
| Cond | Condensation |
| Cycli | Cyclization unit process |
| Dischar | Discharging |
| Emi | Emissions |
| Eng | Energy |
| Env | Environment |
| Equip | Equipment |
| Heat | Heating and cooling |
| InMat | Input material |

Subscripts (Continued)

| | |
|--------|--------------------------------|
| Insul | Insulator |
| Jack | Jacket layer of reactor |
| Latent | Latent heat |
| Limit | Limiting material |
| Loss | Heat loss |
| Misc | Represent for any element |
| Motor | Motor |
| Orig | Original, before the operation |
| OutMat | Output material |
| Oxid | Oxidation unit process |
| Prod | Product or output |
| Pump | Pump |
| Reag | Reagent |
| Rxn | Reaction |
| Salt | Salt formation unit process |
| Sensi | Sensible heat |
| Shaft | Agitator shaft |
| Stir | Agitator |
| Suct | Suction |
| Therm | Thermal fluids |
| Vapo | Vaporization |

Greek Letters

| | |
|----------|---|
| α | Coefficient for calculating N_p of agitator |
| γ | Fraction of nominal power consumed, % |
| η | Efficiency of motor or equipment, % |
| ρ | Density, kg/m^3 |

List of Acronyms

| | |
|-------|--|
| API | Active Pharmaceutical Ingredient |
| CSTR | Continuous Stirred-Tank Reactor |
| GSK | GlaxoSmithKline pharmaceutical company |
| LCA | Life Cycle Assessment |
| LCI | Life Cycle Inventory |
| 4-DEL | 4-D-Erythronolactone |
| TCU | Temperature Control Unit |

1. Introduction

The chemical and pharmaceutical industries are making efforts to reduce environmental burdens from their production processes. The manufacturing of chemical products and active pharmaceutical ingredient (API) encompass complex organic reagents, solvents and catalysts that are toxic to human health and environment. It is essential to select materials and solvents that result in the least environmental burdens, as well as select the

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reaction route and manufacturing technologies that are environmental-friendly in process development stages. Furthermore, most of these toxic solvents and chemicals are disposed as process wastes. Typically, tens to hundreds kg of process wastes are generated for the production of 1 kg of API or chemical products.¹ It is imperative to consider the options of waste management as early on as possible during process development.

A number of pharmaceutical companies have successfully applied life cycle assessment (LCA) in their manufacturing plants. LCA is a proven environmental management tool, which is used to systematically quantify the environmental impacts and evaluate the improvement options throughout the life cycle of a process, product or activity.² LCA provides quantified evidence for decision-making processes towards the design of products with better environmental attributes. Glaxo SmithKline (GSK) conducted cradle-to-gate life cycle assessment on active pharmaceutical ingredient (API) production and developed a systematic methodology for transparency in LCA;^{3,4} Johnson and Johnson compared three routes of API production and compared the resource consumption of batch vs continuous wet granulation in tableting process;^{5,6} Sanofi studied the environmental impacts of life-cycle-based process optimization and intensification of an API production.⁷ These studies further demonstrate that LCA is a valuable tool to quantify energy consumptions and environmental emissions at the full-scale production plants.

However, due to its data-intensive and time-consuming nature, conducting LCA is not easily done for every API, especially when a large proportion of APIs fail clinical trials even before the end of development. Just a basic LCA study with a boundary from gate-to-gate would require the exact amount of each input material and output product, the explicit energy consumption, and the concrete wastes and emissions by each unit process. When the boundary of the LCA is expanded, more data have to be included in LCI, such as transportation mode, distance for shipping intermediate materials and products, information of usage and end-of-life management. Basically, the required LCI data are not directly available or measurable, and collecting data is time intensive and may be arduous for process development.^{8,9}

Generating LCI data at early process development stages can reduce the time and costs involved in data collection. The LCI data from early process developments stages can provide advance information for large-scale manufacturing decisions. Here we present a methodology to generate gate-to-gate LCI data from pilot-plant experimental records and thereafter to scale up it to LCI of full-scale manufacturing plants.

1.1 LCA of Pilot Plant Operation

Pilot plant operation enables companies to evaluate new processes and technologies at a small-scale with limited investment, thus helping to reduce risks before building large process plants.^{10, 11} Pharmaceutical industry operates the pilot plant operation to prove the feasibility of scale up the chemists' successful synthesis from their lab work, and also typically has the function of producing materials for clinical trials.¹¹

Nowadays, with more environmental concerns in the chemical and pharmaceutical industries, conducting LCA at pilot-scale can incorporate environmental considerations together with traditional technical and economic criteria at an early stage of process design and development.^{2,8} This will enable the company to estimate environmental load data, identify environmental hotspots, and provide options for building sustainable manufacturing plants and supply chains at the process design and development stage.^{8,12,13} This will especially help in the aspects of identifying the hot spots of energy consumption, recognizing the equipment or sub-processes with relative high waste generation and environmental emissions. In turn, that supports selecting environmental-friendly material and process alternatives throughout the life cycle by quantitatively comparing different technological production routes, different materials and other experimental options. It is estimated that 80% of a product's environmental effects are determined by the process design and development stage.⁸ Process engineering industries have shown increasing interests in the application of LCA to new material and process design and development.¹⁴⁻¹⁶

Conducting LCA in the pilot-scale raises the challenge of data collection for life cycle inventory (LCI). There are obvious mismatches between LCI data and experimental records in pilot plant operation, as listed in Table 1 and discussed below.

1.2 Gaps between Experimental Records and LCI

Experimental records and LCI have different purposes. Experimental records are mainly used for references of process modeling and understanding, where the production and manufacturing procedures of the conducted experiments are documented in detail; on the other hand, the objectives of LCI data are for further assessment on the environmental impacts from the life cycles of the products.

Experimental records and LCI have different boundaries. Experimental records have gate-to-gate boundaries: they start with the commercially available intermediate materials and energies at the plant's in-gate, and end at the products to the plants' out-gate. However, LCI data typically considers the boundary from cradle-to-gate, and it usually traces back to the sources of the intermediate materials and energy generation.

Experimental records and LCI have different description methods. In experimental records, the system is usually described with a process diagram that lists all the equipment and instruments, showing the material and energy flow from equipment to equipment. However, in LCI data, the studied system is illustrated as reference flowchart based on unit processes. Each unit process is represented by a black box and highlighted with the material and energy inputs and outputs. The types of equipment may not be highlighted in unit process.

Experimental records and LCI have different focuses. Experimental records generally pay attention to product quality, reaction yield and process efficiency. Usually, chemists and lab operators take the system under study as a stream line operation and follow the time sequenced step-by-step action, such as "X kg of Y material is added to reactor at Time Z" and "Heat the solution to M degree and maintain the temperature for N minutes". Meanwhile, the LCI study focuses on the definition of the functional unit and the quantified data for reference flow. Generally, the whole system is divided into a few unit processes, and the data of each unit process is quantifiably listed.

Experimental records and LCI data require different types of data and data sources. The pilot plants run experiments to vary experimental conditions and parameters, collecting data from practical measurements, such as the composition of materials and products, the temperature of the reaction, and the flow rate of the inlet/outlet fluids. On the other hand,

the LCI data favors the consumptions and releases from each unit process, before summarizing the total consumptions and releases from the whole system. Primary data from actual measurements are the first choices for LCI data, and secondary data from calculations, estimations and literature would then be considered for the missing data. There is a need to bridge the gaps between pilot plant experimental records and LCI data.

1.3 Scale up of LCI from Pilot Plant to Designed Commercial Production Process

Conducting LCAs using pilot plant data may overestimate the overall environmental burdens, leading to significant errors on the environmental performance of processes at industrial-scale.^{17,18} Gavankar et al. reported that scaling up of a specific process (from 100 g/day to 1 ton/day) could reduce 84% to 94% of its cradle-to-gate impacts;¹⁷ Hetherington et al. reported the obvious disparity between LCA results obtained from early process development stage and LCA results generated from industrial-scale.¹⁸

It is more important to generate a reliable industrial-scale LCI than to conduct pilot-scale LCA. The overall environmental performance of large-scale manufacturing plant is always the main interest of industry. We propose to scale up the LCI data from pilot-scale to the designed industrial-scale from below considerations.

Compared to lab-scale development stages, the LCI data generated from pilot plant are the closest to those of full-scale manufacturing plant. As pilot plant is at the highest level in process development, its material capacities and equipment dimensions are much bigger than those of laboratory experiments and mini plants.

Pilot plant operation can generate detailed process information that can be used for scaling up to manufacturing plant. With justifications and assumptions of technology applied, equipment deployed, efficiency of material and energy, and interactions between unit processes, it is reasonable to scale up the LCI data of pilot plant, and predict the LCI data for a designed manufacturing plant.

Furthermore, a designed manufacturing plant has set clear targets about the capacities of materials and products, dimensions of reactors, models of equipment and sources of energy. The developed methodology, which is based on established laws of physical systems, is able to calculate the industrial-scale material and energy flows from above

information. Combined with the sensitivity analysis and uncertainty analysis, the developed methodology can generate the ranges of LCI data for the designed manufacturing plant.

1.4 Objective and Structure of this Paper

The main objective of this paper is to bridge the gaps between pilot plant operation and life cycle assessment by presenting a methodology for converting the experimental records into LCI data, thereafter scale up it to industrial-scale LCI. This work is intended to enable industrial process developers to gain a much clear view of the environmental footprint much earlier in design, thereby enabling earlier design changes to reduce impacts.

The rest of this paper is organized as follows. The typical steps of the methodology that converts pilot-scale experimental records into LCI data are described in Section 2. The methodology was further developed to scale up LCI from pilot-scale to industrial-scale in Section 3. In Section 4, the methodology was applied to the experimental records of multi-kilogram synthesis of 4-D-Erythronolactone (4-DEL) that was conducted in our pilot plant as a batch process. The methodology is evaluated in Section 5. Further discussions and conclusions are given in Section 6 and 7 correspondingly.

2. Methodology of Translating Experimental Records to LCI

A systematic methodology is developed to translate the pilot plant experimental records into LCI data. According to the requirements in the ISO 14040 series of standards,^{19, 20} the methodology is based on the material and energy flows and balances within the defined system boundaries, as shown in Figure 1.

2.1 LCA Goal and Scope Definition (Step 1)

The first step to conduct a LCA is to define the objective and goal of the study, clearly stating the reasons to carry out the study as well as the intended application and audience. In pursuing green chemistry and engineering, the main objectives of conducting LCA can be classified as: comparison of reaction route or manufacturing technologies; choice of materials and solvents; identification of environmental hotspots; selection of waste

management options, such as solvent recovery or reduction; development of systematic methodology for quick and convenient LCA assessment.

Based on the objective of the study, certain impact categories are selected. Global warming potential (GWP) and energy consumption are the two impact indicators that attract the most attention.

The process diagram or flowchart should be obtained in step 1.2. They can briefly describe the system under study.

The functional unit is defined in step 1.3. As the key element of LCA study, it provides a quantitative reference to relate the inputs and outputs. According to the objectives of LCA study, we recommend to define the functional units of chemical and pharmaceutical processes in two ways:

- i. For the purposes of comparing reaction routes, selecting waste management options, choosing materials and solvents, the major focus is the production of API or other chemical products. The functional unit can be straightforwardly defined as a specified amount of product that meets certain product quality, such as 1 kg of API product with a purity > 99%;
- ii. For the purpose of comparing manufacturing processes, the productivities of processes are the major focus of study. The functional unit can be defined either as a specified amount of product or as a specific time period of process operation. For example, when a batch process and a continuous process are compared to produce one API, the functional unit can be defined as production of 1 kg of pure API by each process; it can also be defined as 1 week of operation time by each process.

2.2 Identification of Unit Process (Step 2)

The system boundaries are determined in step 2.1. Cradle-to-gate is the common LCA boundary for chemical and pharmaceutical study. However, the cradle data of raw materials are normally out of the companies' control, and may be sourced from the literature suppliers or Ecoinvent database. The chemical and pharmaceutical companies have the production data, which starts from the raw materials delivered to the plants' in-

gate, and ends at the API or products at the plants' out-gate. A gate-to-gate boundary of LCI is highlighted in this study.

The system boundaries decide which processes to be included in the LCA study, such as the processes for by-products and recycling etc. Also, the geographical boundaries, time boundaries and technology boundaries are also defined in the system boundary.

Subdivision of the system into unit processes and composition of a LCI flowchart can clearly describe the system boundary for LCA study and explicitly identify which data to be collected. The number of unit process and the boundary of each unit process should be determined by the level of details required by the objectives of the LCA studies: the more details are required, the more unit processes are subdivided.

Unit processes are connected with intermediate materials and form a LCI flowchart. To ensure valid subdivision of unit processes, the mass and energy balance are compiled in two levels: the input and outputs of each unit process should be balanced; and the sum of all unit processes should be balanced with the overall system.

It should be noted that the allocation of unit process should base on the definition of functional unit, either according to mass of product or according to the process time.

2.3 Translation of Experimental Data (Step 3)

In conducting LCA, the most difficult and time-consuming part is data collection. This section presents the step by step procedures to translate from experimental records to LCI data. All the calculation and data translation procedures are based on each operation conducted in the pilot plant experiments, that is, every piece of experimental records are calculated and translated into LCI.

2.3.1 The data of material flow

Material flow includes input materials, expected main product, secondary by-products, auxiliary material, direct emissions to environment, and wastes. The translation procedures of quantifying material flows from experimental records are stated in Step 3.1 and shown in Figure 2 and 3. The corresponding equations are listed in Table 2.

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2.3.2 The data of energy consumption

Calculation and estimation of the energy consumed in pilot plant operations are the major issues of the developed methodology. For each piece of experimental record, it is essential to identify all the equipment used in the operation, and then check the specifications and the energy sources of the listed equipment. Although this methodology is limited to electrical energy, other sources of energy, such as steam may exist for other pilot plant operations.

The ideal situation is to have the direct measurements and records of energy consumed by the equipment. Otherwise, according to the types of the equipment, different empirical engineering formulas are applied to calculate the energy consumptions. The procedures of calculating energy consumption from experimental records are stated in Step 3.2 and shown in Figure 4 to 6. The corresponding equations are listed in Table 3, 4 and 6.

2.3.3 Intermediate Calculations

The density of mixtures, heat capacity of materials and bond energy of compounds may have to be estimated in calculating the energy consumed by equipment. The corresponding equations are listed in Table 5.

2.3.4 Summary of Data Translation

In summary, the quantification of input materials and output materials is mainly based on mass balance and the mechanisms of reactions that happen during the process operations; the quantification of energy consumption is mainly based on engineering principles and empirical equations of various types of equipment. For the by-products, if they are not allocated within the boundary of the life cycle assessment, they can be considered as emissions to air, water or wastes depending on the gaseous, liquid or solid states of the by-products. Furthermore, the storage of materials and transportation data are not considered in this methodology. The summarization of data translation from pilot plant experimental records to LCI is listed in Table 7.

2.4 Datasets of the Unit Processes (Step 4)

2.4.1 Data Categorization (Step 4.1)

This step describes the procedures to categorize and count up the LCI data for each unit process. For the operations within the n^{th} unit process, the data can be classified into five categories: i) Input materials, $D_{n,InMat}$; ii) Auxiliary and service materials, $D_{n,ASMat}$; iii) Energy consumption, $D_{n,Eng}$; iv) Emissions and wastes, $D_{n,Emi}$; v) Amount of the main output used for the manufacturing of the targeted product, $\|D_{n,OutMat}\|$. A dataset for the n^{th} unit process, D_n , is formed, as shown in Figure 7 and below.

$$D_n = \begin{bmatrix} D_{n,InMat} \\ D_{n,ASMat} \\ D_{n,Eng} \\ D_{n,Emi} \end{bmatrix} \quad (28)$$

It should be noted that input materials participate in the reactions and become part of the products; auxiliary and service materials are input into the process, but do not generally become a part of the products, such as the catalysts and the process water. Furthermore, $D_{n,InMat}$, $D_{n,ASMat}$, $D_{n,Eng}$ and $D_{n,Emi}$ are vectors, while $\|D_{n,OutMat}\|$ is a scalar indicating the total amount of the main output from the n^{th} unit process.

The inventory data for the n^{th} unit process, UP_n , can be obtained by normalizing D_n , which is based on per unit output of main output material, such as per kg production of the main output material from the n^{th} unit process.

$$UP_n = D_n / \|D_{n,OutMat}\| = \begin{bmatrix} UP_{n,InMat} \\ UP_{n,ASMat} \\ UP_{n,Eng} \\ UP_{n,Emi} \end{bmatrix} \quad (29)$$

2.5 Reference Flow and LCI (Step 5)

This section describes the procedures to link unit processes and build a reference flow for the defined functional unit. As shown in Figure 8, the functional unit involves M_n kg of the targeted product, and per 1 kg of product n involves M_{n-1} kg of output material $n-1$ and so on, till the initial stage, per 1 kg of output material 2 involves M_2 kg of output material 1, so the LCI for the functional unit can be expressed as:

$$LCI = \sum_{i=1}^n [(\prod_{i=1}^n M_{n-i+1}) \cdot UP_{n-i+1}] = \sum_n \begin{bmatrix} f_n \cdot UP_{n,InMat} \\ f_n \cdot UP_{n,ASMat} \\ f_n \cdot UP_{n,Eng} \\ f_n \cdot UP_{n,Emi} \end{bmatrix} \quad (30)$$

where, the quantification factor f is defined as:

$$f_n = \prod_{i=1}^n M_{n-i+1} \quad (31)$$

3 Methodology for Scaling Up LCI (Step 3A)

With an extended procedure (step 3A) to step 3, the developed methodology, as illustrated in Figure 1 and explained in section 2, is applicable to scale up LCI from pilot plant scale to industrial scale. This LCI scale up step focus on the estimation of material and energy flows with following assumptions:

- i. Industrial plant deploys the similar technology and operating procedures as pilot plant. Extra new processing steps, which do not exist at pilot-scale, may be added to commercial production plant;
- ii. Commercial production plant has the same study goal, system boundary, functional unit and unit processes as those of pilot plant. The above extra new processing steps can either be included in the existing unit processes or be separated as new unit processes;
- iii. Commercial production plant is preliminarily designed with targeted material capacity, approximated dimensions of reactors, choices of equipment, estimated reaction conversion rate, and predicated energy sources and efficiencies.

LCI scale up procedure is based on each unit process. As demonstrated in Figure 9 and the descriptions below:

Step 3A.1 identifies all the operation steps within the unit process under study. For the steps that are similar as those of pilot plant, step 3A.2 and 3A.3 predict the material flow and energy consumption in industrial-scale; for the extra new processing steps that are added to commercial production plant, step 3A.4 calculates the required material flow and energy consumption.

Step 3A.2 scales up material flow of existing operation steps in pilot plant. Based on the data obtained in step 3.1, efficiency ratio and scale ratio are applied to each reaction mechanism for scaling up the data of materials that were used in reactions; different scale ratios may be applied to other material data, such as service materials and auxiliary materials.

Step 3A.3 scales up energy consumptions of existing operation steps in pilot plant. With the information of selected equipment, step 3.2 is applied to re-calculate energy required by each process operation.

Step 3A.4 calculates material flow and energy consumption of extra new process steps that do not exist in pilot plant operation. With the information from the designed process, steps 3.1 and 3.2 are applied.

Step 3A.5 conducts sensitivity analysis, generates industrial material flow and energy consumption for scenarios with various process parameters. The selectable parameters include reaction conversion rates, energy efficiencies, equipment, and technologies of existing and new processing steps. Step 3A.5 is a repeated procedure of step 3A.1 to 3A.4, but with different parameters.

4 Case Study

This section presents a case study that illustrates application of the developed methodology.

4.1 Description of 4-DEL Pilot Plant Operation

The batch process of 4,D-erythrionolactone (4-DEL, $C_4H_6O_4$) was successfully scaled up to kilogram-scale in the pilot plant operation.³³ As shown in Figure S6, the reaction scheme of synthesizing 4-DEL involves three reactions:

- i. Salt formation, where D- (-) isoascorbic acid ($C_6H_8O_6$, DIAA) reacts with sodium carbonate (Na_2CO_3). The reaction generates main output material of $C_6H_7NaO_6$ and by-product of sodium biocarbonate ($NaHCO_3$).
- ii. Oxidation reaction, where $C_6H_7NaO_6$ reacts with hydrogen peroxide (H_2O_2). The reaction generates a main output material of $C_4H_7NaO_5$ and by-product of NaO_2CCO_2Na .

iii. Cyclization reaction. $C_4H_7NaO_5$ reacts with hydrochloric acid (HCl). The reaction generates main product of 4-DEL, and by-products of oxalic acid (HO_2CCO_2H), sodium chloride (NaCl), carbon dioxide (CO_2) and water (H_2O).

The pilot plant operation was carried out with a 60 L jacketed reactor, as shown in Figure S7. The reaction was agitated by an overhead stirrer, with two pumps being used for input materials from carboys. The temperature of the reactor was controlled by a temperature control unit (TCU) comprising a heat/cooling system.

4.2 LCI Goal and Scope of 4-DEL Pilot Plant Operation (Step 1)

The main goal of this case study is to conduct a life cycle inventory from the experimental records of the batch processing of 4-DEL in pilot plant operation. The generated inventory data can be used by researchers and engineers to assess the energy consumption and environmental impacts of the process, as well as identify the hot spot that has the most energy consumptions or has the most contributions to environmental impacts.

The functional unit of this study is production of 1 kg of 4-DEL with a purity > 99%.

4.3 Identification of Unit Processes (Step 2)

A gate-to-gate life cycle boundary is considered for this case study. The boundary starts from the first reaction of salt formation and ends at the production of 4-DEL compound. As described in the reaction scheme of synthesis 4-DEL, the three sequential reactions are defined as three unit processes, and a final separation process is considered as another unit process. Due to the unavailability of experimental records on separation process, this study focuses on the three unit process of salt formation, oxidation and cyclization for data translation. Figure 10 shows the flowchart of synthesis 4-DEL in pilot plant operation, listing the required input and output data for each unit process.

4.4 Translation of Data of 4-DEL Pilot Plant Operation (Step 3)

Table S1 to S3 in supporting information list the detailed experimental records, the translated LCI data and the corresponding quantification steps of the unit processes of salt formation, oxidation and cyclization, respectively. These tables demonstrate that each piece of the recorded pilot plant operation was translated into material flow and energy

consumption, including the LCI data of input materials, service materials, main output material, by-products, energy consumptions, emissions and wastes. The further details of each translation procedure are demonstrated in supporting information S5.

4.5 Datasets of Unit Process of 4-DEL Pilot Plant Operation (Step 4)

From the translation of each piece of experimental records listed in Table S1 to S3, the overall experimental datasets, D_{Salt} , D_{Oxid} , and D_{Cycli} of the three recorded unit processes of 4-DEL pilot plant operation are summarized in Table S4. According to the weight of the main output from each unit process, mass allocation was applied to obtain the LCI of each unit process, as shown in Table 8.

4.6 Reference flow and LCI of 4-DEL Pilot Plant Operation (Step 5)

The LCI of synthesis of 4-DEL in pilot plant was demonstrated Table 9.

5 Evaluation of Methodology

5.1 Data Quality

Data quality is the key issue in conducting LCA. It generally considers the time period that the study covers, the geographical regions that the study applies to, the representativeness of the technology, and the reproducibility of data. For the data collections from experimental records, these considerations have been inherently set by the experiments itself, before applying the methodology for data translation.

Data sources, completeness, and precision are the major factors affecting data quality in the methodology. To ensure the best available data source, the selection of data sources complies with ISO requirements: direct measurement as the first choice; with calculation and estimation being the second choice; followed by literature data and assumptions as the last choice. It should be noted that experimental records are the bases of the methodology, such that direct measurements are the main data sources, especially for the amounts of materials.

The data completeness depends on the level of detail. The methodology ensures the data completeness by analyzing every material, equipment, and reaction occurred within each piece of record and operation.

The data precision involves numerical accuracy and data uncertainty. In the methodology, numerical inaccuracy may exist due to unavoidable errors in lab measurements, rounding of calculations, inappropriate of literature data and inaccuracy of assumptions. In life cycle assessment, data uncertainty analysis can systematically study how the input uncertainties propagate into output uncertainties of environmental impacts. Monte Carlo simulation is a common way to conduct uncertainty analysis, where a form of probability density distribution function is specified to the input parameters and data.

5.2 Contribution Analysis for Energy Consumption

The energy consumed by pumps and agitators are limited. From the energy calculations in Eq. (6) to (15), the main factors affecting the equipment' energy consumption include: the operation time, the power number, and the mass of fluids to be pumped or agitated. In the case study, as shown in Figure 11, the energy consumed by pumps and agitators was less than 5% of the electricity consumptions, either in individual unit process or in the overall reference flow. This is reasonable due to the small-scale of operation, where the power numbers of instruments and the amounts of materials were scaled down.

However, the heating/cooling system consumes the most of the energy consumption, which are mainly used for sensible heat, or used to counteract the reaction heat and maintain the temperature of the reactor. From the calculations in Eq. (18) to (20), the major factors affecting the reaction heat include the moles, bond energy or enthalpies of formation of each compound in the reaction; the major factors affecting the sensible heat include the variation of temperature, mass and heat capacity of each material in the reactor. In the case study, heating/cooling system accounts for at least 95% of the electricity consumption in individual unit process and in the overall reference flow. This is mainly due to the increase of reactor temperature in the salt formation process, and high reaction heat in the oxidation and cyclization processes.

5.3 Effects of Equipment Efficiency to Energy Consumption

The methodology applies a fixed efficiency number (75%) in calculating the energy consumed by pump, agitator and heating/cooling system. However, the actual equipment efficiency fluctuates with experimental conditions, such as the load of equipment, the flow rate of pump, the geometry of the impeller, and the insulation of heating/cooling

system.^{34, 35} As shown in Figure 12, the overall energy consumption of the reference flow increases 85.7% by decreasing the efficiencies of pump, agitator and heating/cooling system from 75% to 50%, 90% and 40% respectively.

6 Discussion

6.1 Unit Process with Multiple Outputs

Allocation is required for a unit process with multiple output materials. If the n^{th} unit process has m different outputs, $O_{n,1}, O_{n,2} \cdots O_{n,m}$, the amount of the i^{th} output material is expressed as $\|O_{n,i}\|$, and we can define a mass allocation factor as:

$$f_{Alloc,n,i} = \frac{\|O_{n,i}\|}{\sum_m \|O_{n,m}\|} \quad (32)$$

Correspondingly, the LCI of the unit process UP_n is allocated by the m outputs, and the LCI for the i^{th} output material is expressed as:

$$UP_{n,i} = f_{Alloc,n,i} \cdot UP_n \quad (33)$$

6.2 Complicatedly Connected Unit Processes

Unit processes that have complicated connections are suggested to be isolated to multiple serial connections. When more operation stages are involved in the pilot plant experiments, the connections of unit processes usually become more complex. They may be linked serially, in parallel, or as a mixture of both types of connections. To simplify the data translation, we suggest separating the complicated connection into multiple serial connections. An example of complex connections of unit processes is shown in Figure 13, where the outputs from UP_1 were sent to the parallel connections of UP_3 , UP_4 and UP_5 ; UP_7 , UP_4 and UP_8 are parallel connections, which are serially connected to UP_9 ; UP_5 and UP_6 is another parallel connection, which is serially connected to UP_8 . To simplify the assessment of LCI for the functional unit in Figure 15, the flowchart can be isolated into 4 serial connections:

- i. $UP_1 \rightarrow UP_3 \rightarrow UP_7 \rightarrow UP_9 \rightarrow UP_{10}$ (Based on output material $O_{1,1}$)
- ii. $UP_1 \rightarrow UP_4 \rightarrow UP_9 \rightarrow UP_{10}$ (Based on output material $O_{1,2}$)
- iii. $UP_1 \rightarrow UP_5 \rightarrow UP_8 \rightarrow UP_9 \rightarrow UP_{10}$ (Based on output material $O_{1,3}$)

iv. $UP_2 \rightarrow UP_6 \rightarrow UP_8 \rightarrow UP_9 \rightarrow UP_{10}$

The above four serial connections generate four sub LCIs, according to their quantification factor f in the flowchart, the final LCI for the functional unit is added up with Eq. (34) and expressed as:

$$LCI = f_{12} \cdot UP_{10} + f_{11} \cdot UP_9 + (f_6 \cdot UP_7 + f_5 \cdot UP_3 + f_1 \cdot f_{Alloc,1,1} \cdot UP_1) + (f_7 \cdot UP_4 + f_2 \cdot f_{Alloc,1,2} \cdot UP_1) + [f_{10} \cdot UP_8 + (f_8 \cdot UP_5 + f_3 \cdot f_{Alloc,1,3} \cdot UP_1) + (f_9 \cdot UP_6 + f_4 \cdot UP_2)] \quad (34)$$

6.3 LCI Flowchart and Division of Unit Process

LCI flowchart is based on the logical sequence of the operations or the sequence of reactions, instead of the physical equipment in the experimental setup. For example, in the 4-DEL case study, the three sequential reactions of salt formation, oxidation and cyclization were logically isolated as three unit processes. However, the three reactions actually took place in the same reactor, where they were operated as sequential experimental stages in the pilot plant operation.

Unit processes are logically isolated from the whole process operation, but they are physically connected to each other by the connecting material flow. As demonstrated in the case study, there are three separated LCIs corresponding to the three unit processes respectively. However, the main output material from the previous unit process is the input material to the following unit process, such as the main output of $C_6H_7NaO_6$ from the salt formation unit process is the input material to the oxidation unit process; and the output of $C_4H_7NaO_6$ from the oxidation unit process is the material input to cyclization unit process. The connecting material flow is the link of unit processes to the functional unit.

The selection of connecting material is straightforward given if there is only one output material from the previous unit process acting as the input material to the following unit process. However, in cases there are multiple output materials from the previous unit process taking part in the main reaction in the next unit process, it is necessary to judge the limiting reagent and choose it as the connecting material. The example in below demonstrates two sequential reactions corresponding to two connected unit processes. In

the first reaction, the molar ratio of the two outputs D to E is 1:1. The second reaction requires the molar ratio of the two inputs D to E is 1:2. If there is no extra charge of material E during the second reaction, material E is the limiting material and D generates excess material.

First reaction: $A + 2B + C = D + E + F$

Second reaction: $D + 2E + 3G = H + I$

6.4 Excess Input Materials

In the pilot plant trial and error experiments, it may be a general issue of adding excess input materials with the purposes of expediting the desired reactions; maximizing the use of expensive reagents; adjusting the solutions to designed condition, such as specific PH value; or ensuring the complete reaction of specified reagents, such as in combustion.³⁰ The case study of synthesizing 4-DEL in pilot plant indicated that the excess input materials in each unit process were not negligible. In the salt formation process, 16.3 % (0.49 kg) of the 3 kg of input material of $C_6H_8O_6$ is excess material; in the oxidation process, 37.6% (0.94 kg) of the 2.5 kg of input Na_2CO_3 is excessive.

We suggest three possible ways to treat the excess input materials in translating the pilot plant experimental records:

- i. In the case that the excess input materials are separated from the main output of the unit process, they can be treated as process wastes. However, the small amounts of excess materials in pilot plant operations are often not worthy of further separation and purification to recycle or recover.
- ii. In the case that the excess materials are not separated from the output material, and they do not participate in any reactions in the following unit processes, they can be treated as process wastes.
- iii. In the case that the excess materials are not separated from the output material, and they do participate in the reactions in the following unit processes, they can be ignored in the current unit process. But in the following unit processes, the outputs from the reactions they participated in should be listed and assessed.

In the case study, the three unit processes sequentially took place in the same reactor since there was no separation stage to isolate the excess materials from the main product, and the excess materials also took part in the reactions in the following unit process, therefore, we treated the excess materials under case iii. The excess material from the salt formation process, i.e. 0.49 kg of $C_6H_8O_6$, was reacted with the input material of Na_2CO_3 in the following oxidation process and generated 0.55 kg of $C_6H_7NaO_6$. Together with the 2.82 kg of $C_6H_7NaO_6$ generated in the salt formation process, a total of 3.37 kg of $C_6H_7NaO_6$ participated in the oxidation reaction and produced 1.88 kg of $C_4H_7NaO_5$. Similarly, the 0.94 kg of excess Na_2CO_3 and 1.01 kg of excess $C_6H_7NaO_6$ from the oxidation process reacted with the input material of HCl in the following cyclization process, generating CO_2 , NaCl and $C_6H_8O_6$, which were treated as emissions to air and wastes in the final LCI.

6.5 Side-reactions and By-products

In translating the pilot plant experimental records, it is important to understand the compounds inside the reactor, and justify the priority of reactions that possibly take place. Parallel side-reactions are common in the batch processing due to the existence of excess materials and by-products from previous unit processes. As in the case study, both the by-products of $NaHCO_3$ from the salt formation reaction and the NaO_2CCO_2Na from oxidation reaction, together with the two excess materials of $C_6H_7NaO_6$ and Na_2CO_3 from oxidation reaction, reacted with the HCl in the cyclization process. These four side-reactions competed with the main reactions:

- i. Main reaction: $C_4H_7NaO_5 + HCl = C_4H_6O_4 + NaCl + H_2O$
- ii. Side-reaction #1: $Na_2CO_3 + 2HCl = 2 NaCl + H_2O + CO_2$
- iii. Side-reaction #2: $NaHCO_3 + HCl = NaCl + H_2O + CO_2$
- iv. Side-reaction #3: $NaO_2CCO_2Na + 2HCl = HO_2CCO_2H + 2NaCl$
- v. Side-reaction #4: $C_6H_7NaO_6 + HCl = NaCl + C_6H_8O_6$

With an assumption that the above reactions are irreversible and the conversion rates of all reagents are 100%, it needed 75.6 moles of HCl to complete the five reactions. According to the calculation, there is lack of 1.63 moles of HCl, so the priorities of the five reactions have to be decided. Unfortunately, the main reaction of cyclizing $C_4H_6O_4$

from $C_4H_7NaO_5$ is most likely to have the lowest priority of reaction. This is because the four by-reactions are very fast ionic acidification reactions, taking place almost simultaneously at the moment HCl is charged in. The main cyclization reaction is an organic reaction involving the breakage and formation of covalent bonds. We assume this reaction is not completed and the process has excess $C_4H_7NaO_5$ as waste.

As to the treatment of by-products in the data translation of pilot plant experimental records, we suggest:

- i. The by-products can be treated as waste outputs if they are not separated from the process for further usage, and they do not participate in any reactions in the following unit processes.
- ii. Allocated with the main product if the by-products are further processed and separated from the main product within the system boundary.

In the case study, we treated the by-products as process wastes with the consideration that the by-products are not separated for further usage in the following experimental stages. .

6.6 Energy Consumption for Reaction

Regardless of exothermal (-) or endothermal (+) reactions, and regardless of heating or cooling operations, pilot plant operation consumes energy to reach the controlled temperature, instead of generating energy. In the oxidation reaction of synthesis 4-DEL, the calculation from bond energy indicated it was an exothermal reaction with 795 kJ/mol, and the reaction released a total 2.63 kWh of heat in the recorded pilot plant operation. Part of the released reaction heat is used to account for the sensible heat of the fresh input material, and part of the heat lost through the wall of the reactor, 2.38 kWh of electricity is still needed to cool down the reaction. Both exothermal and endothermal reactions require electrical energy to reach the targeted temperature. So they are expressed as energy demanded in pilot plant operation, rendering their “+” or “-” signs redundant. In full scale industrial operations, some released energy may be reused or recovered, and this should be indicated in corresponding LCI.

6.7 Energy Consumption for Heat Loss

Without real-time measurements of circulated thermal fluids in temperature control unit, the energy consumed by heating/cooling system in our 4-DEL case study was estimated through reaction heat, sensible heat, latent heat and heat loss through reactor, as stated in step 3.2.4.2 and Eq. (17) to (24). Two scenarios of heat loss were considered in our methodology: (1) when heating/cooling vessel is operated at a stable fixed temperature, the heat loss through walls of vessels can be calculated with Eq. (22); (2) during heating/cooling operations, integral calculation with Eq. (24) is applied to accumulate the heat loss during the time span of heating/cooling operation. Considering kilogram-scale reactions were carried out in a well-insulated jacket reactor with reaction temperatures ranged from 22°C to 39.7°C, we assume that there is limited amount of heat loss through radiation and evaporation, and negligible heat loss through thermal convections of solutions inside reactor, thermal fluids in jacket layer and environmental air. We predict the major heat loss in our case study is through the conduction of the wall of insulator, and simplify the overall heat transfer coefficient as:

$$U = k_{Insul}/\theta_{Insul} \quad (35)$$

where, $k_{Insul}(W/m/K)$ and $\theta(m)$ represent insulator's thermal conductivity and thickness of wall, respectively.

It may be necessary to re-consider the heat loss for complicated applications. For example, a complex reaction involving many reagents and intermediate products, or a process with large amount of reaction solutions and thermal fluids, or an operations at relative high temperature and fast flow rate, it may require to analyze the dynamic heat fluxes from reaction solution to thermal fluid and followed to external environment. A model-based simulation and characterization is recommended to quantify the overall heat transfer coefficient.

6.8 Batch or Continuous Process

The developed methodology is applicable to chemical and pharmaceutical processes, regardless of batch process, continuous process or hybrid processes that mix the batch and continuous processes. In a continuous process, the reactions may be isolated by

equipment and occurs simultaneously. In another hybrid setup of 4-DEL case study, the salt formation reaction occurred in a static mixer continuously, while the oxidation reaction occurred in another continuous stirred-tank reactor (CSTR), where the effluent of $C_6H_7NaO_6$ from the static mixer reacted with the solution of H_2O_2 that was continuously fed into the CSTR.³³ When desired amount of oxidation output, $C_4H_7NaO_5$, was obtained, HCl was fed into the CSTR and the cyclization reaction occurred batch-wise. From the process aspect, the salt formation reaction and the oxidation reaction occurred simultaneously, thus there is no operation sequence. However, from LCI consideration, salt formation reaction is necessary for the oxidation reaction, so the unit process of salt formation should be positioned before the unit process of oxidation. Furthermore, when the functional unit is generally defined as the amount of final product, LCI is mainly concerned with the overall input materials, energy consumption, output materials, emissions and wastes. The process details about the types of equipment, the technology of production and the time duration of operation, etc. are used for the purpose to generate the LCI data and conduct LCA assessments.

The startup processes are necessary for continuous operation, and they should be included in LCI. We consider the startup processes in two situations:

- i. In the first situation, startup procedure adjusts the flowrates of input and output materials to a steady state. In the above hybrid setup of 4-DEL case study, the startup of salt formation reaction in the static mixer adjusted the flow rates of inlet $C_6H_8O_6$ and Na_2CO_3 solutions until a constant flowrate of output $C_6H_7NaO_6$ reached. Since all the input and output materials in the startup of salt formation are discarded, they should be included in the wastes of LCI, and the energy consumption for the startup should be included in LCI.
- ii. In the second situation, startup procedure accumulates the initial amount of reaction solutions in CSTR before the outlets are switched on to discharge outputs. This is because of the structure of CSTR, where outlets are able to discharge output materials only when the solutions in reactor reach required level. The accumulated solutions can be included in the input and output materials if they are finally discharged to participate in the following reactions and become part of the product; otherwise, they should be considered as wastes, as stated in the first situation.

6.9 Transportation Data

Transportation of materials is not considered in this methodology due to a few of reasons:

- i. Most of the pilot plant operations are performed within limited space of lab, and they involve very little transportation of intermediate materials;
- ii. In a cradle-to-gate boundary, resource consumption and emission from energy production contributed the most to the environmental impacts;³⁶
- iii. We assume different reaction routes apply the similar amount of transportation of raw materials;
- iv. When the pilot plant process is up-scaled to full manufacturing plants, there will be transportation of intermediate materials from unit process to unit process, which may be in different geographical areas.

6.10 Industrial-scale LCI

Reliable industrial-scale LCI data are the essential to generate solid LCA results for manufacturing plants. LCA results for large-scale commercial operation plants are the main interests of companies. However, chemical and pharmaceutical reactions are scale-dependent; the LCI data generated from a small-scale pilot plant are different to the LCI generated from a large-scale manufacturing plant. Conducting LCA at pilot-scale can generate environmental load data and help to analysis hot spots, but direct scaling up of LCA results from pilot-scale to industrial-scale may cause obvious disparity. We recommend to calculating the ranges of industrial-scale LCI data by the developed methodology, thereafter conduct industrial-scale LCA results. This is expected to provide more reliable LCA results than directly scaling up pilot-scale LCA results.

6.11 Assumptions and Limitations

- i. The methodology counts the water produced by reactions as process water, in consideration that it is impossible to separate the water produced by reactions from the water for process service. In the 4-DEL case study, water is a by-product in the oxidation and cyclization reactions, and was counted into the service material in the LCI data.

- ii. Only electrical energy is considered in this methodology. Electricity is the most common energy source in the pilot plant operations, but other types of energy, such as thermal energy from steam or water, may be involved in different experimental setups.
- iii. In both the methodology development and case study, allocation and normalization of unit processes are based on the mass-ratio of the outputs. However, they can be expanded to other types of allocations, an example being their process time.
- iv. The samplings for process tests are not considered in this methodology. Should the numbers of sampling and the amount of each sampling be available, it would be recommended to include the sampling materials into the material flows.
- v. The calculations of material flows are based on ideal situations of irreversible reactions. The calculations of energy consumptions are in accordance to chemical engineering and empirical equations for specific equipment under certain applicable conditions. Despite the limitations, the accuracies of the translated LCI data are reasonable and acceptable.
- vi. The developed methodology excludes recovery/recycle of materials/solvents, also excludes energy which is generated in one operation and used in other operations. They are recommended to be included in the industrial-scale LCI once the detailed data are available.

7 Conclusions

We have presented a systematic methodology to bridge the gaps between pilot plant operation and LCI, thereafter scale-up it to industrial-scale LCI data. Following the requirements of LCA in the ISO 14040 series of standards, and embedding the principles of chemical engineering and the empirical equations of process equipment, we translated each piece of pilot plant experimental records into input materials, output materials, service materials, energy consumptions, emissions and wastes. We demonstrated a step by step procedure to conduct LCI on a case study of multi-kilogram synthesis of 4-D-Erythrionolactone (4-DEL) that was conducted in our pilot plant. The developed methodology provides a reliable, convenient and easily following basis to perform LCA studies during process development. It enables researchers and engineers to perform LCA studies based on pilot plant operations, and predict the industrial-scale LCI data. It

enables industrial process developers to gain a much clearer view of the environmental footprint much earlier in design, thereby enabling earlier design changes to reduce impacts.

Supporting Information

Demonstrations of data translation for unit processes of salt formation, oxidation and cyclization; experimental datasets for unit process of salt formation, oxidation and cyclization; demonstration of translation procedures for salt formation process; reaction scheme of synthesis of 4-DEL; process diagram of pilot plant batch synthesis of 4-DEL. This information is available free of charge via the Internet at <http://pubs.acs.org/>.

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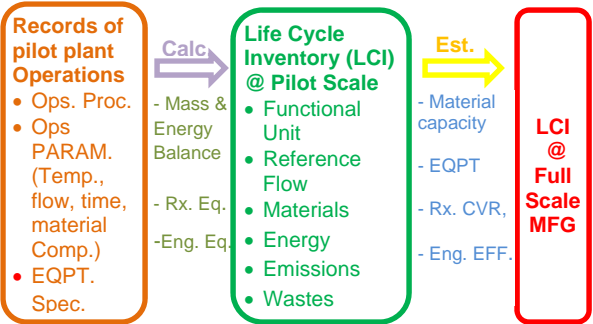
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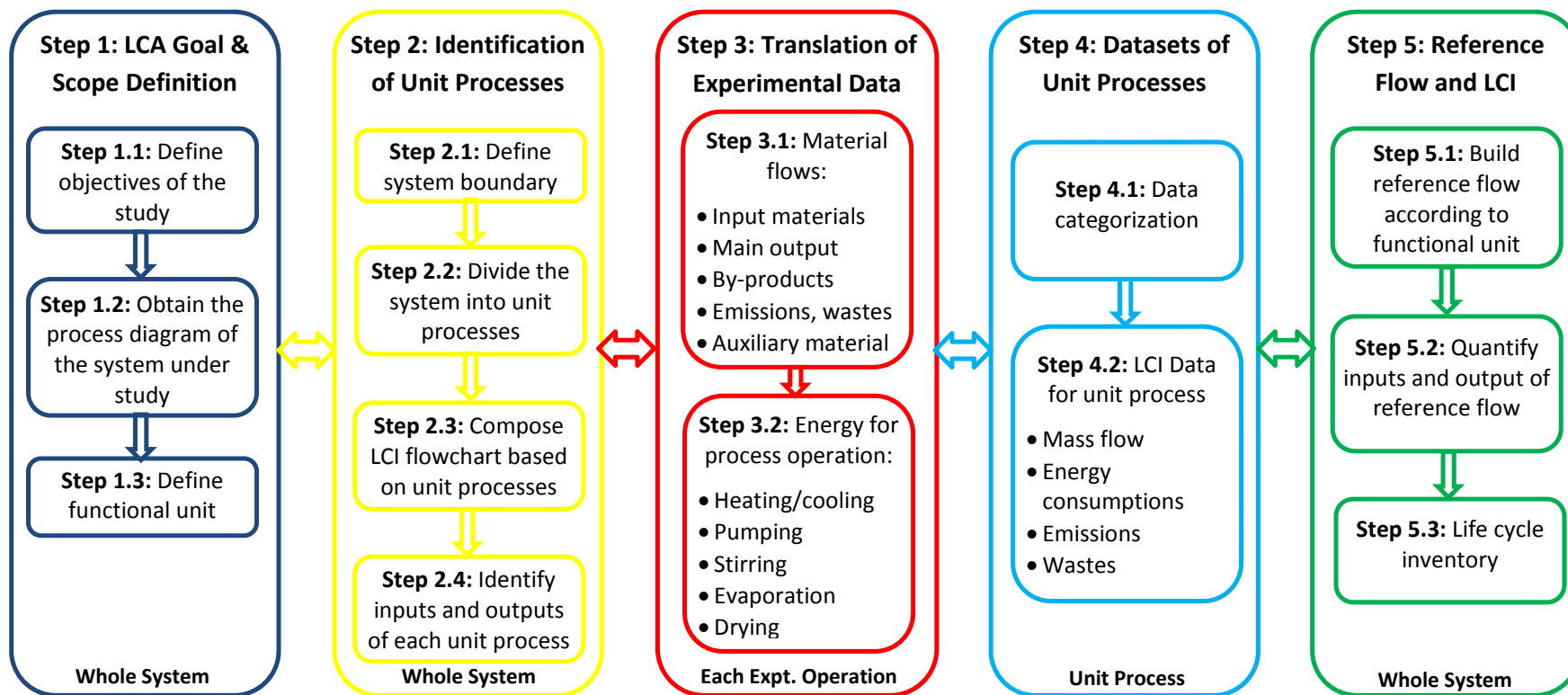
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* Sampling and testing are not considered in this methodology

** The preparation for the reaction, such as flushing or purging the reactors, are considered separately and not included in any unit process.

FIGURE 1. General methodology of converting pilot plant experimental records to life cycle inventory.

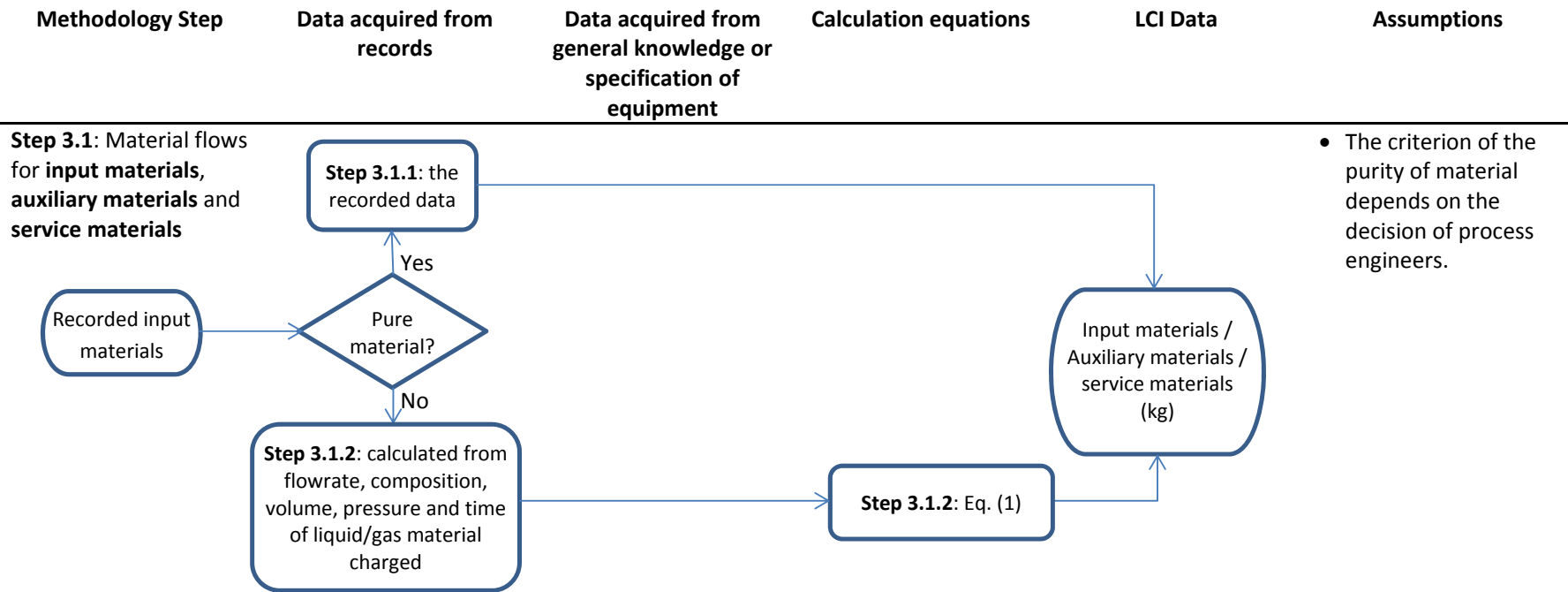


FIGURE 2. Translation from pilot plant experimental records to LCI input materials.

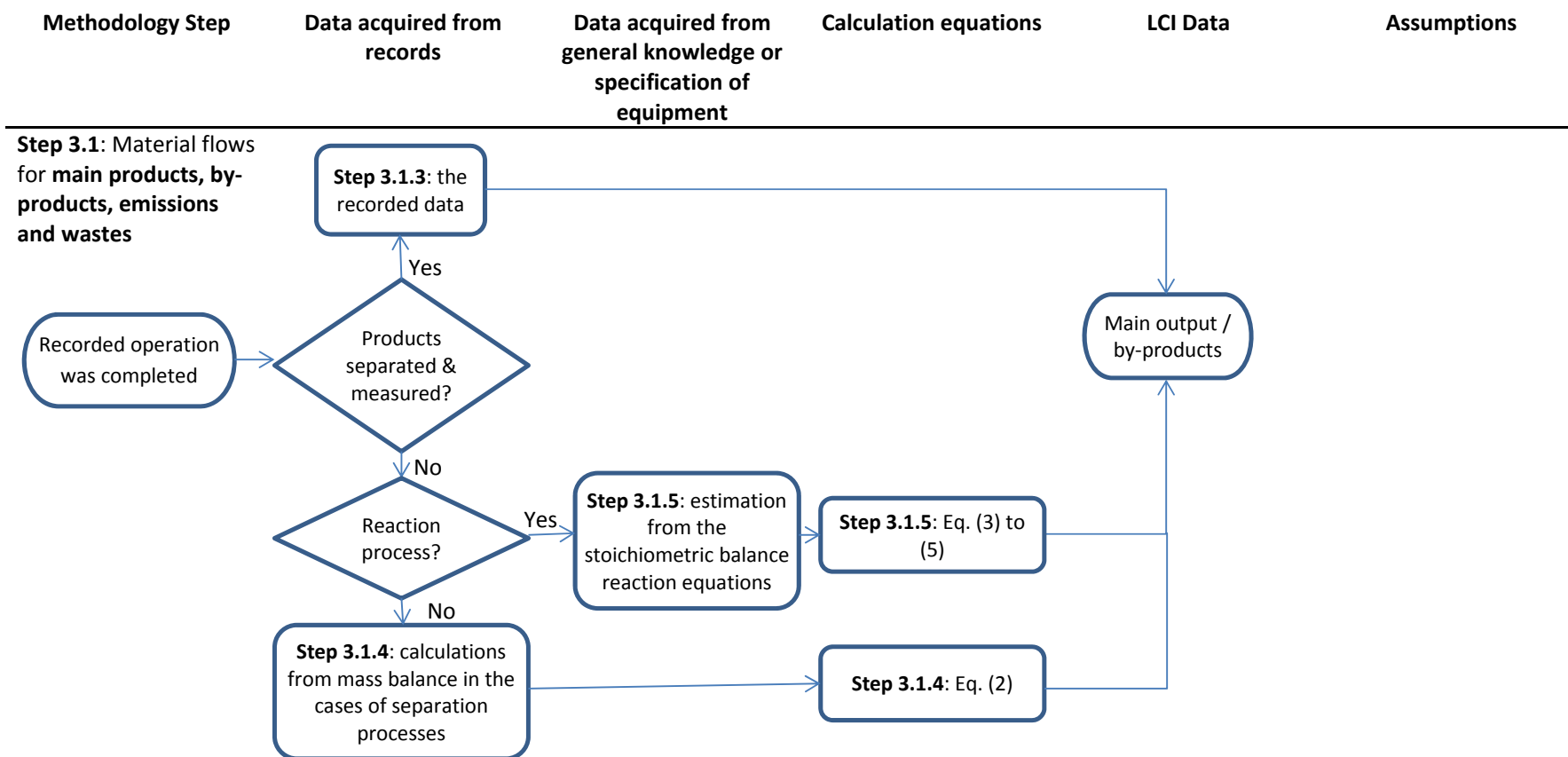


FIGURE 3. Translation from pilot plant experimental records to LCI output materials, emissions and wastes.

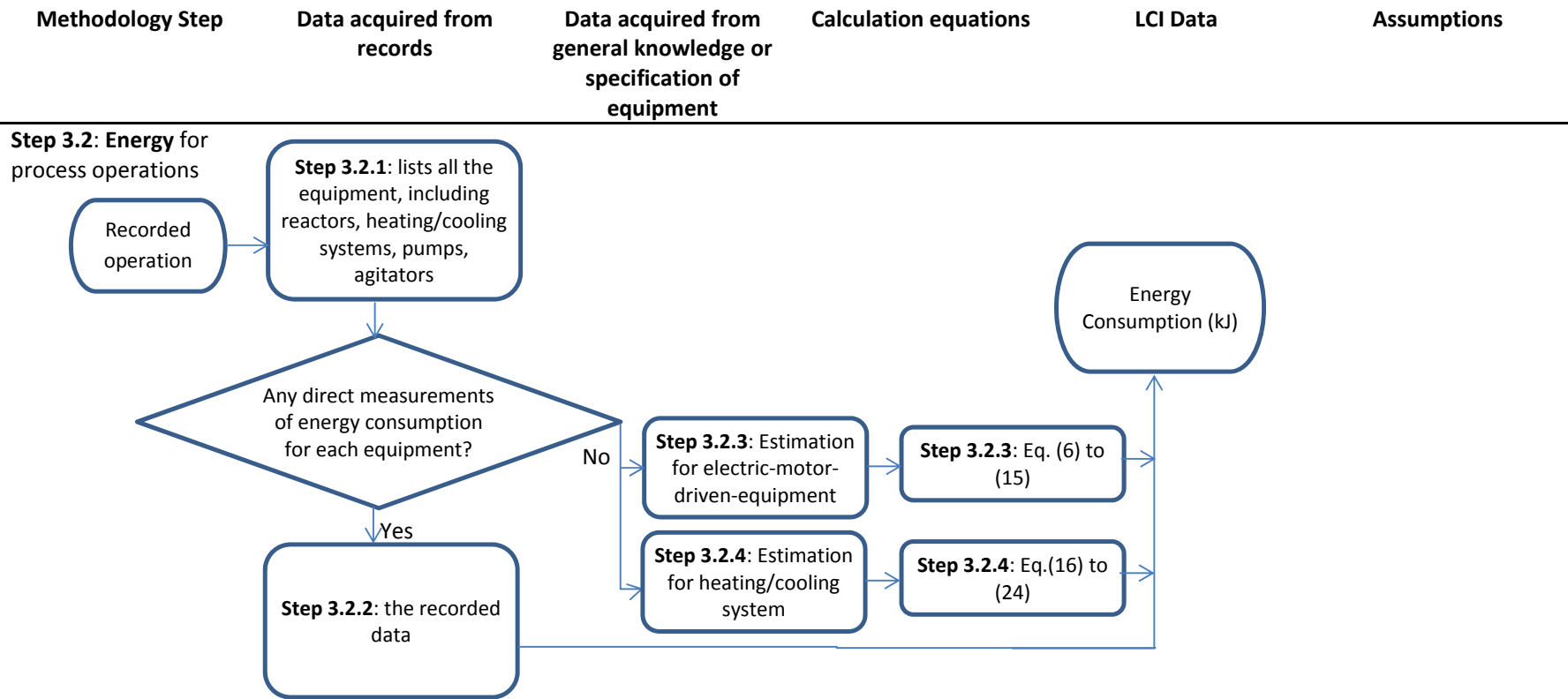


FIGURE 4. Translation from pilot plant experimental records to energy consumptions.

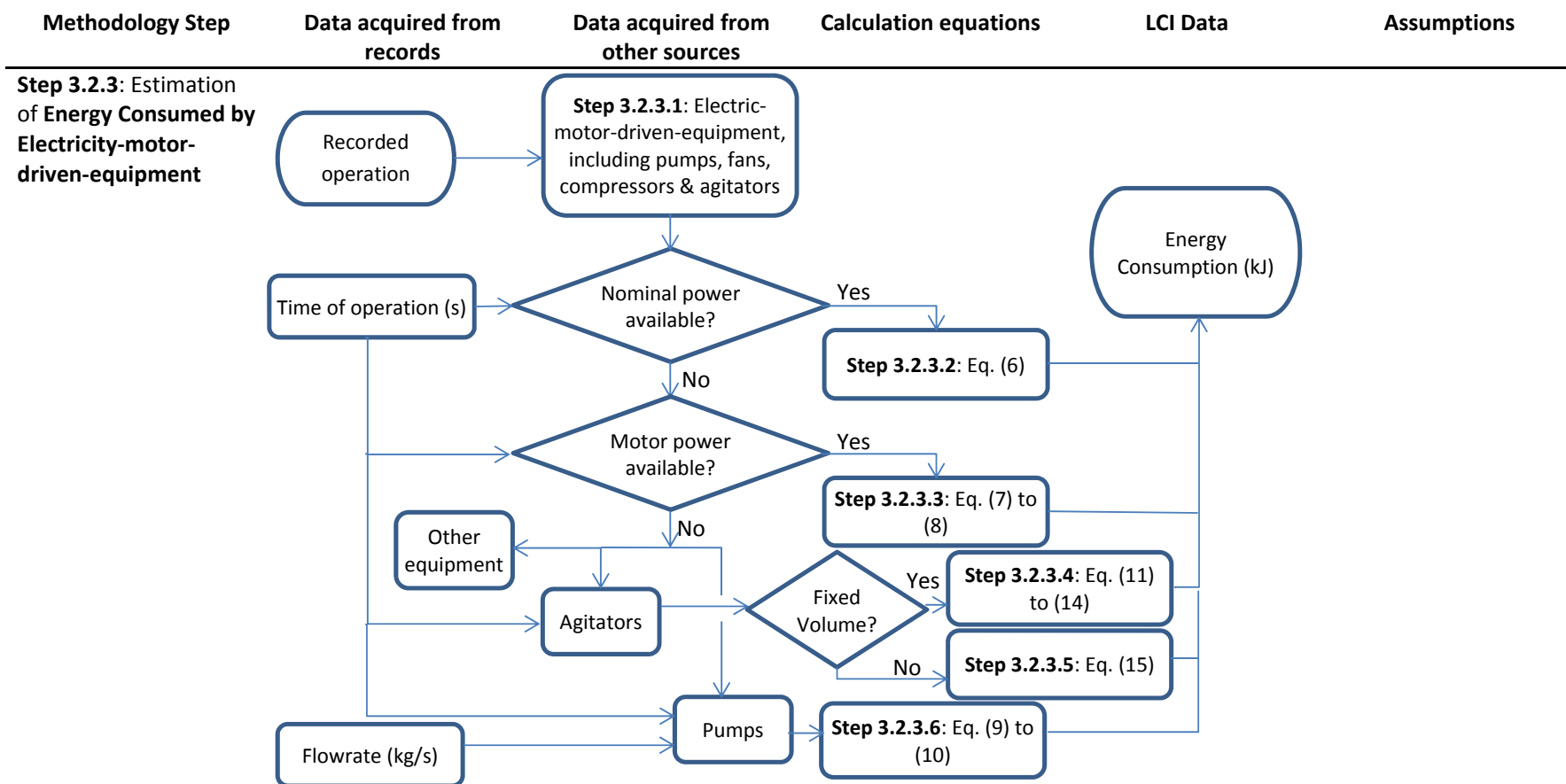


FIGURE 5. Estimation of Energy Consumed by Electricity-motor-driven-equipment.

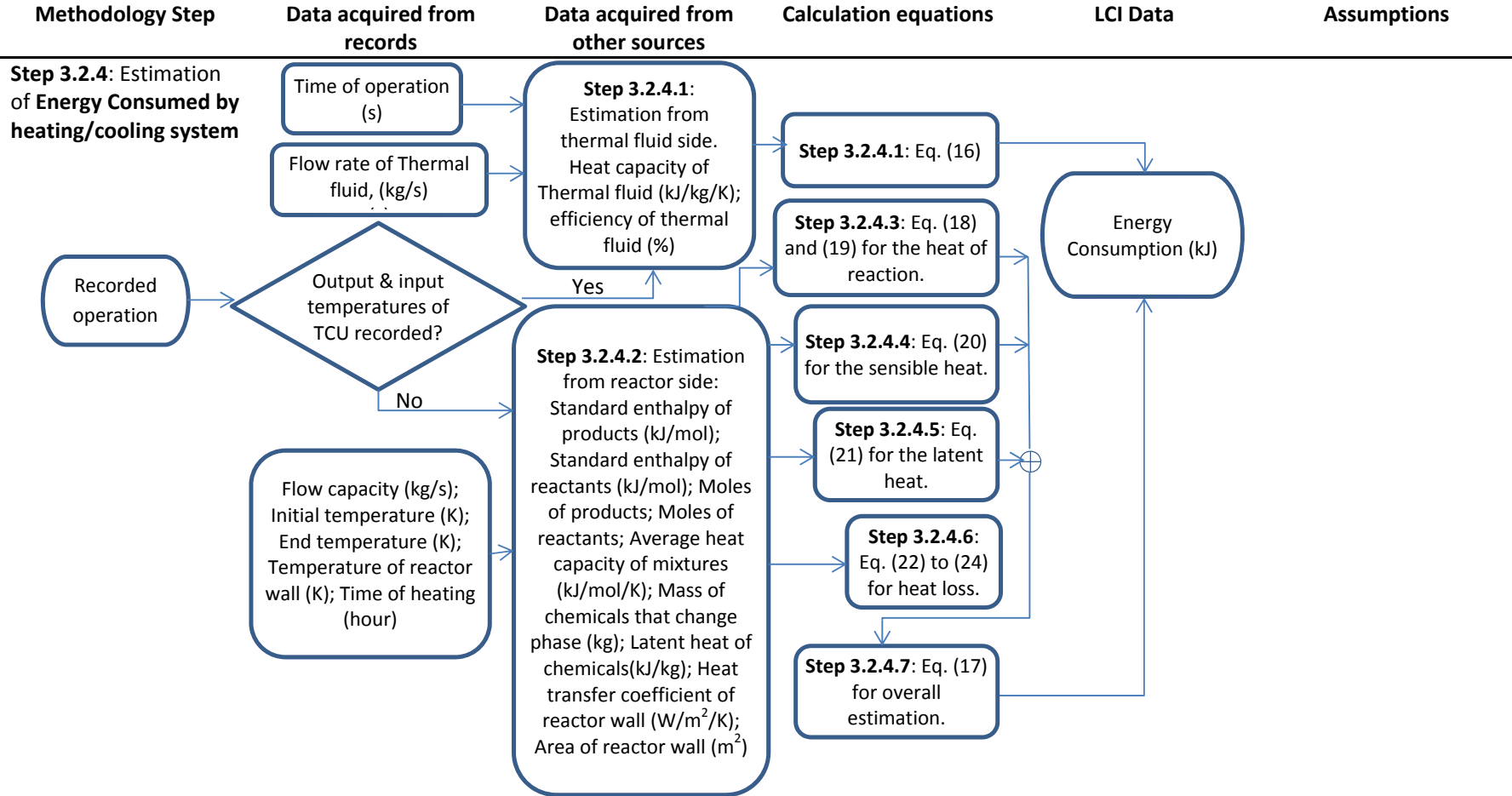


FIGURE 6. Estimation of Energy Consumed by heating/cooling system.

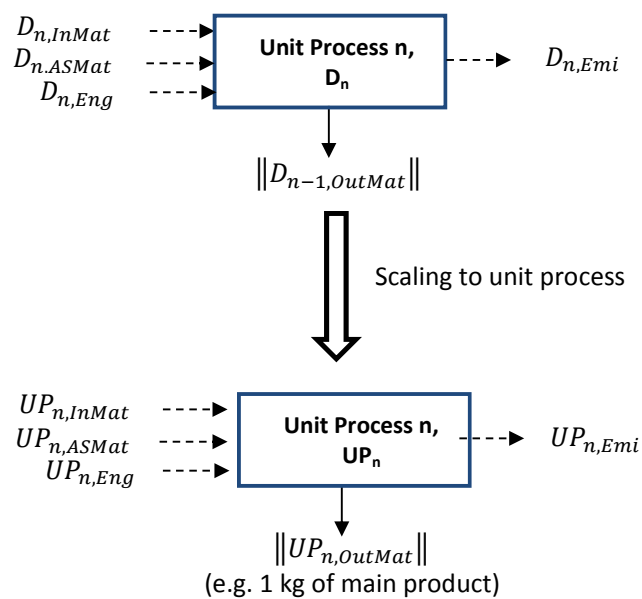


FIGURE 7. Conversion of dataset based on experimental records to dataset of unit process.

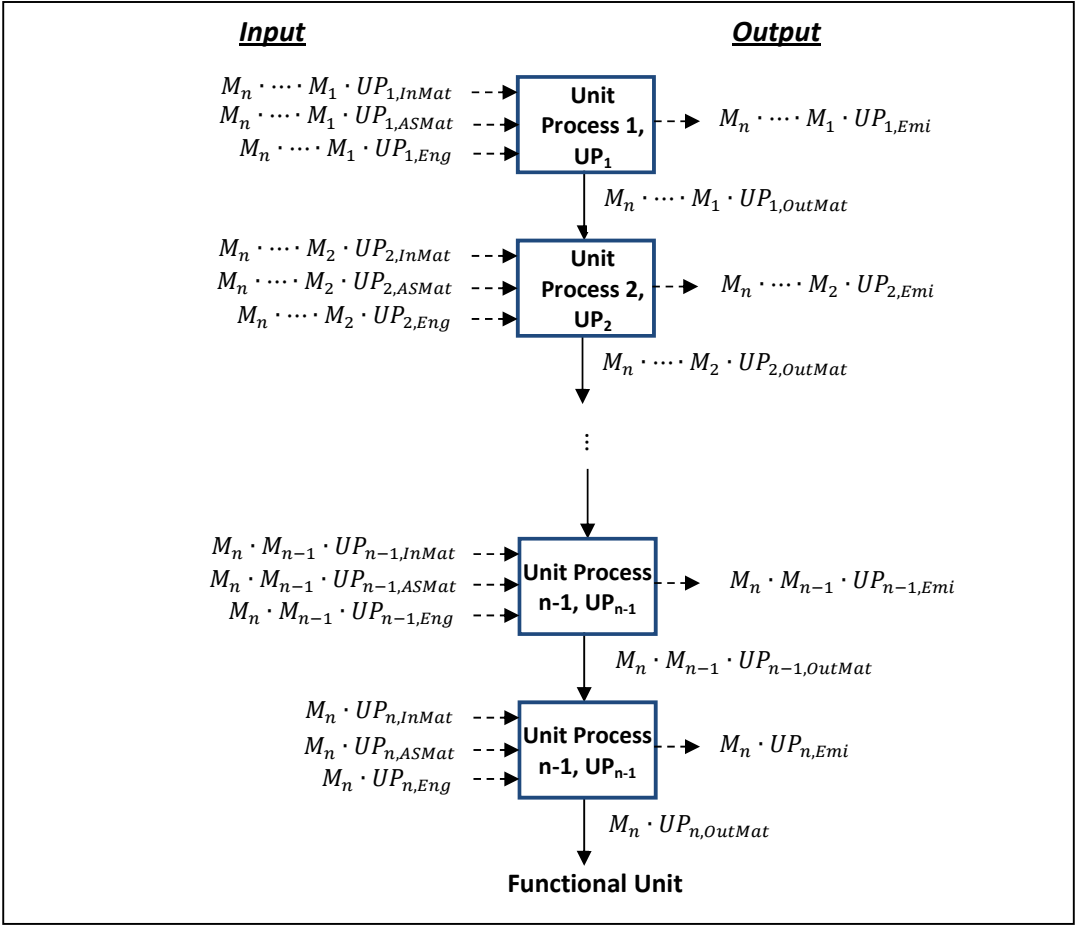


FIGURE 8. LCI data sets based on functional unit.

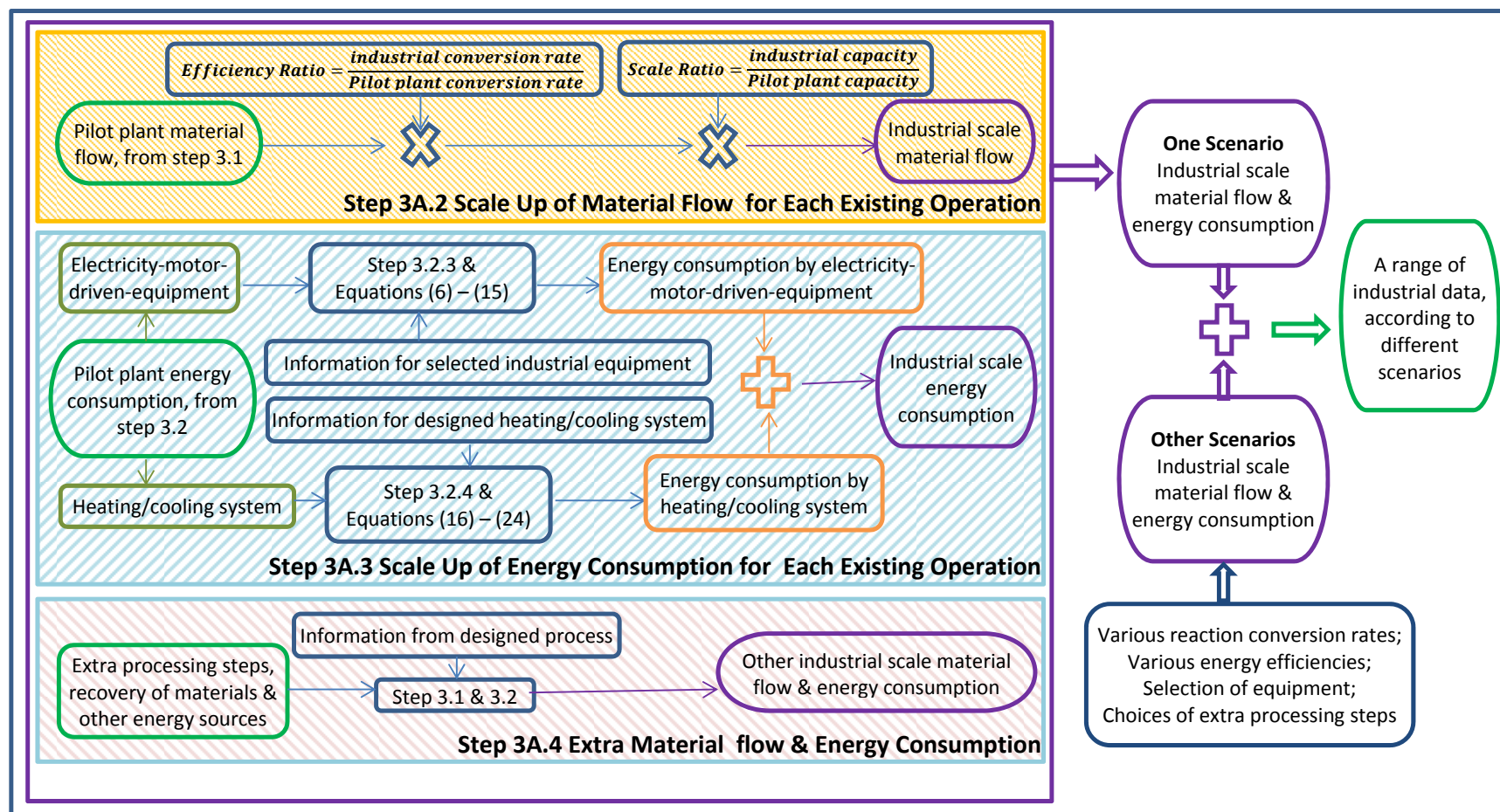


FIGURE 9. Scale-up LCI from pilot plant scale to industrial scale.

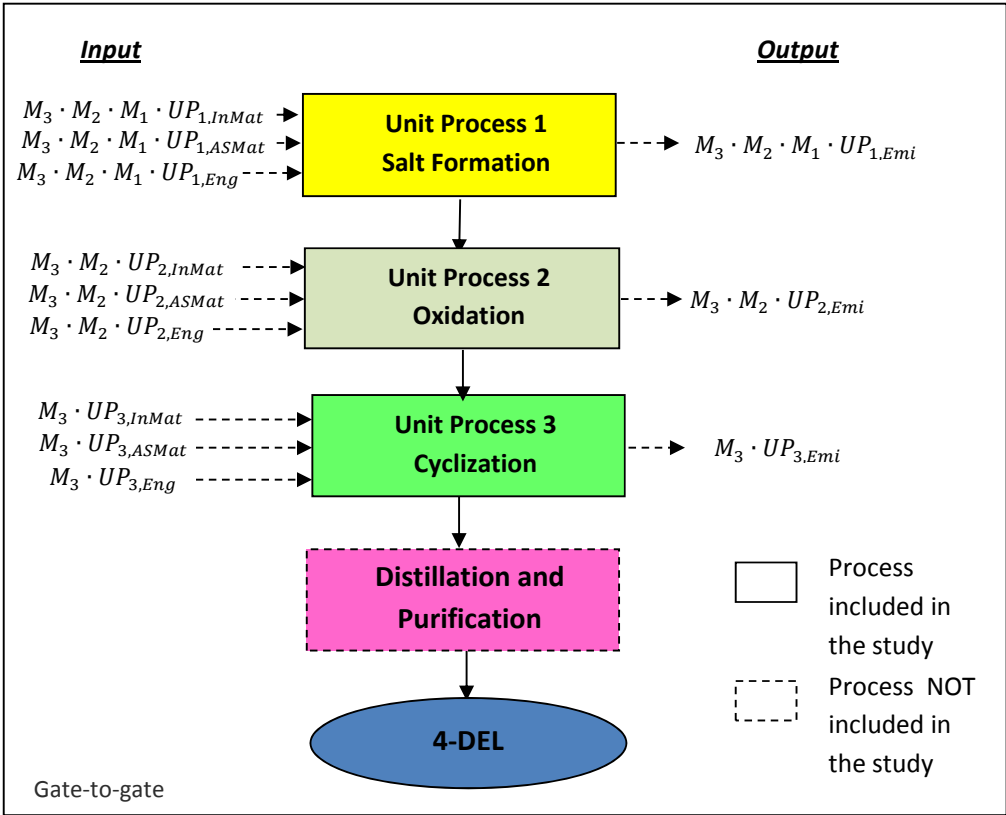


FIGURE 10. LCA flowchart of synthesis 4-DEL in pilot plant batch reactor.

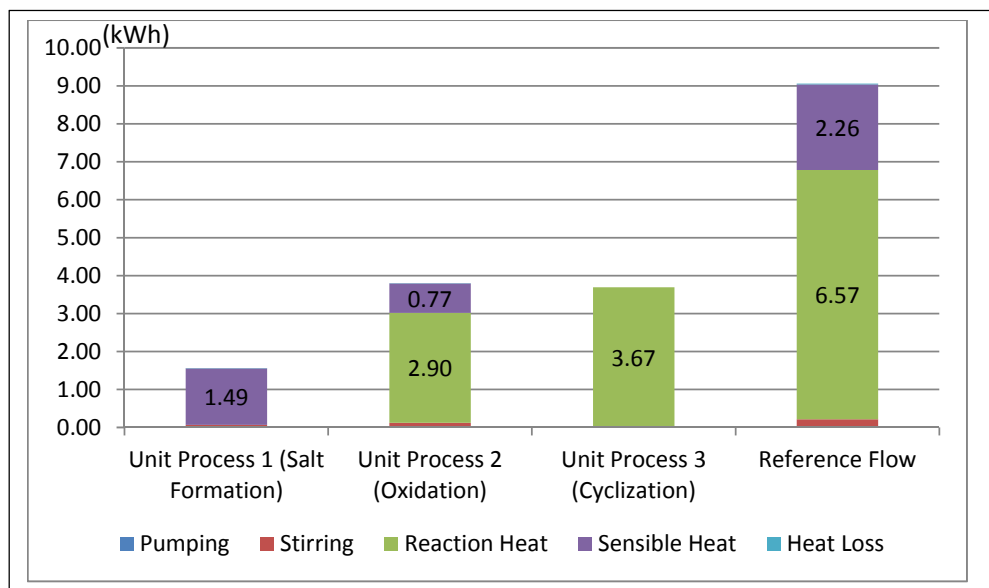


FIGURE 11. Contribution analysis to energy consumption in the reference flow of 4-DEL case study.

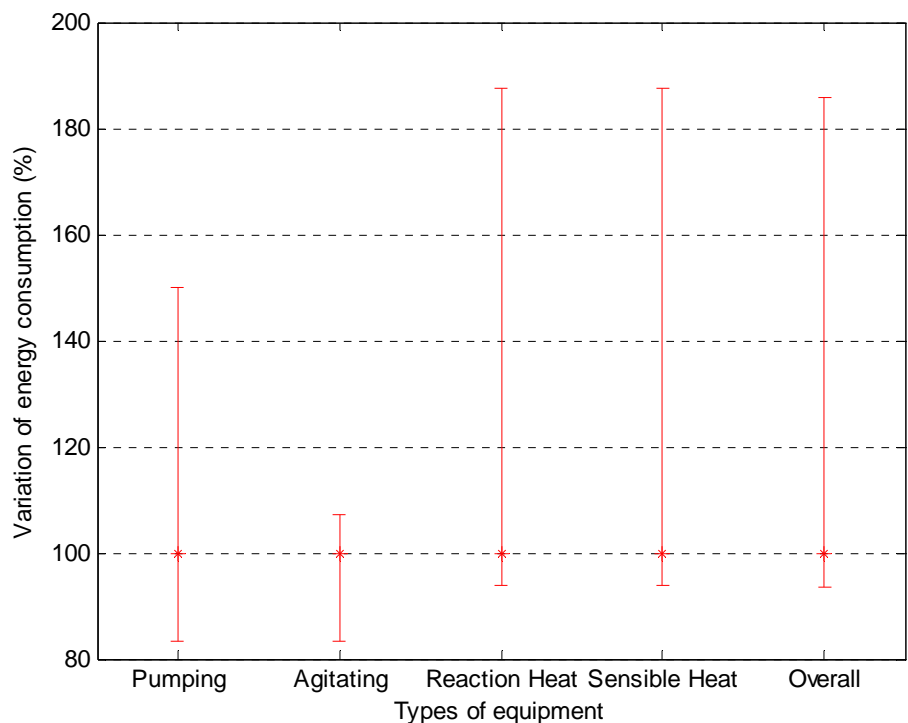


FIGURE 12. Energy consumption varies with efficiency of instruments in the reference flow of 4-DEL case study.

In the reference flow of 4-DEL case study, energy consumption is scaled to 100% when the efficiencies of all instruments are 75%. The overall energy consumption varies from 93.5% to 185.7% by varying the efficiency of pump from 50% to 90%, the efficiency of agitator from 70% to 90%, and the efficiency of heating/cooling system from 40% to 80%.

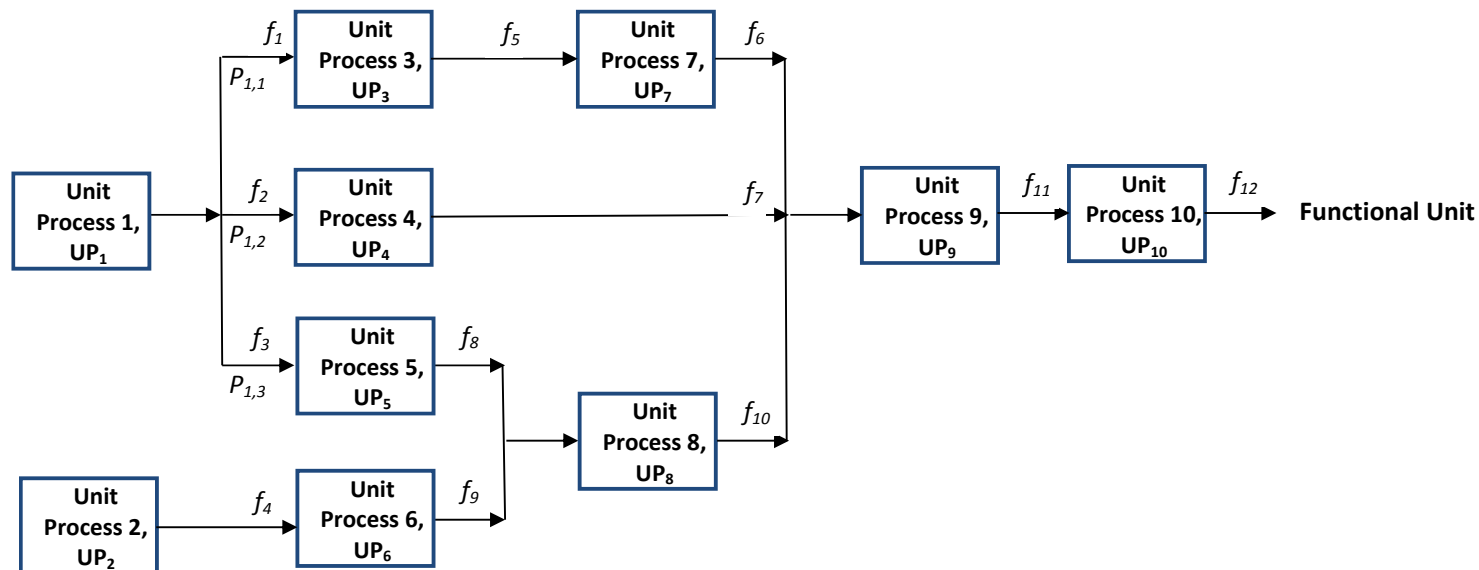


FIGURE 13. Flowchart with complicated connection of unit processes.

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TABLE 1. The main gaps between experimental records and LCI data.

| | Experimental Records | Life Cycle Inventory |
|---------------------------|--|---|
| Objective | <ul style="list-style-type: none"> • Production and manufacturing | <ul style="list-style-type: none"> • Environmental impacts |
| Scope Definition | <ul style="list-style-type: none"> • Gate-to-gate | <ul style="list-style-type: none"> • Cradle-to-gate |
| System Description | <ul style="list-style-type: none"> • Process diagram, • Lists of equipment and instruments | <ul style="list-style-type: none"> • Flowchart, • Highlights the inputs and outputs of each unit process |
| Focus | <ul style="list-style-type: none"> • Product quality • Yield and efficiency of the process <ul style="list-style-type: none"> ✓ Material flow and operations, ✓ Time sequenced step by step operations, ✓ Production conditions | <ul style="list-style-type: none"> • Data of functional unit, • Reference flow per functional unit, lists of <ul style="list-style-type: none"> ✓ input materials, ✓ energy consumption, ✓ air emission, ✓ water emission ✓ wastes |
| Types of Data | <ul style="list-style-type: none"> • Mass and composition of input materials at different process stages • Mass and composition of intermediate products and final output product • Operating parameters, such as <ul style="list-style-type: none"> ✓ temperature, ✓ pressure ✓ pH ✓ flow rate to charge/discharge fluids ✓ stirring speed and time • Equipment specification | <ul style="list-style-type: none"> • Mass of input materials for each unit process • Mass of output materials for each unit process • Energy consumption for operation, such as <ul style="list-style-type: none"> ✓ heat exchange ✓ separation ✓ fluids charge/discharge ✓ agitation |
| Data sources | <ul style="list-style-type: none"> • Measured • Controlled | <ul style="list-style-type: none"> • Measured, • Calculated • Estimated |

TABLE 2. The main mathematic equations used for translating material flows.

| Equation No. | Mathematic Equation | Step | Situations for Applications | Parameters |
|--------------|---|-------|--|---|
| (1) | $M = Q \cdot \Delta t \cdot x$ | 3.1.2 | Liquid or gas materials by charging | M : mass of material, (kg) Q : flowrate of charging, (kg/s) Δt : time of charging, (s) x : composition of material, (%) |
| (2) | $\sum M_{InMat} = \sum M_{OutMat}$ | 3.1.4 | For separation processes, such as, distillation, crystallization, filtration, evaporation, extraction and absorption processes | M_{InMat} : mass of input material, (kg) M_{OutMat} : mass of output material, (kg) |
| (3) | $\begin{cases} m_{Limit} = m_{React,A} \\ C_{Conv,Limit} = C_{Conv,A} \end{cases} \text{ if } m_{Reag,A} \cdot C_{Conv,A} < a/b \cdot m_{Reag,B} \cdot C_{Conv,B}$ $\begin{cases} m_{Limit} = m_{React,B} \\ C_{Conv,Limit} = C_{Conv,B} \end{cases} \text{ if } m_{Reag,B} \cdot C_{Conv,B} < b/a \cdot m_{Reag,A} \cdot C_{Conv,A}$ | 3.1.5 | For output materials from reactions, e.g., for reaction: $aA + bB \rightarrow cC + dD$ | m_{Limit} : moles of limiting reagent m_{Reag} : moles of reagent m_{Prod} : moles of product C_{Conv} : Conversion rate of reagent, (%) $C_{Conv,B}$: Conversion rate of reagent B f_{Stoi} : stoichiometric coefficient of reaction |
| (4) | $f_{Stoi,c} = \begin{cases} c/a & \text{if } m_{Limit} = m_{Reag,A} \text{ and Output C is calculated} \\ c/b & \text{if } m_{Limit} = m_{Reag,B} \text{ and Output C is calculated} \end{cases}$ $f_{Stoi,d} = \begin{cases} d/a & \text{if } m_{Limit} = m_{Reag,A} \text{ and Output D is calculated} \\ d/b & \text{if } m_{Limit} = m_{Reag,B} \text{ and Output D is calculated} \end{cases}$ | | | |
| (5) | $m_{Prod,i} = f_{Stoi,i} \cdot m_{Limit} \cdot C_{Conv,Limit}$ | | | |

TABLE 3. The main mathematic equations used for translating energy consumed by electricity-motor-driven-equipment.

| Equation No. | Mathematic Equation | Step | Situations for Applications | Parameters |
|--------------|---|---------|---|--|
| (6) | $E_{Equip} = P_{Equip} \cdot \Delta t / 3600 / \gamma_{Equip}$ | 3.2.3.2 | Electric-motor-driven equipment, such as pumps, fans, compressors and stirrers. ^{21,22} | E_{Equip} : Energy consumed by equipment, (kWh) P_{Equip} : Nominal power of equipment, (kW) Δt : Operation time of equipment, (s) γ_{Equip} : Fraction of equipment nominal power consumed, (%). Empirical values are 28% for agitators; 52% for vacuum pumps. |
| (7) | $E_{Equip} = P_{Motor} \cdot f_{Load} \cdot 0.746 \cdot \Delta t / \eta_{Motor} / \eta_{Equip}$ | 3.2.3.3 | Assume the motor works under the same conditions during all the operation time, such as with the same mass flow, rotation speed and pressure. ^{23,24} | E_{Equip} : Energy consumed by equipment, (kWh) P_{Motor} : Motor power of equipment, (kW) f_{Load} : Load factor η_{Motor} : Efficiency factor of motor, (%). Normally appeared as NEMA Nominal efficiency. η_{Equip} : Efficiency factor of equipment, (%) Normally appeared as Drive efficiency in product catalog. |
| (8) | $f_{Load} = \frac{\text{average motor load}}{\text{rated motor load}}$ | | | |
| (9) | $E_{Pump} = Q \cdot \Delta P / \rho / \eta_{Shaft} / \eta_{Motor} \cdot \Delta t / 1000 / 3600$ | 3.2.3.6 | For the situation that both nominal power and motor power are not available, the energy consumption by pumps can be calculated with engineering and empirical formulas. ²⁵ | E_{Pump} : Energy consumed by pumps, (kWh) Q : Mass flowrate, (kg/s) ΔP : Pressure difference between the suction pressure (P_{Suct} , Pa) and the discharge pressure ($P_{Dischar}$, Pa). η_{Shaft} : Shaft efficiency, (%). η_{Motor} : Motor Efficiency, (%). |
| (10) | $\Delta P = P_{Suct} - P_{Dischar}$ | | | |

TABLE 3. The main mathematic equations used for translating energy consumed by electricity-motor-driven-equipment (continued).

| Equation No. | Mathematic Equation | Step | Situations for Applications | Parameters |
|--------------|---|---------|---|--|
| (11) | $E_{Stir} = N_p \cdot D_a^5 \cdot n^3 \cdot \rho \cdot \Delta t / \eta_{Stir} / 1000 / 3600$ | 3.2.3.4 | For agitators working at a fixed volume of solution. ²⁶ For various types of impeller, the empirical flow numbers of N_Q are listed in Table 6. | E_{Stir} : Energy consumed by agitators, (kWh) D_a : Diameter of agitator's impeller, (m) n : Rotational speed, (rps) ρ : Density of solution, (kg/m ³) Δt : Operation time of agitator, (s) η_{Equip} : Efficiency factor of agitator, (%) N_p : Agitator's power number N_Q : Agitator's flow number q : volumetric flow rate, (m ³ /s) |
| (12) | $N_p = \frac{\alpha^2 \pi^2}{2} N_Q$ | | | |
| (13) | $\alpha = \frac{\text{radical component of velocity}}{\text{velocity of impeller blade tip}}$ | | | |
| (14) | $N_Q = \text{flow number} = \frac{q}{n D_a^3}$ | | | |
| (15) | $E_{Stir} = \int_0^{\Delta t} N_p \cdot d_a^5 \cdot n^3 / \eta_{Stir} / 1000 / 3600 \cdot \rho(t) \cdot dt$ $= N_p \cdot d_a^5 \cdot n^3 / \eta_{Stir} / 1000 / 3600 \cdot \rho_{Charg} \cdot \left[\left(\frac{M_{Orig}}{Q_{Charg}} - V_{Orig} \cdot \frac{\rho_{Charg}}{Q_{Charg}} \right) \cdot \ln \frac{\left V_{Orig} + \frac{Q_{Charg} \cdot \Delta t}{\rho_{Charg}} \right }{ V_{Orig} } + \Delta t \right]$ | 3.2.3.5 | For agitators working at a variable volume of solution, such as the materials are kept charging in at a fixed flowrate. | M_{Orig} : Original mass in reactor before charging, (kg) V_{Orig} : Original volume in reactor before charging, (m ³) Q_{Charg} : Flowrate of charging solution, (kg/s) ρ_{Charg} : Density of charging solution, (kg/m ³) |

TABLE 4. The main mathematic equations used for translating energy consumed by heating/cooling system.

| Equation No. | Mathematic Equation | Step | Situations for Applications | Parameters |
|--------------|---|---------|---|---|
| (16) | $E_{Heat} = \int_0^{\Delta t} q_{Therm} \cdot \rho_{Therm} \cdot C_{P,Therm} \cdot (T_{Input} - T_{Output}) / \eta_{Therm} / 3600 \cdot dt$ | 3.2.4.1 | Estimation of energy consumption with the real-time measurements of the circulated thermal fluids inside the temperature control unit. | E_{Heat} : Energy consumed by heating /cooling system, (kWh) q_{Therm} : volumetric flow rate of circulated thermal fluid, (m ³ /s) ρ_{Therm} : Density of thermal fluid, (kg/m ³) $C_{P,Therm}$: Heat capacity of thermal fluid, (kJ/kg/K) T_{Input} : Input temperature of circulated thermal fluids inside temperature control unit, (K) T_{Output} : Output temperature of circulated thermal fluids inside temperature control unit, (K) η_{Therm} : Thermal efficiency of temperature control unit, (%) |
| (17) | $E_{Heat} = (E_{Rxn} + E_{Sensi} + E_{Latent} + E_{Loss}) / \eta_{Heat}$ | 3.2.4.7 | Estimation of energy demanded by heating/cooling system from the reactor side. | E_{Rxn} : Heat of reaction, (kWh) E_{Sensi} : Sensible heat of solution in reactor, (kWh) E_{Latent} : Latent heat of solution in reactor, (kWh) E_{Loss} : Heat loss through reactor, (kWh) η_{Heat} : Efficiency of heating/cooling system, (%) |
| (18) | $E_{Rxn} = \left(\sum_i m_i \cdot H^o_{Prod,i} - \sum_j m_j \cdot H^o_{Reag,j} \right) / 3600$ | 3.2.4.3 | Estimation of heat of reaction from enthalpies of formation, with Hess's law. ²⁷ Assumes that the reaction occurs at a constant volume and constant pressure. | m_i : Moles of product i, (mol) $H^o_{Prod,i}$: Standard enthalpy of product i, (kJ/mol) m_j : Moles of reactant j, (mol) $H^o_{Reag,j}$: Standard enthalpy of reactant j, (kJ/mol) |

TABLE 4. The main mathematic equations used for translating energy consumed by heating/cooling system (continued).

| Equation No. | Mathematic Equation | Step | Situations for Applications | Parameters |
|--------------|--|---------|--|---|
| (19) | $E_{Rxn} = \left(\sum_i m_i \cdot BE_{Reag,i} - \sum_j m_j \cdot BE_{Prod,j} + \sum_k m_k \cdot \Delta H_{Vap,k} - \sum_l m_l \cdot \Delta H_{Cond,l} \right) / 3600$ | 3.2.4.3 | Estimation of heat of reaction from bond energies. ²⁸ It is based on the gas state of all materials, including the reactants and output materials. For materials not in gas state, extra vaporization and condensation energy should be considered. | $BE_{Reag,i}$: Bond energy of reactant i in gas state, (kJ/mol) Reactants break bonds, absorbs energy, endothermic, represented with "+". $BE_{Prod,j}$: Bond energy of product j in gas state, (kJ/mol) Products form bonds, release energy, exothermic, represented with "-". $\Delta H_{Vap,k}$: Vaporization energy required to convert material k from liquid to gas state, (kJ/mol), endothermic, represented with "+". ΔH_{Vap} : Condensation energy required to convert material l from gas to liquid state, (kJ/mol) exothermic, represented with "-". m : Moles of material, (mole) |
| (20) | $E_{Sensi} = \left(\sum_i M_i \cdot \bar{C}_{p,i} \cdot (T_{End} - T_{Orig}) \right) / 3600$ | 3.2.4.4 | The heat causes the temperature change of reactor and all the materials inside. ²⁹ | M_i : Mass of material i, (kg) $\bar{C}_{p,i}$: Heat capacity of material i, (kJ/kg /K) T_{End} : Temperature at the end of operation, (K) T_{Orig} : Initial temperature, (K) |
| (21) | $E_{Latent} = \left(\sum_i M_i \cdot L_i \right) / 3600$ | 3.2.4.5 | The heat causes the objects' change in state, but without change of temperature, e.g. from liquid to gas state. ³⁰ | M_i : Mass of material i, (kg) L_i : Standard latent heat of material i, (kJ/kg) |

TABLE 4. The main mathematic equations used for translating energy consumed by heating/cooling system (continued).

| Equation No. | Mathematic Equation | Step | Situations for Applications | Parameters |
|--------------|--|---------|---|--|
| (22) | $E_{Loss} = \left(\sum_i U_i \cdot A_i \cdot (T_i - T_{\infty}) \cdot \Delta t_i \right) / 3600/1000$ | 3.2.4.6 | Heat loss through the vessels of reactors, pipes, condensers at fixed stable temperature. ³¹ | U_i : Heat transfer coefficient of vessel i, (W/m ² /K) A_i : Area of the wall of vessel i, (m ²) T_i : Temperature inside vessel i, (K) T_{∞} : Temperature outside vessel i, (K) Δt_i : The duration of operation on vessel i, (s) |
| (23) | $T_i = T_{Orig,i} + \frac{T_{End,i} - T_{Orig,i}}{t_{Span,i}} \cdot t$ | 3.2.4.6 | Heat loss through the vessels of reactors, pipes, condensers during heating/cooling operation. | T_i : Temperature of vessel i at time t, (K) $T_{Orig,i}$: Initial temperature of vessel i, (K) $T_{End,i}$: Final temperature of vessel i, (K) $t_{Span,i}$: The total duration of operation on vessel i, (s) t : The current duration of operation on vessel i, (s) |
| (24) | $E_{Loss} = \left[\sum_i U_i \cdot A_i \cdot \int_0^{t_{Span,i}} \left(T_{Orig,i} + \frac{T_{End,i} - T_{Orig,i}}{t_{Span,i}} \cdot t - T_{\infty} \right) dt \right] / 3600/1000$ $= \left[\sum_i U_i \cdot A_i \cdot \left((T_{Orig,i} - T_{\infty}) \cdot t_{Span,i} + (T_{End,i} - T_{Orig,i}) \cdot \frac{1}{2} \cdot t_{Span,i} \right) \right] / 3600/1000$ | | | |

TABLE 5. Intermediate calculations.

| Equation No. | Mathematic Equation | Purpose | Situations for Applications | Parameters |
|--------------|---|--|--|---|
| (25) | $\frac{1}{\rho_{Mix}} = \sum_i \left(\frac{x_i}{\rho_i} \right)$ | Estimation of average density of mixtures. | For pumping and stirring, usually there are at least two materials existing in the reactor or pumps. | ρ_{Mix} : Average density of mixed solution, (kg/m^3) x_i : Mass fraction of component i in the mixture, (%) ρ_i : Density of component i, (kg/m^3) |
| (26) | $C_p = \sum_i (C_{p,i} \cdot N_i) + C_{p,Misc} \cdot N_{Misc}$ | Estimation of heat capacity of compounds. | In the case that the heat capacities of some liquid and solid compounds are not available in the literature, we can estimate them by the modified Kopp's rule. ³² | C_p : Overall heat capacity of the compound, $(J/K/mol)$ $C_{p,i}$: Constant heat capacity associated with each element i in the compound, $(J/K/mol)$ N_i : Number of occurrences of element i in the Compound $C_{p,Misc}$: An associated number for the element that does not have a specific constant heat capacity, $(J/K/mol)$. Usually 26 is used for solid compound and 33 used for liquid compound. N_{Misc} : Number of occurrences of element that does not have a specific constant heat capacity. |
| (27) | $BE = \sum_i (n_i \cdot BE_{Bond,i})$ | Estimation of bound energy of compounds. | Estimating the average values of energy required to break chemical bonds at 298 K. | BE : The total bond energy of a compound, (kJ/mol) n_i : The number of bond i in the compound. $BE_{Bond,i}$: The standard bond energy of each bond i in the compound, (kJ/mol) |

TABLE 6. Empirical flow numbers for various types of impeller.

| | Impeller Type | Values of Flow Number, N_Q |
|---|---|------------------------------|
| 1 | Marine propellers (square pitch) | 0.5 |
| 2 | Four-bladed 45o turbine (W/Da)=1/6 | 0.87 |
| 3 | Disk Turbine, standard six-bladed turbine | 1.3 |
| 4 | HE-3 high-efficiency impeller | 0.47 |

TABLE 7. Summary of translating experimental data to LCI.

| Data Types | Data Sources |
|----------------------------|--|
| • Material inputs/outputs | • Recorded data (direct measurements) • Calculation from mass balance and mechanisms of reactions • Data beyond the boundary of experimental records are sourced from vendors, literature records or database |
| • Input energies/ services | • Recorded data (direct measurements) • Gas from lab data (pressure, flowrate, time) • Electricity for process equipment from engineering principles and empirical equations • Heat for circulation system: ✓ Integral of the power of the temperature control unit (TCU) ✓ Heat calculation from the thermal fluid ✓ Heat calculation from reactor? |
| • Emissions to Air | • Recorded data |
| • Emissions to water | • Calculation from mass balance or mechanisms of reactions |
| • Wastes | • By-products (if no allocation) ✓ Gaseous by-products as Emissions to Air ✓ Liquid by-products as Emissions to Water ✓ Solid by-products as Wastes • Excess reagents |
| • Storage | • Not included |
| • Transportation data | • Not included |

TABLE 8. Life cycle inventory for unit process of salt formation, oxidation and cyclization.

| | Salt Formation, UN_{Salt} | | | | Oxidation, UN_{Oxid} | | | | Cyclization, UN_{Cycli} | | | |
|------------------|---|-----------------------|------|------------|---|-----------------------|------|--------------|---|-------------------------|------|----------------|
| | List of Inputs | Amount | Unit | Comments | List of Inputs | Amount | Unit | Comments | List of Inputs | Amount | Unit | Comments |
| Input Materials | C ₆ H ₈ O ₆ | 1.064 | kg | Fresh | Na ₂ CO ₃ | 1.330 | kg | Fresh | C ₄ H ₇ NaO ₅ ** | 1.554 | kg | |
| | Na ₂ CO ₃ | 0.535 | kg | material | H ₂ O ₂ | 0.431 | kg | material | NaO ₂ CCO ₂ Na | 1.322 | kg | From |
| | | | | | C ₆ H ₇ NaO ₆ ** | 1.500 | kg | From salt | NaHCO ₃ | 1.182 | kg | oxidation or |
| | | | | | C ₆ H ₈ O ₆ | 0.261 | kg | formation | Na ₂ CO ₃ | 0.777 | kg | salt formation |
| | | | | | | | | | C ₆ H ₇ NaO ₆ | 0.835 | kg | |
| Output Material | | | | | | | | | HCl | 2.231 | kg | Fresh |
| | C ₆ H ₇ NaO ₆ ** | 1 | kg | | C ₄ H ₇ NaO ₅ ** | 1 | kg | | C ₄ H ₆ O ₄ | 1 | kg | |
| Service Material | N ₂ | 0.005 | kg | | H ₂ O | 7.104 | kg | | H ₂ O | 7.231 | kg | |
| | H ₂ O | 11.729 | kg | | | | | | | | | |
| Energy | Pumping | 1.62x10 ⁻³ | kWh | | Pumping | 1.04x10 ⁻³ | kWh | | Pumping | 1.08 · 10 ⁻³ | kWh | |
| | Stirring | 0.028 | kWh | | Stirring | 0.077 | kWh | | Stirring | 0.023 | kWh | |
| | Heating/cooling | 0.638 | kWh | | Heating/cooling | 2.484 | kWh | | Heating/cooling | 3.669 | kWh | |
| Emissions, Waste | NaHCO ₃ * | 0.426 | kg | By-product | CO ₂ | 0.277 | kg | Air Emission | CO ₂ | 0.942 | kg | Air Emission |
| | C ₆ H ₈ O ₆ * | 0.174 | kg | Excess | NaO ₂ CCO ₂ Na* | 0.851 | kg | By-product | C ₄ H ₇ NaO ₅ | 0.207 | kg | Excess |
| | | | | | Na ₂ CO ₃ * | 0.500 | kg | Excess | C ₆ H ₈ O ₆ | 0.744 | kg | By-product |
| | | | | | C ₆ H ₇ NaO ₆ * | 0.537 | kg | Excess | HO ₂ CCO ₂ H | 0.884 | kg | By-product |
| | | | | | | | | | NaCl | 3.579 | kg | By-product |

* By-products or excess materials reacted in the following unit processes.

** Connecting materials that connect the unit processes.

TABLE 9. Life cycle inventory for functional unit.

| | Salt Formation $1.554 * 1.500 * UN_{Salt}$ | | | Oxidation $1.554 * UN_{Oxid}$ | | | Cyclization $1 * UN_{Cycli}$ | | | Overall $UN_{Cycli} + 1.347 * UN_{Oxid}$ $+ 1.347 * 1.255 * UN_{Salt}$ | | |
|---------------------|---|----------------------|------|--|--|-------------------|--|--|-------------------|--|----------------------|------|
| | List of Inputs | Amount | Unit | List of Inputs | Amount | Unit | List of Inputs | Amount | Unit | List of Inputs | Amount | Unit |
| Input Materials | C ₆ H ₈ O ₆ | 2.480 | kg | Na ₂ CO ₃ H ₂ O ₂ | 2.067 0.670 | kg kg | HCl | 2.231 | kg | C ₆ H ₈ O ₆ | 2.480 | kg |
| | Na ₂ CO ₃ | 1.247 | kg | | | | | | | Na ₂ CO ₃ | 3.314 | kg |
| | | | | | | | | | | H ₂ O ₂ | 0.670 | kg |
| | | | | | | | | | | HCl | 2.231 | kg |
| Service Material | H ₂ O | 27.340 | kg | H ₂ O | 11.040 | kg | H ₂ O | 7.231 | kg | H ₂ O | 45.611 | kg |
| | N ₂ | 0.012 | kg | | | | | | | N ₂ | 0.012 | kg |
| Energy | Pumping | $3.78 \cdot 10^{-3}$ | kWh | Pumping Stirring Heating /cooling | $1.62 \cdot 10^{-3}$ 0.120 3.860 | kWh kWh kWh | Pumping Stirring Heating /cooling | $1.08 \cdot 10^{-3}$ 0.023 3.669 | kWh kWh kWh | Pumping | $6.48 \cdot 10^{-3}$ | kWh |
| | Stirring | 0.065 | kWh | | | | | | | Stirring | 0.208 | kWh |
| | Heating | 1.487 | kWh | | | | | | | Heating | 9.016 | kWh |
| | /cooling | | | | | | | | | /cooling | | |
| Emissions, Waste | | | | CO ₂ | 0.430 | kg | CO ₂ | 0.942 | kg | CO ₂ | 1.372 | kg |
| | | | | | | | C ₄ H ₇ NaO ₅ | 0.207 | kg | C ₄ H ₇ NaO ₅ | 0.207 | kg |
| | | | | | | | C ₆ H ₈ O ₆ | 0.744 | kg | C ₆ H ₈ O ₆ | 0.744 | kg |
| | | | | | | | HO ₂ CCO ₂ H | 0.884 | kg | HO ₂ CCO ₂ H | 0.884 | kg |
| | | | | | | | NaCl | 3.579 | kg | NaCl | 3.579 | kg |