TOWARDS SUSTAINABLE PRACTICES IN PHARMACEUTICAL RESEARCH AND DEVELOPMENT: A LIFE CYCLE APPROACH

by

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Dalhousie University is located in Mi'kma'ki,
the ancestral and unceded territory of the Mi'kmaq.
We are all Treaty people.

Dedication

To my dearest friends, mentors, and colleagues,

This thesis is dedicated to you with profound gratitude and love for your unwavering support, encouragement, and sacrifices throughout my journey towards achieving my Masters of Applied Science. Your boundless patience, understanding, and belief in me have been the pillars upon which I've built my academic pursuits.

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With heartfelt appreciation,

Adam LeBlanc

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Abstract

This project is an environmental impact and cost analysis of commonly used crystallization processes for isolating and purifying active pharmaceutical ingredients (APIs) at Solid State Pharma Inc., a pharmaceutical research organization. A comprehensive Life Cycle Inventory (LCI) has been compiled for cooling, antisolvent, evaporative, and reactive crystallization processes, covering aspects from raw material extraction to waste disposal, providing a cradle-to-gate evaluation for the API and a cradle-to-grave evaluation for the solvent. Relevant environmental impact categories such as global warming potential, fossil fuel potential, and human toxicity potential have been considered to quantify environmental burdens across the life cycle stages. A comparison between solvent recycling and incineration scenarios has been made to evaluate environmental impacts.

The project's main objective was to identify resource consumption hotspots in these crystallization processes. This was achieved by compiling a detailed LCI for selected processes and developing a life cycle model for environmental impact assessment. Among the processes investigated, reactive crystallization proves most prevalent (38.9%), followed by antisolvent processes (25.9%), while evaporative and cooling processes showed similar occurrence rates.

Solvent usage analysis revealed that water was the most prevalent solvent (22.6% usage), with class 3 solvents predominating (74.1% usage). Reactive and evaporative processes tended to use higher solvent amounts compared to other types, though some reactive processes exhibited lower solvent usage akin to cooling processes. Dichloromethane emerged as a significant class 2 solvent, notably present in process P32, which constituted 75% of the total amount used in all processes.

Environmental impact assessment indicated that solvent production was the primary contributor in the incineration option. However, implementing solvent recovery systems significantly reduced these impacts, making the recovery option more environmentally favorable. Economic analysis showed that operating costs are predominantly associated with solvent procurement, with cooling crystallization generally exhibiting the lowest costs due to reduced solvent usage. Further, solvent recovery systems showed high returns on investment at larger production scales, suggesting their viability for cost savings and profitability.

Overall, the project provided valuable insights into the environmental and economic implications of different crystallization processes, emphasizing the importance of solvent choice and recovery systems in pharmaceutical manufacturing. It laid the groundwork for developing expert systems for comparative assessments of crystallization technologies, furthering environmental sustainability and cost-effectiveness in the pharmaceutical industry.

Chapter 1: Introduction

The objective of this project is to perform an environmental impact and cost analysis for the crystallization processes commonly used for isolation and purification of active pharmaceutical Ingredients (API). A Life Cycle Inventory (LCI) will be compiled for common crystallization processes, designed for isolation of 50 APIs at Solid State Pharma Inc, a pharmaceutical research organization. Crystallization processes that will be investigated include cooling crystallization, antisolvent crystallization, evaporative crystallization, and reactive crystallization. The scope of analysis includes extraction of raw materials, crystallization process, transportation, and waste disposal/treatment, etc., providing a full cradle-to-gate evaluation for the API and a cradle-to-grave evaluation of the solvents. Relevant environmental impact categories (e.g., global warming potential, fossil fuel potential, human toxicity potential, etc.) will be considered to quantify the environmental burdens related to energy requirements, resource consumption in extraction, production, waste disposal/treatment stages of life cycle. Relevant environmental impact categories will be evaluated and compared for the two cases of solvent/reagent recycling versus incineration. A life cycle approach enables evaluation of alternative crystallization processes from a holistic perspective and will further inform designing processes with reduced environmental impact. This approach paves the route to developing an expert system, which would provide comparative assessment of environmental, safety, and cost of various crystallization technologies in pharmaceutical industries.

The project's main objective is the identification of hotspots in resource consumption of common crystallization processes from a cradle-to-gate/grave perspective. This will be accomplished by compiling a life cycle inventory for selected common crystallization processes (antisolvent, cooling, evaporative, and reactive) and developing a life cycle model for environmental impact assessment of crystallization processes.

To evaluate the environmental sustainability of the company's portfolio of crystallization processes and pinpoint process hotspots, we will develop a thorough inventory of materials and energy consumed in multiple crystallization processes, enabling us to analyze the associated environmental impact of resource and energy consumption. Additionally, we will conduct a cost analysis of commonly employed processes, providing valuable insights into financial implications of solvent recycling versus the common approach of incineration.

In more detail, we will compile site-specific information concerning selected crystallization processes, taking into account various factors such as the type and quantity of solvents and materials, as well as process conditions such as temperature and operation time. Our investigation encompasses the analysis of 54 crystallization processes, spanning four distinct categories: antisolvent crystallization, cooling crystallization, evaporative crystallization, and reactive crystallization.

We will investigate the environmental impact of 54 cases of crystallization processes. The data compiled will be accurately entered into the OpenLCA software. To support site-specific information, we will leverage the extensive Ecoinvent database, which includes background processes such as solvent and reagent manufacturing, enabling us to perform a comprehensive cradle to grave environmental impact analysis. Simultaneously, we will complete the cost analysis of the crystallization processes at this stage.

In conjunction with the case study approach employed in our project objective, our goal is to propose an innovative tool that facilitate the prediction of environmental sustainability. This tool would enable us to assess the impact of changes in process conditions and input parameters, ultimately enhancing the overall sustainability of the processes. While the case studies conducted in our first objective offer valuable insights, they can be intricate, time-consuming, and may not be directly applicable to other scenarios (non-predictive). Therefore, the knowledge that we have in this project can be used to develop a streamlined approach to bypass the need for laborious, case-by-case studies.

During the hotspot identification process, we will gather valuable information regarding inventory data, enabling us to comprehensively identify influential process parameters. We anticipate that key factors such as the quantity and type of solvent, process time, and temperature will play pivotal roles in determining the environmental impact of crystallization processes. By analyzing these parameters, we aim to gain valuable insights into their influence on the overall sustainability of the processes.

Chapter 2: Current Trends in Life Cycle Assessment for Pharmaceutical Industry

In 1992, R.A. Sheldon introduced the E-factor which became a framework for a more sustainable attitude towards our environment (Sheldon, 1992). Then, in 1998, Anastas at the United States Environmental Protection Agency (US EPA) developed green chemistry principles (P. T. Anastas & Warner, 1998, p. 30). In 2015, all member states adopted the United Nations Sustainability Development Goals (UN-SDGs) (P. T. Anastas & Zimmerman, 2018). More specifically, UN-SDG Goal 3 'ensure healthy lives and promote well-being for all at all ages' and Goal 12 'ensure sustainable consumption and production patterns' provide a framework for the fine chemicals and pharmaceutical industry to rethink processes and to contribute to the sustainability goals.

Measurable sustainability metrics help guide process, product design and development, and provide benchmarks for future improvements. Life cycle assessment (LCA), as described in International Organization for Standardization (ISO) standard 14040:2006, quantifies the environmental impact associated with all life cycle stages of a product. LCA is applied in the bulk chemical industry, especially for new bulk products, green, and brownfield projects (International Organization for Standardization, 2006). LCA, although not as common as the bulk chemical industry, has started to gain more attention in the bulk pharmaceutical industry (Becker et al., 2022a).

To develop new pharmaceutical processes in rigorous time frames, tools to appropriately address the environmental impact in a time-efficient manner are required to avoid delays. Glaxo Smith Kline (GSK) has focussed the LCA on a cradle-to-gate analysis and further developed the fast life cycle assessment of synthetic chemistry (FLASC) tool (Curzons et al., 2007). The GSK FLASC tool is tailored toward pharmaceutical processes which, in most cases, have much lower production volumes than the bulk chemical industry. However, these pharmaceutical processes can involve more complex synthetic steps and reagent use. The strength of simplified methodologies, like GSK FLASC, is that these address two key challenges of pharmaceutical manufacturing: often, limited data regarding supplied precursors is available which is solved by the lifecycle inventory (LCI) methodology and increased time and cost pressure on drug discovery and development required LCA methodologies and metrics which have a lower adoption hurdle (Becker et al., 2022a; Curzons et al., 2007).

2.1 Green Chemistry Principles and Good Manufacturing Practices

To design commercial-scale good manufacturing practice (GMP) processes for pharmaceuticals, process development must address the regulatory guidelines during the clinical and manufacturing phase to obtain regulatory approval at the launch of the product. Table 2-1 shows an overview of the twelve green chemistry principles and selected regulatory guidelines for the pharmaceutical industry (*12 Principles of Green Chemistry*, n.d.; Becker et al., 2022a; European Medicines Agency, 2014, 2024; Food & Drug Agency, 2017; Sargent et al., 2016). As seen in Table 2-1, several regulatory guidelines are in close alignment with the principles of green chemistry. However, some regulatory expectations on drug substance quality and process make it more challenging to implement green chemistry principles and process changes (Becker et al., 2022b). For each pharmaceutical process development program, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) need to resemble the green chemistry principles.

Table 2-1. Green chemistry principles and selected regulatory guidelines.

Green Chemistry Principles	Regulatory Guidelines
• Prevent waste instead of treating it. • Design atom-efficient synthetic methods. • Choose synthetic routes using nontoxic compounds where possible. • Design new products that increase functionality while reducing toxicity. • Minimize the use of auxiliary reagents and solvents. • Design processes with minimal energy requirements. • Preferable to use renewable raw materials. • Avoid unnecessary derivatization. • Replace stoichiometric reagents with catalytic cycles. • Design new products with biodegradable capabilities. • Develop real-time and on-line process analysis and monitoring methods. • Choose feedstocks and design processes that minimize the chance of accidents.	• **ICH Q11:** Development and manufacture of drug substances • **ICH Q3C:** Residual solvents • **ICH M7:** Assessment and control of DNA reactive (mutagenic) impurities in pharmaceuticals to limit potential carcinogenic risk. • **ICH Q8:** Pharmaceutical development • Cleaning procedures to avoid cross contamination: EMA guideline of setting health-base exposure limits • FDA Guidance Advancement of Emerging Technology Applications • **ICH Q3A/B:** Impurities in new drug substances/products • **ICH Q6A:** specification and acceptance criteria for new drug substances and new drug products: chemical substances. • **ICH Q1A-F:** Stability of drug substances and drug product.

	- FDA Guidance Quality Considerations for Continuous Manufacturing. - **ICH Q9:** Quality Risk Management

The green chemistry principle ‘choose synthetic routes using nontoxic compounds where possible’ is very well reflected by the ICH guidelines on impurities (ICH Q3A), residual solvents (ICH Q3C), and mutagenic impurities (ICH M7). These ICH guidelines generate the selection and use of non or less toxic solvents (ideally ICH class 3 solvents) and limit toxic impurities in drug substances and products originating from toxic reagents and/or by-products.

2.2 Environmentally Sustainable Solvent Practices

Over the years, industry and process chemistry have been transitioning toward more environmentally sustainable solvent practices. Specifically, the substitution of chlorinated solvents is an area of ongoing interest (Becker et al., 2022a).

In the pharmaceutical industry, it is common to have multipurpose facilities that synthesize different APIs because of the low annual yield requirement for market (Becker et al., 2022a). APIs are typically synthesized in batch processes. Once the desired annual market quantity of API is achieved, multipurpose facilities clean the equipment and transition to another API requiring a similar equipment setup. In these cases, it is more challenging to limit the use of solvents while assuring appropriate cleaning of the pharmaceutical reactors and equipment. To avoid cross-contamination of pharmaceuticals and pharmaceutical intermediates, target values according to the acceptable daily intake (ADI) and maximum allowable carry over (MACO) of one compound to the next product have to be adhered to (Becker et al., 2022a). They are set for each API based on health-based exposure limits. Therefore, for batch processes, the in-between batch cleaning and the cleaning before product switches are performed until these limits are reached. In most cases, this typically requires extensive cleaning with organic solvents and water (Becker et al., 2022a). It is also important to note that the amount of cleaning solvent can be much higher in the development phase of a drug than actual solvent amounts used in the processes batches (Becker et al., 2022a).

Green chemistry principles aim to reduce the process mass intensity (PMI), see equation (2-1), or the E-factor, see equation (2-2).

$$PMI = \frac{total\ \ input\ [kg]}{total\, product\ [kg]} \tag{2-1}$$

$$E\ factor = \frac{total\, waste\ [kg]}{total\ \ product\ [kg]} \tag{2-2}$$

Organic solvents can often contribute to more than 50% to these metrics in the pharmaceutical industry (Jimenez-Gonzalez et al., 2011). The amounts of cleaning solvents needed to avoid cross-contamination in GMP processing can significantly contribute to the PMI. Typically, reactor rinses are performed with polar solvents, such as acetone, followed by water rinses until the total carbon (TC) values or substance-specific cleaning thresholds are met (Becker et al., 2022a).

In 2010, the Green Chemistry Institute Pharmaceutical Roundtable started a program which was looking at suitable replacements for dipolar aprotic solvents and solventless reactor cleaning (Jimenez-Gonzalez et al., 2011; Rogers & Jensen, 2019). The use of green solvents, alternative mechanics, and chemical cleaning procedures are ways to improve the solvent utilization. Technical advancements like continuous processes with dedicated small reactor racks can further reduce solvent use during cleaning procedures if it can be shown that impurities do not accumulate and if the technical challenges of reactor fouling can be solved (Rogers & Jensen, 2019).

2.3 Rational Drug Design

Anastas et al. (2018) discussed how rational drug design can be further expanded to guide safer chemical design. They also indicated that it is important to assess the impacts besides the actual hazards and risks for the end user (patient), manufacturer, and the environment. For example, switching a process for a high volume, low potency peptide with good biodegradability to a greener solvent or, at best, to ‘chemistry in water,’ being able to discharge waste streams to aqueous wastewater treatment, can have a huge impact on the environment. Starting development programs for such changes can be justified (N. D. Anastas et al., 2018). For example, switching a very potent cytotoxic API process with low biodegradability and relatively small annual needs (e.g., low kilogram range) to aqueous reaction media will likely provide relatively little effect on the overall total waste generation and treatment of the LCA, unless significant improvements to yield, purity, or process safety can be achieved (N. D. Anastas et al., 2018). Anastas et al. (2018) suggested that other parts of the chemical industry can learn and adopt some of the pharmaceutical product design procedures to improve sustainability.

Significant progress has been made in academia, industry, and on the regulatory side in the last few years to expand methodologies and to promote the realization of green chemistry principles and process optimization based on green chemistry and sustainability metrics (Becker et al., 2022a).

2.3.1 Chemistry in Water

Organic solvents are a key contributor to the PMI of API processes (Becker et al., 2022a). Therefore, the reduction of solvents as well as the substitution with alternative reaction media are efficient strategies for sustainability improvements.

Lipshutz et al. (2013, 2017) demonstrated that surfactants in water can be used to allow classical organic reactions to be performed in water. This is because the surfactants in water form nanoreactors in organic media (Lipshutz, 2017; Lipshutz et al., 2013). Bailey et al. (2021) were able to lower the overall cumulative PMI of the synthesis of a 5-HT_4 agonist receptor manufacturing process from 350 to 79 by utilizing chemistry in water. Further, the reduction of the PMI of used organic solvents was reduced from 233 to 13 and the amount of process water was reduced by 48% (Bailey et al., 2021). Additionally, Krell et al. (2021) from Novartis recently showed how to treat aqueous waste streams from surfactant chemistry to allow for discharge into wastewater treatment plants.

2.3.2 Continuous Processing

Innovative technologies like novel reactor designs and applications of continuous processing can significantly contribute to sustainability (Rogers & Jensen, 2019). The green chemistry principle ‘design processes that minimize the chance of accidents’ is often a key driver to switch a batch process to a continuous process during scale-up phases of pharmaceutical products. The development of a continuous process requires a deep understanding of reactions. Kinetic data acquisition is crucial and a combination of in-line process analytical technologies and modeling techniques can provide a highly efficient development and scale-up technique (Fath et al., 2020).

An impressive set of sustainable process development efforts have been made for the synthesis of MK-7264, a chronic cough treatment currently in clinical phase III studies (Basu et al., 2020; Otte et al., 2020, p. 4; Ren et al., 2020). Since the API production was expected to exceed 50 MT annually, a large emphasis was placed on developing a process that was cost-effective, robust, and sustainable in the long term. The initial route, designed for speedy manufacturing of early preclinical and clinical trials supplies, contained 11 steps, a PMI of 366, a total yield of 16%, and several hazardous reagents and conditions and expensive reagents. Initially, an improved batch process was developed, resulting in a step-PMI reduction from 80 to 17. However, the batch process had limitations with excess reagents and the addition of another compound to deal with the impurity profile of an intermediate. Therefore, a continuous process for the commercial-scale API intermediate manufacturing was developed to further achieve process control and sustainability improvements. The switch to a continuous flow process showed a 90% reduction of the PMI, a PMI reduction of 54% compared with the improved batch process, and a 70% reduction of carbon monoxide formation. With further process development, a yield of 91% was achieved, along with a six-fold reduction in raw material costs (Basu et al., 2020; Otte et al., 2020, p. 4; Ren et al., 2020).

2.4 Life Cycle Assessment in Pharmaceutical Industry

Although the application of LCA metrics in the pharmaceutical industry is not yet widespread, it has become more common in recent years compared to a decade ago (Jiménez-González & Overcash, 2014). LCA is now used in various applications within the pharmaceutical industry. To address the challenges faced and gain insights within reasonable timelines, streamlined LCA tools have been developed and used in the pharmaceutical industry (Jiménez-González & Overcash, 2014). There is a need for reliable, user-friendly, and standardized tools to facilitate LCA implementation.

2.4.1 API Synthesis Case Studies in Pharmaceutical Industry

Initially, companies focused on case studies to understand the environmental impacts of specific activities and identify opportunities for improvement. LCAs have been conducted for specific APIs (de Jonge, 2003; Jiménez-González, 2000; Jiménez-González et al., 2004), but these studies are limited in their applicability to other APIs as they are compound- and synthesis-specific.

The study conducted by de Jonge (2003) examined case studies of two pharmaceutical products (Exelon and Tegretol). These case studies examined the primary energy requirements of various life-cycle components of the drug. Exelon is a drug used to treat Alzheimer's disease that was approved by the Food and Drug Agency (FDA) in 2000. The LCA included recovery of the natural resources, chemical production, transportation, pharmaceutical production, packaging, distribution, and disposal of the packaging. Results showed that the primary energy requirements were 38% distribution and transport, 34% packaging, 12% API synthesis, 5% formulation, and 1% end-of-life treatment. Tegretol is a drug used to treat epilepsy and was first introduced in 1965. Results showed that the primary energy requirements were 62% API synthesis, 20% distribution, 14% packaging, and 4% formulation.

In the study by Jiménez-González (2000), the LCA of Sertraline Hydrochloride (an chiral antidepressant) was evaluated. The goal of the study was to facilitate the evaluation, comparison, and selection of alternative synthesis routes by incorporating the overall environmental impact routes by using a cradle-to-gate approach (i.e., packaging and distribution of the drug was not examined). It was found that there was a strong relationship between the complexity of the system and the environmental aspects in the early stages of Sertraline synthesis. When more steps, intermediate isolation, and solvents were used, more waste was generated. Overall, two main factors had a great influence over environmental performance: solvent utilization and energy usage.

In the 2004 study by Jiménez-González *et al.*, a cradle-to-gate LCI/A was conducted to determine environmental impacts in the synthesis of a typical API. Their results showed that solvent use accounts for the majority of the potential cradle-to-gate impacts associated with the manufacture of the commercial pharmaceutical product. Further, if spent solvent is incinerated instead of recovered, the life-cycle profile and impacts are considerably increased.

2.4.2 Sub-System Case Studies in Pharmaceutical Industry

Subsequently, LCA was used to assess specific sub-systems such as solvents, catalysts, equipment, waste streams, and processing options. The pharmaceutical industry has employed LCAs to evaluate different materials, such as solvents (Jiménez-González & Overcash, 2014). GSK and AstraZeneca have integrated LCA into their solvent selection processes (AstraZeneca, n.d.; Folić et al., 2008). Capello et al., (2007) developed a framework that combined Environment Health and Safety (EHS) assessments with LCA.

Nielsen et al., (2007) performed a cradle-to-gate LCA for industrially produced enzyme products. Enzymes are biological catalysts that have a large capacity to increase the speed of a wide variety of biochemical reactions. They are able to increase the quality, speed, and yield of processes and also reduce energy consumption and use of hazardous chemicals. This study investigated a cradle-to-gate LCA for five representative enzymes. The environmental impacts of producing these enzyme products vary by a factor of 10 or more. This variation was explained by differences in fermentation time, formulation type, production yield, and strength of the final product. The main source of environmental impact was usually the fermentation process due to the electricity and ingredient consumption.

Adams et al., (2013) contributed to the development of GSK's reagent guide, which incorporated LCA into reagent selection. They developed a reagent guide that ranked the commonly used reagents for 15 transformations to reduce the environmental impact of drug discovery and development. The reagents were scored by a combination of health, safety, and environmental risk phases, life cycle analysis, and an assessment of the chemistry including considerations of atom efficiency, stoichiometry, work-up, and other issues Guides covered alkene reduction, amide formation, C-H bromination, C-H chlorination, deoxychlorination, epoxidation, ester formation, ether formation, fluorination, iodination, ketone reduction, nitro reduction, oxidation of alcohols to aldehydes and ketones, reductive amination, and sulfur oxidation (Adams et al., 2013)..

2.4.3 Alternative Chemical Route Case Studies in Pharmaceutical Industry

The next stage involved comparing different chemical routes or processing alternatives. This included comparing chemical and biological routes or evaluating the impacts of producing different molecules (Jiménez-González & Overcash, 2014). LCAs have explored various chemical routes for different APIs.

For instance, Henderson et al., (2008) conducted an LCA comparing a chemical route to an enzymatic route for producing 7-aminocephalosporic acid. The routes studied were a chemical synthetic process and a two-enzyme catalyzed process. A cradle-to-gate LCI was conducted, and results compared the synthetic efficiency, environment, health, safety, and life cycle metrics for both processes. It was found that the chemical synthetic process had a higher yield, but a much lower reaction mass efficiency and half the mass productivity of the enzymatic process. Further, the chemical process used more hazardous materials and solvents and required about 25% more process energy than the enzymatic process. Overall, the chemical process had a larger environmental impact, mainly due to the production of raw materials.

2.4.4 Formulation Case Studies in Pharmaceutical Industry

As understanding grew, LCA was extended to assess the environmental profiles of formulated products, including dosage forms such as devices, tablets, liquids, and creams (Jiménez-González & Overcash, 2014). Some companies conducted full LCAs, while others focused on carbon footprints. Additionally, companies examined environmental and carbon footprints for their global operations, often as part of corporate responsibility reporting and to identify areas for improvement (Jiménez-González & Overcash, 2014).

2.4.5 Crystallization Specific LCAs in Pharmaceutical Industry

From the literature review of LCA in the pharmaceutical industry it was found that there is a significant research gap regarding the application of LCAs specifically to the crystallization steps of API purification. To date, there have been no studies focusing on this crucial aspect and will be the focus of this project.

Chapter 3: Background Information

This chapter will present key background information on crystallization, solvents, life cycle assessment, and solvent recovery systems.

3.1 Crystallization

Solids can be either crystalline (ordered structure) or amorphous (unordered structure). Crystalline solids have a regular arrangement of particles into a fixed, rigid pattern (i.e., lattice). They are anisotropic because their mechanical, electrical, magnetic, and optical properties vary with dimension. The regularity of their internal structure allows crystals to have smooth faces develop as the crystal grows and have the planes of the faces parallel to the atomic planes of the lattice (Mullin, 2001).

3.1.1 Crystal Symmetry and Structure

There are three simple elements of symmetry: central, axial, and planar. From the elements of symmetry, a total of 32 point groups can be constructed. The point groups are categorized into seven different systems: regular (5), tetragonal (7), orthorhombic (3), monoclinic (3), triclinic (2), trigonal (5), and hexagonal (7). By combining the seven crystal systems with the 32 point groups, there are a total of 320 space groups (Mullin, 2001).

3.1.2 Types of Crystalline Solids

There are four main types of crystalline solids: ionic, covalent, molecular, and metallic. Ionic crystals are charged ions held in place by electrostatic forces. Covalent crystals' atoms do not carry effectives charges and are connected by a framework of covalent bonds. Molecular crystals hold molecules together by weak attractive forces (e.g. π-bonds, and H-bonds). Metallic crystals contain an ordered array of identical cations (Mullin, 2001).

3.1.3 Isomorphs & Polymorphs

When two or more substances crystallize in almost identical forms, they are termed isomorphs. Isomorphs are usually chemically similar. At times, isomorphs can crystallize together out of solution to created mixed crystals. In these cases, no fixed pattern is found due to the composition of homogeneous solid phase deposited. Mixed crystals depend largely on the relative concentrations and solubilities of the substances in the original solvent. Additionally, isomorphs commonly show formation of overgrowth crystals (Mullin, 2001).

Polymorphs are substances capable of crystallizing into different, but chemically identical crystalline forms. Polymorphs sometimes undergo transformations without a change of external form. This results in an aggregate of very small crystals of stable modification confined within the boundary of the original unstable form. When polymorphs are not interconvertible, the crystal forms are monotropic. Sometimes the term isopolymorphism is used when each of the polymorph's forms of one substance is isomorphous with the respective polymorphous form of another substance (Mullin, 2001).

3.1.4 Chirality

Enantiomers are two crystals of the same substance that are mirror images of each other. In these cases, they do not have planes or centres of symmetry. An optically inactive solution that has enantiomers is termed a racemate. Crystalline racemates have two main classes. Conglomerates are an equimolar mechanical mixture of two pure enantiomers. Racemic compounds are equimolar mixtures of two enantiomers homogeneously distributed throughout the crystal lattice (Mullin, 2001).

3.1.5 Crystal Habit

The faces of crystals can vary considerably in relative size and nearly all crystals are distorted to some degree. Hence, perfect geometric symmetry is rarely observed in crystals. For example, a stunted growth in the vertical direction results in a tabular crystal; an elongated growth in the vertical direction yields a needle or acicular crystal (Mullin, 2001).

The relative growth of crystal faces can be altered, and often controlled, by several factors. Rapid crystallization can result in formation of needle crystals. Impurities in the crystallization solution can stunt growth of a crystal in certain directions. Changing solvents can produce different changes in the habit of the crystal. The degree of supersaturation or supercooling of a solution can also exert a considerable influence on crystal habit (Mullin, 2001).

3.1.6 Crystal Formation

Rapid crystallization from supersaturated solutions frequently produces tree-like formations (i.e., dendrites). These produce a main crystal stem quite rapidly and then grow primary (and sometimes secondary) branches, usually at a 90° angle. Dendrites most often form during the early stages of crystallization. At later stages, more uniform growth occurs. Dendrite formation tends to be favoured by substances that have high enthalpy of crystallization and a low thermal conductivity (Mullin, 2001).

Commonly, crystals exhibit some form of aggregation or intergrowth. The presence of aggregates in a crystalline mass can spoil the appearance of the product and interfere with its free-flowing nature. Aggregation is also most often indicative of impurities and these aggregates increase difficulties with removal all the mother liquor, even after efficient washing (Mullin, 2001).

Composite crystals may occur in simple symmetrical forms or in random clusters. Parallel growth occurs when individual forms of the same substance grow on top of one another in such a way that all corresponding faces and edges of individuals are parallel. Twins (or macles) are composed of two intergrown individuals similar in form and joined symmetrically about an axis or a plane. Parallel growth or twinning are usually encountered when crystallization has been allowed to take pace in an undisturbed medium. Certain impurities in the crystallization medium can also cause twin formation, even under vigorously agitated conditions (Mullin, 2001).

3.1.7 Crystal Imperfections

Very few crystals are perfect. There are three main set of defects found in crystals: point, line, and surface defects.

Point defects occur only at a single point within the lattice network. There are a few types of point defects. Vacancies, lattice sites where units are missing, leave holes within the lattice structure. Interstitials are foreign atoms that occupy interstices between the matrix atoms of the crystal and often lead to distortions in the lattice. Substitutional impurities occur when a foreign atom takes the place of a matrix atom (Mullin, 2001).

Line defects occur when a slip or shearing of the crystal occurs. There are two main types of line defects. A slip dislocation causes the dislocation in a linear fashion whereas screw dislocations cause atoms to be displaced around the dislocation line. Screw dislocations can result in the development of a spiral growth pattern over the crystal face (Mullin, 2001).

Surface defects are produced in crystalline materials because of mechanical or thermal stresses or irregular growth. Grain boundaries are created between individual crystals of different orientation in a polycrystalline aggregate. Tilt boundaries are equivalent to a line of edge dislocations and twist boundaries can be considered a succession of parallel screw dislocations (Mullin, 2001).

3.1.8 Yield

Theoretical crystal yield can be calculated if the solubility data for substance in a particular solvent is known. This is the maximum yield of pure crystals that could be obtained by cooling or evaporating crystallization for the given solution. Actual yield may be higher than the theoretical yield because crystal masses retain some of the mother liquor, even after filtration (Mullin, 2001).

Drying can help remove remnants of the mother liquor but can also cause the topcoat of crystals to become more brittle and be of lower grade than the rest of the crystals. An alternative method would be to wash the crystals to reduce the amount of mother liquor retained. However, this adds the danger of reducing the final yield by redissolving some of the crystals into the wash solution. The efficiency of washing is largely dependent on the shape and size of the crystals (Mullin, 2001).

3.1.9 Effect of Impurities

Pure solutions are rarely encountered because some level of impurity will always be present. For example, a third substance (i.e., the impurity) in a binary system may result in no change (unlikely), a reaction, supersaturating a solution (salting in), or undersaturating a solution (salting out) (Mullin, 2001).

3.1.10 Phase Change Detection

To understand the complete picture of the behaviour of a system, a phase diagram is often developed over a wide range of temperatures and pressures. The number of parameters needed is the minimum number of chemical compounds required to express the composition at any phase. Phases are a homogeneous part of a system.

The heat effects accompanying a crystallization process may be determine by conducting heat balances over the system. Through thermal analysis, phase change is always accompanied by an enthalpy change. The heat effect can be observed if a cooling curve is plotted for the system (Mullin, 2001).

3.1.10.1 Differential Thermal Analysis

Differential Thermal Analysis (DTA) method is used to observe the phase changes and measures the associated change in enthalpy (Mullin, 2001). The process involves heating a small sample near a reference material in an identical container. The reference material must not exhibit any phase change.

3.1.10.2 Differential Scanning Calorimetry

Differential Scanning Calorimetry (DSC) is a calorimetric technique for observing the solid-liquid phase change (Mullin, 2001). Two independently controlled heaters allow the sample and reference pans to be heated at a fixed rate. The instrument detects the change in temperature between the sample and reference and records the amount of heat added or removed. Sharp peaks would represent more pure samples than broader peaks.

3.1.10.3 Dilatometry

Dilatometry detects a phase change by measuring changes in volume. It is widely used in the analysis of melts and usually quite simple since solids absorb heat on melting and expand (Mullin, 2001).

3.1.11 Nucleation

Supersaturation and supercooling are not usually sufficient for a system to begin to crystallize. For a system to crystallize, several minute particles (i.e., seeds) must be present. The seeds act as centres of crystallization.

3.1.11.1 Primary Nucleation

Primary nucleation is considered to not contain any crystalline matter prior to nucleation (i.e., no induced seeding) (Mullin, 2001). For a homogeneous nucleation, the formation of crystal nuclei requires molecules to coagulate consistently and become oriented in a fixed lattice. The number of molecules in a stable crystal nucleus can vary from ten to thousands.

3.1.11.2 Secondary nucleation

Secondary nucleation occurs when a seed is introduced to the solution to induce nucleation (Mullin, 2001). A supersaturated solution nucleates much more readily when crystals of the solute are already present or deliberately added. Small crystalline fragments often grow much more slowly than macrocrystals (Mullin, 2001).

Seeding is the best method for inducing crystallization (Mullin, 2001). Seeding is the inoculation of a supersaturated solution with small particles of the material to be crystallized. Deliberate seeding is frequently employed in industrial crystallization to affect a control over the product size. Seed crystals do not necessarily have to consist of the material being crystallized to be effective (Mullin, 2001). Large seed sizes generate more secondary nuclei in agitated systems than do small seeds because of their greater contact probabilities and collision energies.

3.1.11.3 Effect of Impurities on Nucleation

The presence of impurities in a system can affect nucleation behaviour. The presence of colloidal substances can suppress nucleation. Certain surface-active agents and traces of foreign ions also exert a strong inhibiting effect. Increasing cation charge will also increase inhibition. Ionic impurities can reduce the induction period and the presence of soluble impurities can also affect the induction period (Mullin, 2001).

3.1.12 Recrystallization

It is often possible to remove the impurities from a crystalline mass by dissolving the crystals in a small amount of fresh hot solvent and cooling the solution to produce a fresh batch of purer crystals. To reach a specific purity, the recrystallization step may need to be repeated several times. Eutectic systems can yield near-pure crystals in a single recrystallization step (Mullin, 2001).

During recrystallization, solvent choice depends on the nature of the required substance and the impurity. The impurity should be very soluble in the chosen solvent at the lowest temperature operated. The substance should have a high temperature coefficient of solubility so that high yields can be obtained within a small temperature range.

3.1.13 Crystallization Types

There are four main crystallization types: cooling, antisolvent, evaporative, and reactive. At times, some processes contain a mix these crystallization types. For example, most processes will usually contain an element of cooling to return the solution to room temperature. However, to properly classify these processes as a specific crystallization type, the main process step involved in the crystallization of the API will be its crystallization type (e.g., if an antisolvent addition causes the majority of the crystallization to occur, it would be classified as an antisolvent crystallization process even if some solvent evaporation and cooling occurs).

3.1.13.1 Cooling Crystallization

Cooling crystallization uses temperature differences to crystallize a substance. This is conducted by dissolving a substance to its saturated level at a high temperature and then quickly cooling it so it can crash out. A typical scheme for cooling crystallization is found in Figure 3-1 and an equipment and stream tables found in Table 3-1 and

Table 3-2, respectively.

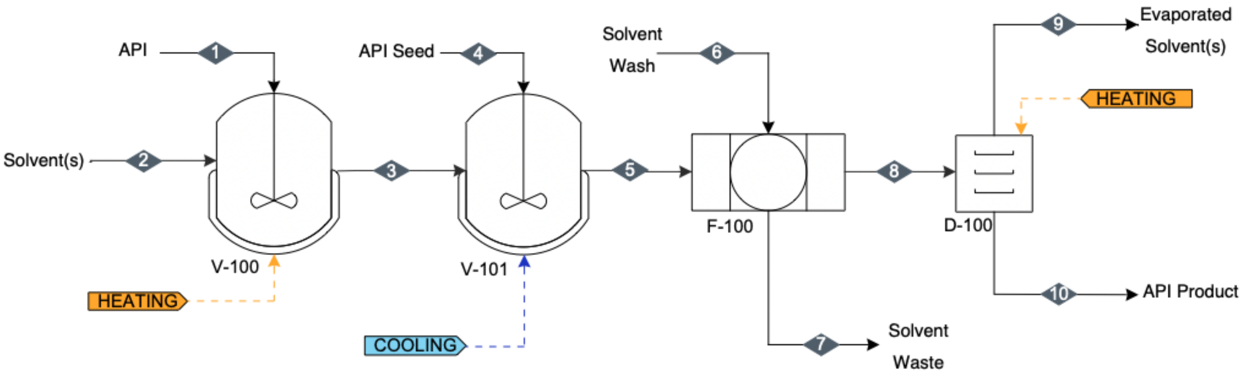

Figure 3-1. A typical process flow diagram of a cooling crystallization process.

Table 3-1. Typical Equipment Table for a Cooling Crystallization Process.

Equipment Label	**V-100**	**V-101**	**F-100**	**D-100**
Equipment	Heating Vessel with Mixing	Cooling Vessel with Mixing	Filtration Unit	Vacuum Dryer

Table 3-2. Typical Stream Table for a Cooling Crystallization Process.

Stream Label	**Stream Description**	**Phase**
1	Starting API	Solid
2	Solvent mixture	Liquid
3	Solvent mixture containing dissolved API	Liquid
4	API Seed	Solid
5	Crystallized API in solvent mixture	Slurry
6	Solvent mixture used as wash	Liquid
7	Liquid solvent waste with trace amounts of undissolved API	Liquid
8	API wet with remains of solvent	Wet solid
9	Evaporated solvent	Gas
10	Final API product	Solid

3.1.13.2 Evaporative Crystallization

Evaporative crystallization uses heat to crystallize a substance. This is conducted by dissolving a substance to its saturated level and then applying heat to the solution to evaporate some of the solution until the product precipitates. A typical scheme for evaporative crystallization is found in Figure 3-2 and equipment and stream tables are found in Table 3-3 and Table 3-4, respectively.

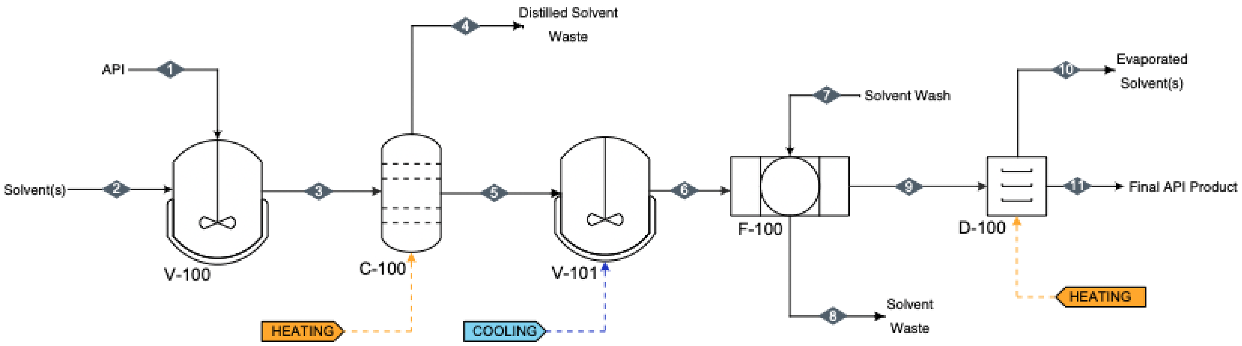

Figure 3-2. A typical process flow diagram of an evaporative crystallization process.

Table 3-3. Typical Equipment Table for an Evaporative Crystallization Process.

Equipment Label	**V-100**	**C-100**	**V-101**	**F-100**	**D-100**
Equipment	Heating Vessel with Mixing	Distillation Column	Cooling Vessel with Mixing	Filtration Unit	Vacuum Dryer

Table 3-4. Typical Stream Table for an Evaporative Crystallization Process.

Stream Label	**Stream Description**	**Phase**
1	Starting API	Solid
2	Solvent mixture	Liquid
3	Solvent mixture containing dissolved API	Liquid
4	Distilled solvent	Liquid
5	Crystallized API in solvent mixture	Slurry
6	Crystallized API in solvent mixture	Thick Slurry
7	Solvent mixture used as wash	Liquid
8	Liquid solvent waste with trace amounts of undissolved API	Liquid
9	API wet with remains of solvent	Wet solid
10	Evaporated solvent	Gas
11	Final API product	Solid

3.1.13.3 Antisolvent Crystallization

Antisolvent recrystallization is commonly carried out as part of a standard polymorph screening and are usually carried out at room temperature. Two different regimes can be used for antisolvent recrystallization: direct and reverse. The direct method involves slowly adding the antisolvent to solution. The reverse method adds the solution directly into the antisolvent. A typical scheme for antisolvent crystallization is found in Figure 3-3 and equipment and stream tables are found in Table 3-5 and Table 3-6, respectively.

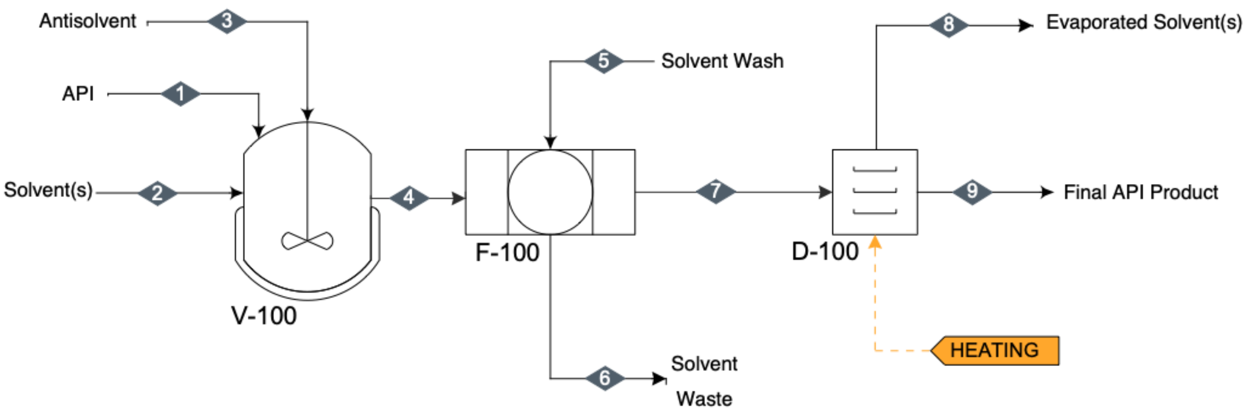

Figure 3-3. A typical process flow diagram of an antisolvent crystallization process.

Table 3-5. Typical Equipment Table for an Antisolvent Crystallization Process.

Equipment Label	**V-100**	**F-100**	**D-100**
Equipment	Vessel with Mixing	Filtration Unit	Vacuum Dryer

Table 3-6. Typical Stream Table for an Antisolvent Crystallization Process.

Stream Label	**Stream Description**	**Phase**
1	Starting API	Solid
2	Solvent mixture	Liquid
3	Antisolvent	Liquid
4	Crystallized API in solvent mixture	Slurry
5	Solvent mixture used as wash	Liquid
6	Liquid solvent waste with trace amounts of undissolved API	Liquid
7	API wet with remains of solvent	Wet solid
8	Evaporated solvent	Gas
9	Final API product	Solid

3.1.13.4 Reactive Recrystallization

Reactive crystallization uses a reactant that will cause a reaction with the compound dissolved in solution. The product created is not as soluble in solution and then precipitates. A typical scheme for reactive crystallization is found in Figure 3-4 and equipment and stream tables are found in Table 3-7 and Table 3-8, respectively.

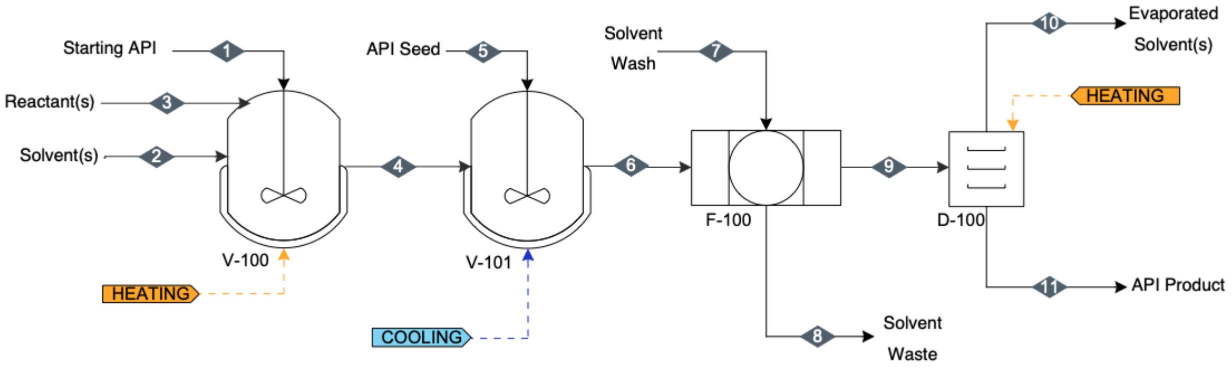

Figure 3-4. A typical process flow diagram of a reactive crystallization process.

Table 3-7. Typical Equipment Table for a Reactive Crystallization Process.

Equipment Label	**V-100**	**V-101**	**F-100**	**D-100**
Equipment	Heating Vessel with Mixing	Cooling Vessel with Mixing	Filtration Unit	Vacuum Dryer

Table 3-8. Typical Stream Table for a Reactive Crystallization Process.

Stream Label	**Stream Description**	**Phase**
1	Starting API	Solid
2	Solvent mixture	Liquid
3	Reactant(s)	Solid
4	Solvent mixture containing dissolved API	Liquid
5	API Seed	Solid
6	Crystallized API in solvent mixture	Slurry
7	Solvent mixture used as wash	Liquid
8	Liquid solvent waste with trace amounts of undissolved API	Liquid
9	API wet with remains of solvent	Wet solid
10	Evaporated solvent	Gas
11	Final API product	Solid

3.1.14 Polymorphism

Polymorphisms represent crystal systems where a substance can exist in structures characterized by different unit cells while each form still consists of the same elemental composition (Brittain, 2009). Additionally, solvatomorphism, occurs for crystal variations where the crystal structure of the substance is defined by other unit cells where these unit cells differ in elemental composition through inclusions of one or more molecules of solvent (Brittain, 2009).

Due to differences in dimensions, shape, symmetry, capacity, and void volume of the unit cells, the different polymorphs of a given substance have different physical properties arising from differences in molecular packing. Some properties include molecular volume, molar volume, density, refractive index along a given crystal axis, thermal conductivity, electrical conductivity, and hygroscopicity (Brittain, 2009). These differences among the crystal forms of a polymorphic system have become extremely interesting to pharmaceutical scientists because they can sometimes lead to observable difference that have implications on processing, formulation, and drug availability (Brittain, 2009).

3.1.14.1 Enantiotropy & Monotropy

The difference in free energy between the forms is a decisive factor for polymorph stability. The form exhibiting the lowest free energy is the most stable. For two different polymorphs, if the temperature dependence of the free energies of the forms differs, the curves cross at a certain temperature and are considered isoenergetic (Brittain, 2009).

For two enantiotropic polymorphs, the enthalpy and free energy curves of the liquid state can be examined. A reversible transition between forms can be observed at the transition temperature (i.e., where the free energy curves cross). The existence of enantiomorphism in the system is indicated by the fact that the free energy curve for the liquid phase intersects the free energy curves of both polymorphs at a temperature that is higher than the temperature of the transition point (Brittain, 2009).

Several rules have been developed that serve to aid in the elucidation of the relative order of stability of polymorphs, and to facilitate the determination of the existence of enantiotropism or monotropism in a polymorphic system. The most applicable rules are the heat of fusion and heat of transition.

The heat of fusion rule states that for enantiotropic systems, the enthalpy of fusion of its first form is less than its second form, whereas the enthalpy of fusion of its first form is more than its second form for monotropic systems (Brittain, 2009). The heat of transition rule states that for enantiotropic systems, the phase transition of its second form to first form is endothermic, whereas the phase transition of its second form to first form is exothermic for monotropic systems (Brittain, 2009). The sign and magnitude of enthalpy change can also be determined by DSC.

3.1.14.2 Nucleation & Crystal Growth

For substances capable of existing in two or more polymorphic forms, each polymorph would have its own characteristic curves. It will also have its own characteristic value of critical radius and free energy (Brittain, 2009).

When it was discovered that compounds could be obtained in more than one form, several cases were documented where the metastable form of a compound crystallized first and then subsequently transformed into a more stable form (i.e., Ostwald's Law of Stages) (Brittain, 2009). Since the stable form would have the lower solubility, a process of solution-mediated phase transformation is set up where, over time, the metastable phase transforms into the stable phase.

Concomitant crystallization refers to the situation where both polymorphs are obtained in a process. Epitaxial crystallization refers to the situation where a stable or metastable crystal form is obtained on foreign surfaces (Brittain, 2009).

3.1.14.3 Structural Aspects of Polymorphism

An ideal crystal is constructed by the infinite regular repetition in space of identical structural units. When considering structures of organic molecules, different polymorphic crystal forms can be formed along two distinguishable routes. If the molecules can be constrained to exist in a rigid grouping of atoms that lacks conformational lability, these may be packed in different motifs to occupy the points of different lattice types (i.e., packing polymorphism) (Brittain, 2009). If the molecules are not rigidly constructed we can transpire that each of these conformationally are distinct modifications packed into its own characteristic structure (i.e., conformational polymorphism) (Brittain, 2009).

3.1.15 Aspects of Solvatomorphic Systems

A solvatomorph is a system where crystal structures of the substance are defined by different unit cells but and where unit cells differ in their elemental composition through the inclusion of one or more molecules of solvent. It has also been defined as a crystalline solid in which solvent molecules have become included in the structure through positional substitution at positions that are site-specific and that are related to other solvent molecules through translational symmetry (Brittain, 2009). They can be classified by the ratio of drug substance that is either stoichiometric fixed ratios of API and solvent or non-stoichiometric. Many solvents are known to form solvatomorphs (Brittain, 2009).

Although the presence of most of the solvents in an API might raise toxicity concerns, there are several reasons for which solvatomorphs of an organic solvent would be of interest (Brittain, 2009):

- Solvatomorph could be the penultimate solid form;
- Solvatomorph could be specifically chosen for recovery or purification;
- Solvatomorph could be characterized by a crystal morphology that facilitates performance of a step in the manufacturing process;
- Solvatomorph could be the poly crystalline form suitable for crystal structure determination of the drug substance by means of single-crystal X-ray;
- Solvatomorph could be useful in a desolvated form that facilitates its dissolution;
- Solvatomorph could constitute new intellectual property and be patentable.

Water is the solvent that forms the largest number of pharmaceutically useful solvatomorphic solids. It has been estimated that approximately one-third of drug substances can form crystalline hydrates (Brittain, 2009). Dehydration may lead to amorphous phase formation and, in some cases even degradation of the API.

Aqueous granulation, particle size reduction, film coating, and tablet compression all provide opportunities to “trap” a compound in a metastable form that may “relax” to a more stable form at some unpredicted point in the life of a dosage form (Brittain, 2009). Alternatively, a kinetically favoured but thermodynamically unstable form may be converted during these processes to a more stable and less soluble form (Brittain, 2009).

Monohydrates are common, but the occurrence of hydrates beyond trihydrates is far less common. Hemihydrates (0.5 water) and sesquihydrates (1.5 water) are also relatively frequent (Brittain, 2009).

3.1.15.1 Hydrates

In non-stoichiometric hydrates, the hydrogen bonding is weak. When hydrogen bonding is strong, it is typically stoichiometric and rigidly incorporated in the structure of the crystal (Brittain, 2009). Van der Waals forces account for most of the lattice energy in less polar molecules. Coulomb interaction is more common for polar molecules. The consideration of these forces leads to isolated site hydrates, channel hydrates, and metal ion-associated hydrates (Brittain, 2009).

Isolated site hydrates occur when water molecules are isolated from direct contact with other water molecules by intervening drug molecules (Brittain, 2009). Water molecules are an integral part of the lattice and have no or limited contacts with other water molecules. When dehydrated, the crystal lattice collapses and forms an unstable form or amorphous phase.

Channel hydrates occur when the water molecules included in the lattice lie next to other water molecules of adjoining unit cells along an axis of the lattice, forming channels through the crystal (Brittain, 2009). Water molecules in these hydrates form wormholes along an axis of the lattice. Once dehydrated the crystal structure usually remains intact.

Metal ion-associated hydrates occur when water molecules are bound directly to a metal ion, either as part of a coordination complex in the case of transition metal ions, or through strong ionic bonds as in the case of an alkali metal and alkaline earth ions (Brittain, 2009). The water molecules are coordinated to a metal cation through the lone-pair electrons of the oxygen atoms of bound water molecules. Dehydration usually takes place at a very high temperature.

3.1.15.2 Behaviour of Solvatomorphs During Processing, Handling, and Storage

If the crystalline state of the bulk drug substance is a metastable polymorph or solvatomorph, the introduction of sufficient energy to overcome any activation energy barrier may cause a phase transformation into a more stable form during processing. A solution mediated transformation of a metastable form to a stable form may also happen during processing (Brittain, 2009).

3.2 Solvents

It is often difficult to determine the best solvent for a substance. Sometimes mixtures of solvents possess the best properties for a given substance. Other times, a second solvent is added to reduce the solubility and initiate crystallization (i.e., antisolvent crystallization). In the case of antisolvent crystallization, both solvents must be miscible with one another. The fundamental driving force for crystallization is the difference between the chemical potential of the given substance in the transferring solution and that in the transferred (i.e., crystal) state (Mullin, 2001).

3.2.1 Choosing a Solvent

There are several considerations that must be made when choosing an appropriate solvent for a crystallization process. It is important to consider the substances' solubility in the given solvent and whether the substance is easily deposited in the desired crystalline form. Polar solvents tend to dissolve polar substances and nonpolar solvents tend to dissolve nonpolar substances. It is important to ensure that the solute and solvent do not have close to the same solubilities with one another. Otherwise, crystallization may not occur (Mullin, 2001).

Additionally, no deleterious impurities should be introduced into crystallization systems. Solvents should be as pure as possible and stable under all foreseeable operating conditions (i.e., will not decompose or oxidate). The solutes and solvents should not react, and highly viscous solvents should be avoided. Since most organic solvents are flammable, stringent operating conditions and safety precautions must be in place (Mullin, 2001).

3.2.2 Residual Solvent Classes

All organic solvents are toxic to some degree. However, some are more dangerous than others. The International Council for Harmonisation (ICH) has put in place a Guideline for Residual Solvents (2016). They organized solvents into three classes (1, 2, and 3) according to their risk. Class 1 solvents were solvents to be avoided, Class 2 solvents were solvents to be limited, and Class 3 solvents were solvents with low toxic potential (International Council of Harmonisation, 2016). Table 3-9 shows the list of solvents commonly used in crystallization processes and their associated residual solvent classification.

3.2.3 Solvent Types

There are four main types of solvents: polar protic, polar aprotic, dipolar aprotic, and nonpolar aprotic. Table 3-9 contains a list of common solvents used in crystallization processes and their associated solvent type.

Table 3-9. Example of Solvent Classification According to the International Council of Harmonisation's Guideline for Solvents As Well As Their Associated Solvent Type.

Solvent Name	*Solvent Class*	*Solvent Type*
1,4-Dioxane	2	Non-Polar Aprotic
Acetonitrile	2	Polar Aprotic
Dichloromethane	2	Polar Aprotic
Dimethyl Acetamide	2	Polar Aprotic
Methanol	2	Polar Protic
Tetrahydrofuran	2	Polar Aprotic
1-Propanol	3	Polar Protic
Acetic Acid	3	Polar Protic
Acetone	3	Polar Aprotic
Dimethyl Sulfoxide	3	Polar Aprotic
Ethanol	3	Polar Protic
Ethyl Acetate	3	Polar Aprotic
2-Methyl Tetrahydrofuran	3	Polar Aprotic
Heptane	3	Non-Polar Aprotic
Isopropyl Alcohol	3	Polar Protic
Isopropyl Acetate	3	Polar Aprotic
Methyl Tert-Butyl Ether	3	Non-Polar Aprotic
Ultra-Pure Water	3	Polar Protic

Polar protic solvent molecules interact by forming strong H-bonds. These solvent molecules have dissociable hydrogen atoms. Polar protic solvents tend to contain OH or NH groups that are able to form these hydrogen bonds. To dissolve the solute, the solvent must be able to break the H-bonds and replace them with bonds of similar strength. Polar aprotic solvent molecules have no dissociable hydrogen atoms and are unable to form hydrogen bonds. They usually lie within the medium range of polarity and are polar due to bonds such as C=O (Mullin, 2001).

Dipolar aprotic solvents have high dielectric constants. These solvents interact by dipole-dipole integrations. If the solute is also dipolar or aprotic, they can form similar dipole-dipole bonds. Non-polar substances are unable to interact with dipoles and cannot dissolve. Protic solutes are soluble in basic dipolar aprotic solvents due to the high number of H-bonds formed (Mullin, 2001).

Non-polar solvents have low dielectric constants and interact by weak Van der Waals forces. Non-polar solutes are readily soluble due to their weak Van der Waals forces that interact with the similar strength forces of the solvent. Dipolar and polar protic solutes have low solubility in these solvents except when non-polar complexes are formed (Mullin, 2001).

3.2.4 Solubility

Solubility tends to increase with temperature (Mullin, 2001). The solubility characteristics of the solute in each solvent have considerable influence on the method of crystallization. For example, if a solute's solubility does not change much with temperature, cooling crystallization should be avoided due to low yield. Effects of pressure are usually considered to be negligible in most crystallization processes (Mullin, 2001).

3.2.5 Measuring Solubility

When measuring solubility, temperature control is essential. Agitation is usually necessary to bring the liquid-solid phases into contact. However, agitation in an open vessel is not recommended due to potential loss of solvent. The achievement of equilibrium (i.e., solubility) presents one of the major experimental difficulties. Several instrumental methods have been used to calculate the solubility of a substance in a solvent, and databases are available for known combinations (Mullin, 2001).

3.2.6 Supersaturation

Supersaturation occurs when a saturated solution is in a thermodynamic equilibrium with the solid phase at a specific temperature. The state of supersaturation is required for all crystallization operations. In labile supersaturation, spontaneous nucleation occurs whereas in metastable supersaturation, spontaneous nucleation would not occur (Mullin, 2001).

3.3 Solvent Recovery Systems

Solvent recovery systems are usually implemented to avoid sending waste solvent to incineration. For this project, distillation columns were used as the main separation unit for solvent recovery systems. Although distillation can be more energy intensive than other separation methods (e.g. pervaporation or membranes), it is used widely in industry.

3.3.1 Distillation

Distillation is a separation process based on differences in the volatilities and boiling points of chemicals in a liquid mixture. In distillation, one or more feed mixtures of two of more components are separated into two or more products, and often limited to, an overhead distillate and a bottoms product. These products' compositions differ from those of the feed(s) (Seader et al., 2016). Usually, the feed(s) are a vapour-liquid mixture. The bottoms product is almost always a liquid and the distillate may be a liquid, vapour, or a mixture of the two (Seader et al., 2016). Some of the condensed vapour returns to the column as reflux to aid the separation process (Aboagye et al., 2021). In distillation, separation requires a second phase to be formed so that both liquid and vapour are present and can make contact while flowing counter-current to each other in a trayed or packed column (Seader et al., 2016).

The relative volatility of the components in a liquid mixture indicates the effectiveness of the separation between the more volatile (light key) and less volatile components (heavy key). From experimental data, for relative volatilities higher than 1.2, distillation should be a suitable separation process. If the values fall between 1.2 and 1.05, distillation could still be a good option, but some other separation methods should also be considered. If the relative volatility falls below 1.05, then distillation should be avoided (Aboagye et al., 2021). The most common distillation types include flash, fractional, steam, extractive, and azeotropic distillation.

3.3.1.1 Equipment Design and Considerations

Distillation columns can either have trays or be packed. There are several factors that influence the design or analysis of binary-distillation operation (Seader et al., 2016). They are:

- Feed flow rate, composition, temperature, pressure, and phase
- Desired degree of component separation
- Operating pressure (which must below critical pressure of mixture)
- Pressure drop (particularly from vacuum operation)
- Reflux ratio
- Number of equilibrium stages and stage efficiency or HETP
- Type of condenser (total, partial, or mixed)
- Degrees of liquid reflux subcooling
- Type of reboiler (partial or total)
- Type of trays or packing
- Column height
- Feed-entry stage
- Column diameter
- Column internals and materials of construction
- Heat lability and chemical reactivity of feed components
- Corrosion and materials of construction
- Toxicity and flammability.

3.3.1.2 Initial Considerations of Design Factors

Temperature and phase of the feed are determined at the feed-tray pressure by an adiabatic-flash calculation across the feed valve. As the feed vapour fraction increases, the required reflux rate increases, but the boilup rate decreases (Seader et al., 2016). As column operating pressure increases, temperatures in the column also increase. The operating pressure at the top of the column should correspond to a saturated distillate temperature that is somewhat higher than the supply temperature of the cooling water to the overhead condenser. It is important to note that if the pressure approaches the critical pressure of the more volatile component, then a lower pressure must be used, and a refrigerant is required as the coolant. For a given feed, desired degree of separation, and operating pressure, a minimum reflux ratio exists that corresponds to an infinite number of theoretical stages. The design trade-off is between the number of stages and the reflux ratio (Seader et al., 2016).

3.3.1.3 Simulation Packages for Distillation

Due to the complexity of calculations involved in distillation, software simulation packages are usually used to perform the calculations. However, the McCabe-Thiele method can be used to get as a simplified method. For non-binary mixtures and multiple component distillation, simulation software is used due to the complications (Seader et al., 2016).

3.3.1.4 Multicomponent Distillation

Approximation methods do also exist for multicomponent distillation. They are often used for preliminary design, parametric studies to establish optimal conditions, process synthesis studies to determine optimal separation sequences, and to determine initial input approximations for rigorous, iterative methods (Seader et al., 2016).

The Fenske-Underwood-Gilliland (FUG) method can quickly provide estimates of operating pressure, equilibrium stages, and reflux ratio for a desired separation between two key components (Seader et al., 2016). These inputs can then be added to simulations where a more rigorous method can be used. Since the FUG method is useful for making preliminary multicomponent distillation calculations prior to rigorous ones, it is often included in all process simulators. The FUG method is particularly useful for the design of distillation columns for the separation of hydrocarbon mixtures (Seader et al., 2016).

3.3.1.5 Types of Distillation

There are many types of distillation processes used in industry. This section will discuss flash, fractional, steam, extractive, azeotropic, and multicomponent distillation.

3.3.1.5.1 Flash Distillation

Flash distillation is a process where a single stage process partially vaporizes the liquid feed under vacuum or atmospheric pressure in a column. This creates two phases in thermodynamic equilibrium (see Figure 3-5) (Aboagye et al., 2021). A vacuum is used for the separation of components with a high boiling point. By creating a vacuum, these compounds can be boiled at a lower temperature. Flash distillation is usually applied to separate components that have a difference in boiling points of more than 70ºC (Szekely, 2021).

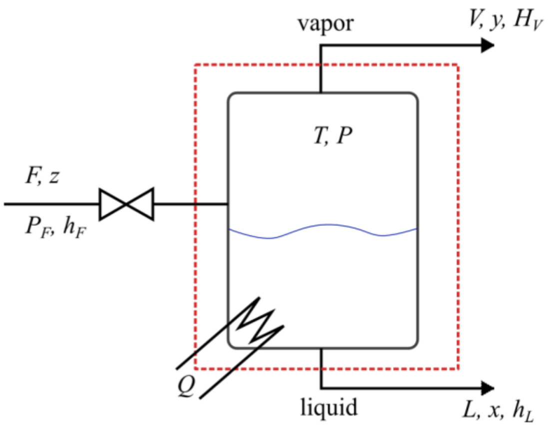

Figure 3-5. Schematic of a flash distillation unit (Iggland & Mazzotti, 2015).

3.3.1.5.2 *Fractional Distillation*

Fractional distillation is a technique that is used to separate components with similar boiling points (i.e., less than 25ºC difference) (Szekely, 2021). This separation is performed by repeated vaporizations and condensations in a fractionating column (see Figure 3-6). These columns consist of several plates and the more volatile component will move towards the top while the less volatile component will move to the bottom.

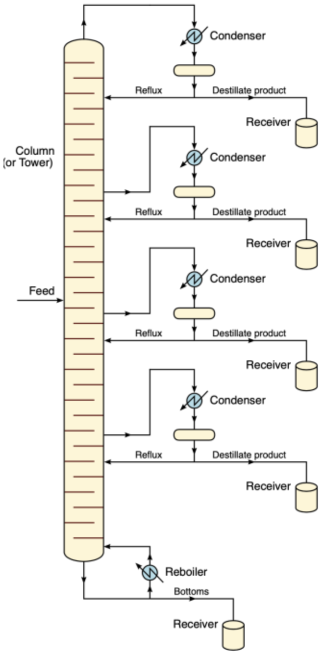

Figure 3-6. An example of a continuous fractional distillation column (Wikipedia, 2020).

3.3.1.5.3 *Steam Distillation*

Steam distillation is applied for the separation of heat-sensitive compounds. Steam is used because it provides good heat transfer rates without the need for high temperatures. For example, steam distillation is commonly used in the extraction of essential oils (see Figure 3-7) (Aleksic & Knezevic, 2014). Steam is produced in a boiler and is brought into the still. It contacts a mixture of water and plant material at the base of the still. The steam transfers the energy to the water mixture and water and essential oil vapour exits the still. The vapours are condensed using cooling water and are sent to a gravity separator where the oil is collected at the top and the plant water is collected at the bottom. This process is typically operated in batch (Aleksic & Knezevic, 2014).

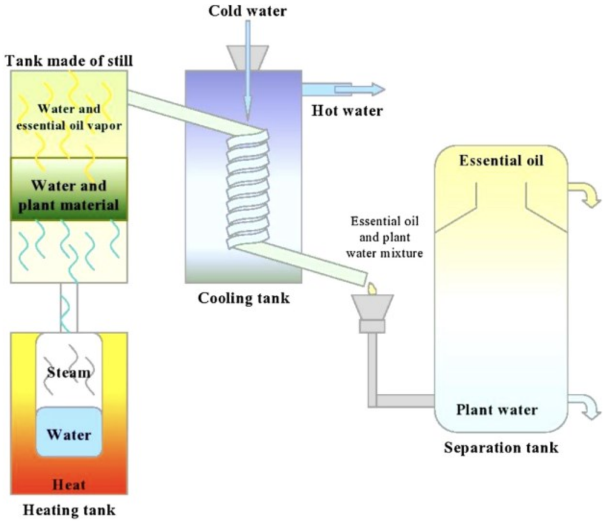

Figure 3-7. Essential oil extraction by steam distillation (Aleksic & Knezevic, 2014).

3.3.1.5.4 *Extractive Distillation*

Extractive distillation is a separation process that uses a third component (entrainer) that is miscible with the feed stream. It is commonly used to separate close boiling components and azeotropes by introducing the entrainer. The entrainer does not form an azeotrope with any other substance in the mixture and allows for easier separation between the components in the original mixture (Aboagye et al., 2021). By adding a large volume of, usually, high-boiling entrainer the liquid-phase activity coefficients can be altered so that the relative volatility of key components becomes more favourable. It is important that the proper selection of entrainer is used so that each species of the mixture has a varying affinity to the selected entrainer (Seader et al., 2016).

A typical extractive distillation set up is shown in Figure 3-8. A binary feed mixture (species A and B) is added to the first column along with an entrainer. After separation in the first column, the distillate contains a purified stream of species A and the bottoms contain the entrainer and species B. The bottoms feed is then sent to the second column where species B is extracted as a purified distillate and the entrainer is collected in the bottoms and recycled back to the first column (Wang et al., 2018). In this case, the entrainer has a lower boiling point than both species A and B; however, some entrainers have boiling points between those of species A and B. Extractive distillation is a suitable method for the separation of mixtures with low relative volatility (Aboagye et al., 2021).

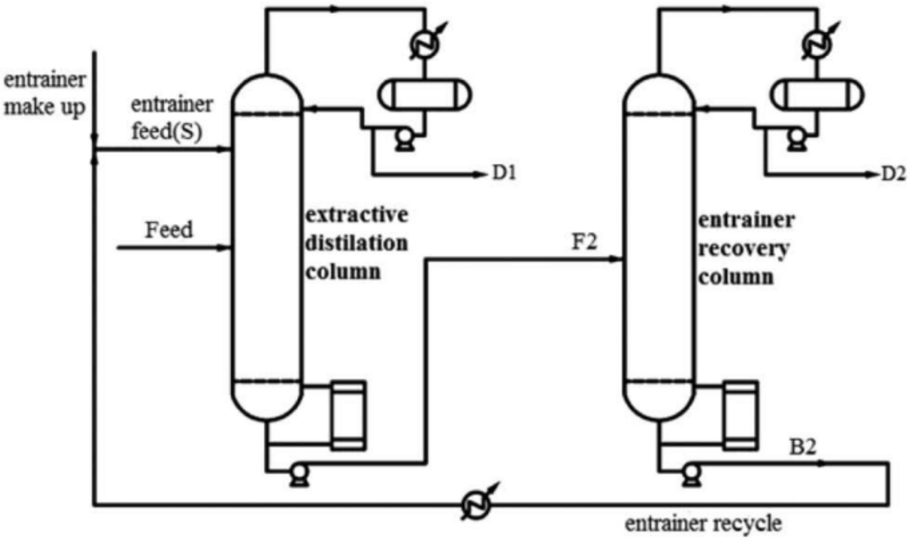

Figure 3-8. An example set up of an extractive distillation system (Wang et al., 2018).

3.3.1.5.5 *Azeotropic Distillation*

Like extractive distillation, azeotropic distillation also adds an entrainer to the mixture. However, the entrainer can form an azeotrope with the other components in the mixture. This facilitates the separation by altering the relative volatility of close-boiling or azeotrope-forming components (Aboagye et al., 2021).

3.3.1.5.6 *Conventional Distillation Sequence for Multi-Component Mixtures*

Often, distillation is required for a feed that contains more than a binary mixture. Conventional distillation sequence for multi-component mixtures is shown in Figure 3-9. A, B, and C denote the most volatile, middle, and least volatile components, respectively. A is removed as distillate in the first column, and then B and C are separated in the second column.

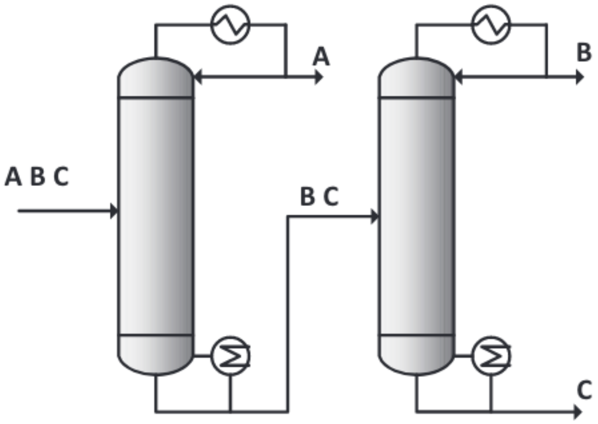

Figure 3-9. Conventional direct distillation sequence (Chaniago et al., 2015).

3.3.1.5.7 Thermally Coupled Distillation

In conventional sequence distillation, every column contains a condenser and a reboiler for heat transfer. However, it is possible to use a material flow to provide some of the necessary heat transfer by direct contact (i.e., thermal coupling). Thermally coupled distillation (TCD) systems can be constructed through the carrying of two interconnecting streams (one in the liquid phase and the other in the vapour phase) between the two columns. A popular TCD configuration is the sequence with a side rectifier (see Figure 3-10a). The side rectifier is topologically and thermodynamically equivalent to the thermally coupled direct sequence (Figure 3-10b) but has practical difficulty in engineering. The thermally coupled direct sequence system is easier to be analyzed than the side rectifier (Chaniago et al., 2015). In the thermally coupled distillation sequences, A is still separated from the first column. B is then separated in the second column. C is separated in either the first column or in the second column with the absence of one reboiler in the operation, depending on the configuration.

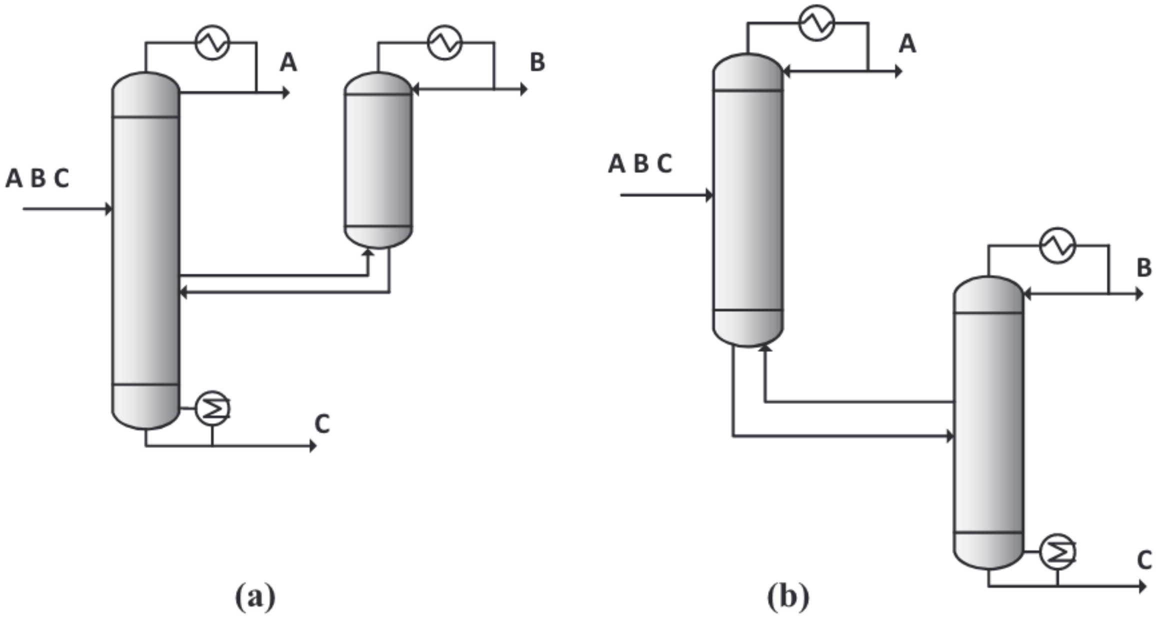

Figure 3-10. Thermally coupled distillation sequences. (a) side rectifier configuration (b) thermally coupled direct sequence (Chaniago et al., 2015).

3.3.1.5.8 Thermal Integration of Heat Pump Assisted Distillation

Distillation columns are thermodynamically comprised of a heat source (condenser) and a heat sink (reboiler). Conventionally, the column uses hot utility to supply heat to the bottom reboiler and wastes heat to cold utility at the overhead condenser. Therefore, an obvious way to reduce energy consumption is to integrate heat removal at the condenser to the reboiler. The heat pumping system has emerged as one of the widely used schemes for continuous distillation columns among various heat integrated distillation techniques (Chaniago et al., 2015). In these systems, excess heat from one part of the process is pumped to another part of the process. Usually this is done to pre-heat a feed stream prior to entering one of the columns. This provides thermal integration into the system and allows for increased efficiency and lower utility costs.

3.3.1.6 Solvent Recovery System Layout

The solvent recovery system for this project (shown in Figure 3-11) consists of a set distillation units to separate the required amount of solvent to their necessary purity levels followed by a filtration unit to collect the remaining solvent and then a vacuum dryer to collect any additional portion of API. An equipment table of the solvent recovery system can be found in Table 3-10.

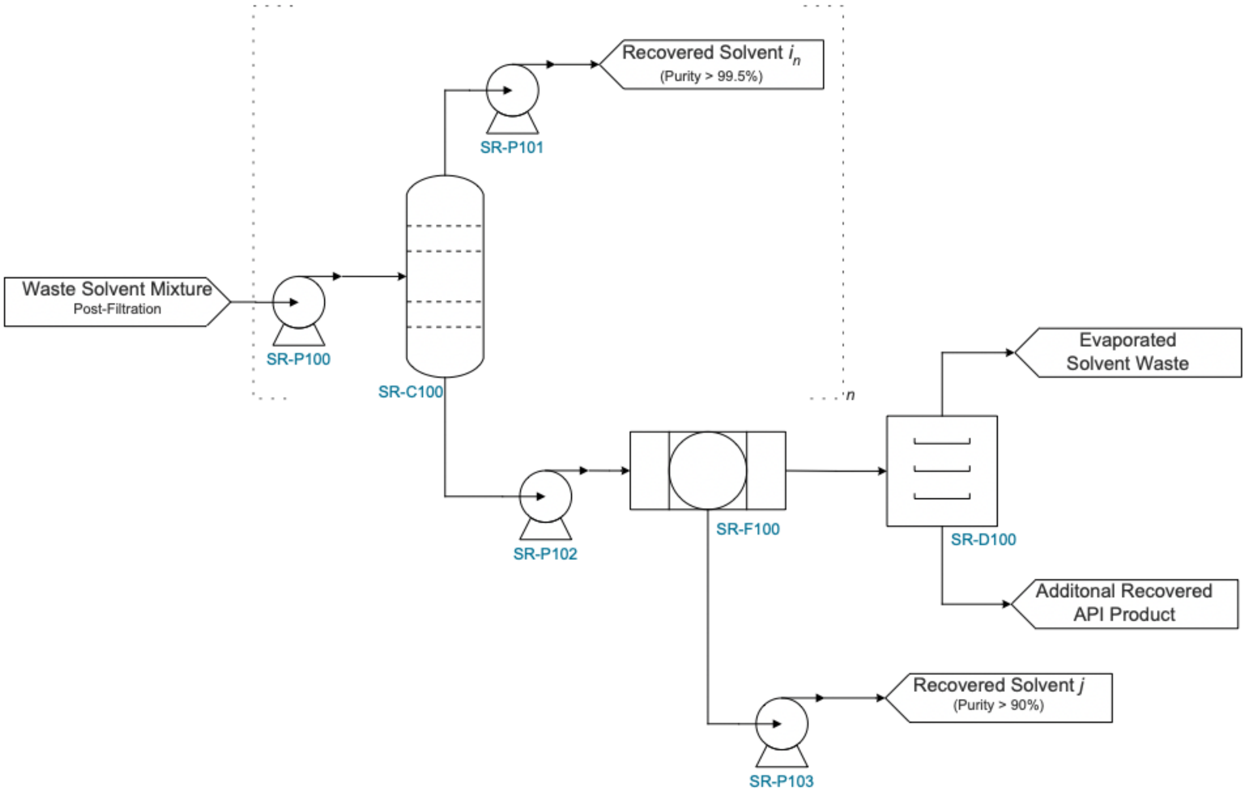

Figure 3-11. PFD of solvent recovery system.

Table 3-10. PFD of solvent recovery system.

Equipment Label	**SR-C100**	**SR-F100**	**SR-D100**	**SR-P10X**
Equipment	Distillation Unit	Filtration Unit	Vacuum Drying Unit	Centrifugal Pumps

3.4 Life Cycle Assessment

Life cycle assessment (LCA) stands as a universally recognized framework employed to assess the potential environmental impacts across all stages of a process, product, or service's life cycle. By using LCA, one can quantify the resource consumption (including materials and energy), emissions, and subsequent environmental consequences throughout the entire supply chain. This encompasses raw material extraction and conversion, manufacturing, transportation, sales, distribution, use, and eventual disposal (Matthews et al., 2014).

The four fundamental steps involved in conducting an LCA are as follows (Matthews et al., 2014):

1. Goal and scope definition, where the objectives and boundaries of the assessment are established.
2. Life cycle inventory analysis (LCI), which entails collecting and compiling data on the inputs and outputs of the system being studied.
3. Life cycle impact assessment (LCIA), where the collected inventory data is evaluated to assess its potential environmental impacts.
4. Interpretation of the results, involving the comprehensive analysis and communication of the findings.

The primary objectives of conducting an LCA can vary, but commonly include identifying process hotspots associated with significant environmental impacts, comparing the environmental performance of alternative processes used to produce the same product, or evaluating the environmental impact of various products serving the same function.

The initial LCA study conducted at Coca-Cola in 1969 marked a milestone in the field. It aimed to compare the environmental trade-offs between glass and plastic bottles, shedding light on their respective impacts (Matthews et al., 2014). Since then, the capabilities of LCA have significantly evolved, transforming it from a limited number of case studies to a recognized decision-making tool for strategic direction. To provide a standardized framework for conducting LCA, the International Standards Organization (ISO) issued a set of standards, namely ISO 14040 and its subsections 14041, 14042, and 14043, between 1997 and 2006 (Jiménez-González & Overcash, 2014). These standards serve as guidance for conducting LCA studies, ensuring consistency and reliability in the process.

During the goal and scope definition stage, which is the initial phase of LCA, the study's boundary is determined based on the specific objectives. This boundary can encompass the entire supply chain, covering the cradle-to-grave life cycle, or it may be limited to a specific section, such as a chemical plant, known as gate-to-gate analysis. The project’s boundary will be a cradle-to-gate analysis.

Moving on to the second stage of LCA, known as life cycle inventory analysis, the focus is on quantifying input energy, materials, output byproducts/products, and emissions. Collecting inventory data involves various methods, including industrial surveys to gather site-specific information, perform calculations, and establishing mass and energy balances across the system boundary. It is worth noting that inventory compilation is often the most time-consuming aspect of LCA. In the context of pharmaceutical processing, obtaining reliable life cycle inventory data can be particularly challenging. This is primarily due to the use of fine chemicals with complex molecular structures, which are often produced through intricate synthetic procedures. Additionally, the confidentiality of certain active pharmaceutical ingredient (API) synthetic procedures limits the availability of data (Ott et al., 2014).

The third stage of LCA, known as life cycle impact assessment (LCIA), entails using the results obtained from the life cycle inventory analysis to evaluate the potential human and ecological effects associated with the process or product under study. This assessment enables researchers to gain insights into the environmental implications and potential impacts throughout the life cycle.

In the final stage of LCA, the interpretation stage, the results obtained are carefully examined and discussed by researchers. The aim is to identify areas that require improvement to enhance the overall sustainability of the process or product. This stage serves as a crucial step in identifying opportunities for process optimization, product innovation, and sustainable development.

When conducting LCA, several challenges are commonly encountered (Jiménez-González & Overcash, 2014). These challenges include:

- Developing a comprehensive strategy for inventory compilation that aligns with the study's objectives, ensuring that all relevant aspects of the system are considered.
- Interpreting the LCA outcomes to inform decision-making processes, which may involve modifying the existing process, exploring innovative technologies, or developing new sustainable products.

Although not yet a routine practice in many businesses, the significance of LCA as a tool for promoting environmental sustainability is gaining increasing attention. In recent decades, various green metrics have emerged to facilitate the identification of bottlenecks and areas for improvement within business operations (Adams et al., 2013; Prat et al., 2013). Examples of such metrics include:

- Process mass intensity (PMI): The ratio of input materials (in kilograms) to the product (in kilograms).

- Reaction mass efficiency (RME): The ratio of reactants (in kilograms) to input materials (in kilograms).
- E-factor: The ratio of waste (in kilograms) to the product (in kilograms).

Additionally, these metrics have been used to estimate the potential CO_2 emissions associated with specific target products (Ott et al., 2014). Consequently, guidelines have been formulated to encourage sustainable practices in the pharmaceutical industry (Jiménez-González et al., 2011). For instance, the E-factor in the pharmaceutical sector tends to be significantly higher compared to that of oil refining and bulk industries, primarily due to factors such as complex synthetic procedures, API isolation, and purification processes (Ott et al., 2014). Therefore, pharmaceutical industries are seeking to innovate by exploring alternative raw materials, designing novel synthetic routes, and implementing advanced isolation and purification techniques to minimize waste generation (Becker et al., 2022a). Despite these efforts, the pharmaceutical industry still faces a considerable waste management challenge, with organic solvents accounting for a significant portion of the waste generated (Prat et al., 2013).

Chapter 4: Methods

4.1 Mass Balance

The mass of substances and solvents added to the crystallization processes was determined through the number of volumes in relation to the mass of API added and density (g/mL) of the chemical. All densities of the solutions were calculated at room temperature (i.e., 25°C).

$$m_{sol} = \rho V_{sol} m_{api} \tag{4-1}$$

where m_{sol} is the mass of solvent (g), ρ is the density of the solvent (g/L), V_{sol} is the volume ratio of solvent to API mass (mL/g), and m_{api} is the mass of the API (g).

4.2 Energy Requirements

The heat required to change temperatures of the solutions was determined through the following equations:

$$\Delta H = m c_p \Delta T \tag{4-2}$$

$$\int_{H_1}^{H_2} dH = m \int_{T_1}^{T_2} c_{pL}(T) dT \tag{4-3}$$

where m is the mass of solvent (kg), c_p is the heat capacity of the solvent (kJ/K•kg), and ΔT is the temperature difference (K).

The integrated specific heat portion of the specific heat calculation for most solvents is shown below:

$$\int_{T_1}^{T_2} c_{pL}(T) dT = C_1(T_2 - T_1) + \frac{C_2(T_2^2 - T_1^2)}{2} + \frac{C_3(T_2^3 - T_1^3)}{3} + \frac{C_4(T_2^4 - T_1^4)}{4} + \frac{C_5(T_2^5 - T_1^5)}{5} \tag{4-4}$$

where $c_{pL}(T)$ is the heat capacity of the solvent between two temperatures (kJ/kg), T_1 is the initial temperature (K), T_2 is the final temperature (K), and C_1 to C_5 are constants.

For heptane, the integrated specific heat portion is:

$$\begin{aligned}\int_{T_1}^{T_2} c_{pL}(T)dT = {} & C_1^2 T_c \log(T_c - T_1) - C_1^2 T_c \log(T_c - T_2) - C_2(T_2 - T_1) \\ & - 2C_1C_3\left((T_2 - T_1) - \frac{(T_2^2 - T_1^2)}{2T_c}\right) \\ & - C_1C_4\left(\frac{T_2^3 - T_1^3}{3T_c^2} - \frac{T_2^2 - T_1^2}{T_c} + T_2 - T_1\right) + \frac{C_3^2 T_c}{12}\left(1 - \frac{(T_2 - T_1)}{T_c}\right)^4 \\ & - \frac{C_3C_4T_c}{10}\left(\frac{(T_2 - T_1)}{T_c} - 1\right)^5 + \frac{C_4^2 T_c}{30}\left(1 - \frac{(T_2 - T_1)}{T_c}\right)^6\end{aligned} \tag{4-5}$$

where T_c is the critical temperature of the solvent (K).

To determine the total heat required for heating or cooling, each solvent's heat was calculated from the solution. The API was ignored in these calculations. The energy required to heat or cool each solvent to its desired temperature was then combined with their masses to determine the total energy required to heat that mass of solution. It was assumed that all solvents added to the processes were added at room temperature (i.e., 25°C).

According to Parvatker et al. (2019) pumping, filtration, drying, distillation, and stirring energy requirements could be calculated using equations found in Table 4-1. E_{pump}, E_{filt}, E_{dry}, E_{dist}, and $E_{stir(1000L)}$ are the energy requirements for pumping, filtration, drying, distillation, and stirring, in units of kWh, respectively. m is the mass of the chemical species in kg. Subscripts $F, ES, liq,$ and D refer to feed, evaporated solvent, liquid solution, and distillate, respectively. ΔT is the temperature difference in ºC; ΔH_v is the enthalpy of vaporization in kWh; T_r is reduced temperature; T_c is the critical temperature in ºC. η is the efficiency; R_{min} is the minimum reflux ratio; α is the relative volatility; X_{LD} is the mole fraction of the light key in the distillation; X_{LF} is the light key in the feed; $T_2 - T_1$ is the boiling point difference between of the separating mixture in ºC; T_{boil} is the boiling point of the mixture; C_i is a constant used to calculate specific heat or heat of vaporization; C_p is the specific heat capacity in kWh/kg•K; ρ_{mix} is the density of the mixture in kg/m^3; and t is time in seconds. Sample calculations can be found in Appendix B.1

Table 4-1. Energy equations used for various unit operations. Units for energy are all in kWh.

Name	***Equation***	***Reference***
Pumping	$E_{pump} = 0.01153\ \times 10^{-5}\ m_{liq}$	(4-6)
Filtration	$E_{filt} = 0.01\, m_{sol}$	(4-7)
Drying	$E_{dry} = \dfrac{m_F \Delta H_{c_p}^{F} + m_{ES} \Delta H_v^{ES}}{\eta_{heat}}$ $\Delta H_v = C_1(1 - T_r)^{(C_2 + C_3 T_r + C_4 T_r^2)}\ where\ T_r = T/T_c$ $\Delta H_{c_p} = C_1(T_2 - T_1) + \dfrac{C_2(T_2^2 - T_1^2)}{2} + \dfrac{C_3(T_2^3 - T_1^3)}{3} + \dfrac{C_4(T_2^4 - T_1^4)}{4} + \dfrac{C_5(T_2^5 - T_1^5)}{5}$	(4-8) (4-9) (4-10)
Distillation	$E_{dist} = \dfrac{m_D \Delta H_v (1.3 R_{min} + 1)}{\eta}$ $R_{min} = \dfrac{1}{\alpha - 1}\left(\dfrac{X_{LD}}{X_{LF}} - \dfrac{\alpha(1 - X_{LD})}{(1 - X_{LF})}\right)$ $\log \alpha = \dfrac{T_2 - T_1}{T_{boil}}(3.99 + 0.001939 T_{boil})$	(4-11) (4-12) (4-13)
Stirring	$E_{stir(1000L)} = 0.0180 \rho_{mix} t$	(4-14)
Heating	$E_{heat} = m_F c_p \Delta T$	(4-15)

To determine the power required by the vacuum pump, a typical size factor has to be determined using:

$$SF = \frac{Air\ equivalent\ flow\ rate\ [kg/h]}{Operating\ pressure\ [mmHg]} \tag{4-16}$$

The typical air filtration rate for a vacuum pump is 10 m^3/h (Sanatron, 2022) and operating pressure of 29 inHg (i.e., 737 mmHg), the typical size factor for a vacuum pump was determined to be 0.02. The power of the vacuum pump was then calculated using (Parvatker et al., 2019):

$$Power = 4.242 \times SF^{1.088} \tag{4-17}$$

This resulted in a typical vacuum pumping power of 0.048 kW.

4.3 Nova Scotia Electricity Production Mix

The province of Nova Scotia's electricity production mix can be found in Table 4-2 (Canada Energy Regulator, Government of Canada, 2022).

Table 4-2. Nova Scotia's Electricity Production Mix as of 2020.

Electricity Source	*Percentage*
Coal	51.37%
Natural Gas	15.95%
Renewables	14.57%
Hydro	13.81%
Biomass	3.21%
Oil	1.08%

The Ecoinvent database v3.9.1 contains inventory information for Nova Scotia's electricity production mix up to this date and will be used for the impact assessment.

4.4 Economic Analysis

There are several aspects that are involved in evaluating the cost of a crystallization process. For this study, the following costs will be considered: the cost of solvent, cost of electricity from the energy requirements of the equipment, cost of incineration of solvent, capital cost of implementing solvent recovery systems, and cost savings from reuse of solvents using solvent recovery systems.

4.4.1 Capital Cost Estimation

A shortcut method was used to determine the capital cost of the solvent recovery system. According to Towler & Sinnott (2022)., a step-count method can be used to provide order of magnitude estimates on capital cost. Their research has shown that 80% of capital cost is associated with distillation and product purification sections (Towler & Sinnott, 2022). The capital cost can be estimated based on the cost of a known process if the separation and recovery system have a similar size and complexity to that of the known process. The Bridgewater method can then be used to correlate plan cost to the number of processing steps (Towler & Sinnott, 2022) and can be described as:

$$Q \geq 60{,}000\colon C = 4320N\left(\frac{Q}{s}\right)^{0.675} \tag{4-18}$$

$$Q < 60{,}000\colon C = 380{,}000N\left(\frac{Q}{s}\right)^{0.3} \tag{4-19}$$

where C is the capital cost in USD, January 2010 basis (CEPCI = 532.9), Q is the plant capacity in metric tons/year, s is the recovery rate of the product in the distillate, and N is the number of functional units. A functional unit includes all equipment and ancillaries needed for a significant process step or function of the separation (Towler & Sinnott, 2022). However, pumping and heat exchangers are not normally considered functional units unless they have substantial cost. For this study, it was assumed that N is equal to the number of distillation columns in the proposed recovery system and s was assumed to be 0.995 since the recovery was 99.5%.

4.4.2 Operating Cost Estimation

There are five main operating costs that will be considered throughout this project: solvent purchase cost, electricity cost for energy requirements, waste incineration cost, depreciation cost, and labour cost.

4.4.2.1 Solvent Purchase Cost

A literature review was conducted to determine the cost of various solvents. A baseline of 55 gallons or 200 L of solvent was used as the base unit to determine the cost of solvent per millilitre. The majority of the solvent costs were found at Spectrum Chemical, Lab Alley, or Fisher Scientific (Fisher Scientific, 2024; Lab Alley, 2024; Spectrum Chemical, 2024). Values can be found in Table C-1 in Appendix C: Solvent Information.

4.4.2.2 Electricity Cost for Energy Requirements

In January 2024, the medium industry electricity tariff in Nova Scotia was \$0.10711/kWh (Nova Scotia Power, 2024). This value aligns well to the \$0.10/kWh that was reported by Savelski et al. (2017). For the purpose of this project, it will be assumed that all energy requirements came from the electrical grid.

4.4.2.3 Waste Incineration Cost

Waste incineration cost will be assumed to be \$0.13/kg of waste incinerated (Savelski et al., 2017). This cost will be used to calculate initial operating cost of the API crystallization processes but will also be used for calculating the payback period of the implementation of the solvent recovery systems.

4.4.2.4 Depreciation Cost

All physical assets such as solvent recovery systems equipment decrease in value with time. For the purpose of this analysis, it will be assumed that a solvent recovery system has a service life of 25 years and will have a no scrap value (Chea et al., 2020).

Annual depreciation can be determined through:

$$d = \frac{C_i - C_S}{n} \tag{4-20}$$

where d is the annual depreciation cost (USD), C_i is the initial cost of equipment (USD), C_S is the scrap value of the equipment, and n is the service life of the equipment (Cooper & Alley, 2011).

4.4.2.5 Labour Cost

Labour cost will be taken into consideration when implementing a solvent recovery system to properly determine payback period of the capital investment. For a continuous process, it will be assumed that labour cost of a solvent recovery system is \$30/hour for 330 working days annually (Chea et al., 2020). Further, some labour goes into collecting waste to be sent to incineration. Since this does not always require constant attention, it will be assumed that labour cost for waste collection takes up 8 hours per working day and cost the same \$30/hour for 330 working days annually.

4.4.3 Payback Period

Payback period is a simple measure of profitability. It represents the length of time required to recover the depreciable fixed capital investment of a project. It can be defined by the following equation (Cooper & Alley, 2011):

$$Payback\ Period = \frac{fixed\ capital\ investment}{(annual\ profit + annual\ depreciation)_{avg}} \quad (4\text{-}21)$$

The fixed capital cost would be the total capital cost of each solvent recovery system calculated in equation (4-18) or (4-19). The annual profit would consist of the amount of cost savings from recovered solvent and waste incineration minus the additional utilities and labour cost. Annual depreciation is calculated from equation (4-21).

4.4.4 Rate of Return on Investment

Another frequently used measure of profitability of an investment is the rate of return on investment (ROI). It can be defined as:

$$ROI = \frac{P}{I} \times 100\% \quad (4\text{-}22)$$

where P is the annual profit from the investment (income – expenses) in $USD and I is the total investment in $USD (Cooper & Alley, 2011).

4.4.5 Process Scale Up

To scale up the solvent recovery system to industrial scale, a scaling factor had to be determined. A 2022 report by the Canadian Generic Pharmaceutical Associated that 4,898,000 kg of API were produced or imported between 2019 and 2021 (Canadian Generic Pharmaceutical Association, 2022). In terms of production scale, three scales will be examined: 100, 1000, and 10,000 kg of API produced annually. The 100 kg production scale was chosen because it is the typical scale at which clinical trial batches start. Two additional scales were used 10-fold and 100-fold increase from clinical trial batches to assess various payback periods.

4.5 Life Cycle Impact Assessment Information

Delta Green's OpenLCA software with the addition of Ecoinvent v3.9.1 database were used to conduct the LCI. ReCiPe 2016 Midpoint (H) impact method that was used to for the analysis. Eighteen impact categories were examined: terrestrial acidification potential (TAP), global warming potential (GWP100), freshwater ecotoxicity potential (FETP), marine ecotoxicity potential (METP), terrestrial ecotoxicity potential (TETP), fossil fuel potential (FFP), freshwater eutrophication potential (FEP), marine eutrophication potential (MEP), human toxicity potential – carcinogenic (HTPc), human toxicity potential – non-carcinogenic (HTPnc), ionising radiation potential (IRP), agricultural land occupation (LOP), surplus ore potential (SOP), ozone depletion potential ($ODP_{infinite}$), particulate matter formation potential (PMFP), photochemical oxidant formation potential – humans (HOFP), photochemical oxidant formation potential – ecosystems (EOFP), water consumption potential (WCP). The functional unit used in this study was 1 kg of API final product.

4.5.1 Life Cycle Perspectives

For this project, the hierarchist perspective was selected. However, a brief description of the two other perspectives (individualistic and egalitarian) will also be discussed.

4.5.1.1 Individualistic Perspective

The individualistic perspective is based on the short-term interest. There is technological optimism regarding human adaptation (Huijbregts et al., 2016). In terms of climate change, an individualistic perspective looks at a 20-year time horizon, an optimistic future socio-economic development, but no climate-carbon feedback of non-CO_2. For ozone depletion, a 20-year time horizon is used and includes skin cancer effects. Ionizing radiation uses a 20-year time horizon and a 10 dose-and-dose rate effectiveness factor, and includes effects like thyroid, bone marrow, lung, and breast cancer as well as hereditary disease. Fine particulate matter contains effects of primary aerosols only. Toxicity is examined in a 20-year time horizon with all exposure routes for human toxicity for organic compounds and drinking water and air for metals. Sea and oceans are examined for marine ecotoxicity for organic compounds and non-essential metals. However, for essential metals, only seas are included. Only carcinogenic chemicals classified as 1, 2A, 2B by IARC are included. Further, ecotoxicity requires a minimum of four tested species. For water use, a high regulation of stream flow is implemented, and 1000 m^3/year/capita water requirement is used for food production with no impact on terrestrial ecosystems considered. Mineral resource scarcity examines future production as reserves only (Huijbregts et al., 2016).

4.5.1.2 Hierarchist Perspective

The hierarchist perspective is based on the scientific consensus regarding the time frame and plausibility of impact mechanisms (Huijbregts et al., 2016). In terms of climate change, an hierarchist perspective looks at a 100-year time horizon, a baseline future socio-economic development, and climate-carbon feedback of non-CO_2. For ozone depletion, a 100-year time horizon is used and includes skin cancer effects. Ionizing radiation uses a 100-year time horizon and a six dose-and-dose rate effectiveness factor, and includes effects like thyroid, bone marrow, lung, breast, bladder, colon, ovary, skin, liver, oesophagus, and stomach cancer as well as hereditary disease. Fine particulate matter contains effects of primary aerosols and secondary aerosols from SO_2, NH_3, NO_x. Toxicity is examined in a 100-year time horizon with all exposure routes for human toxicity for all chemicals. Sea and oceans are examined for marine ecotoxicity for all chemicals. All chemicals with reported carcinogenic effects are included. Further, ecotoxicity requires a minimum of one tested species. For water use, a standard regulation of stream flow is implemented, and 1350 m^3/year/capita water requirement is used for food production as well as the impact on terrestrial ecosystems. Mineral resource scarcity examines future production as the ultimate recoverable resource (Huijbregts et al., 2016).

4.5.1.3 Egalitarian Perspective

The egalitarian perspective is the most precautionary perspective. This considers the longest time frame and all impact pathways where data is available (Huijbregts et al., 2016). In terms of climate change, an egalitarian perspective looks at a 1000-year time horizon, a pessimistic future socio-economic development, and no climate-carbon feedback of non-CO_2. For ozone depletion, an infinite time horizon is used and includes skin cancer and cataract effects. Ionizing radiation uses a 100,000-year time horizon and a two dose-and-dose rate effectiveness factor, and includes effects like thyroid, bone marrow, lung, breast, bladder, colon, ovary, skin, liver, oesophagus, stomach, bone surface and remaining cancer as well as hereditary disease. Fine particulate matter contains effects of primary aerosols and secondary aerosols from SO_2, NH_3, NO_x. Toxicity is examined in an infinite time horizon with all exposure routes for human toxicity for all chemicals. Sea and oceans are examined for marine ecotoxicity for all chemicals. All chemicals with reported carcinogenic effects are included. Further, ecotoxicity requires a minimum of one tested species. For water use, a standard regulation of stream flow is implemented, and 1350 m^3/year/capita water requirement is used for food production and for the impact on terrestrial ecosystems. Mineral resource scarcity examines future production as the ultimate recoverable resource (Huijbregts et al., 2016).

4.5.2 Environmental Impacts

Eighteen impact categories were investigated using ReCiPe 2016 Midpoint (H) method. They are described in more detail below.

4.5.2.1 Climate Change

An emission of a greenhouse gas (GHG) leads to an increased atmospheric concentration of GHG. This will increased the radiative forcing capacity and lead to an increase in the global mean temperature. Increase global temperature will result in damage to human health and ecosystems (Huijbregts et al., 2016).

The global warming potential (GWP), expressed in units of CO_2 equivalents, expresses the amount of additional radiative forcing integrated over 100 years caused by an emission of 1 kg of GHG relative to the additional radiative forcing integrated over that same time horizon caused by the release of 1 kg of CO_2. The amount of radiative forcing integrated over time caused by the emission of 1 kg of GHG is expressed as the absolute global warming potential (AGWP) in units of W/m^2 kg. GWP is calculated as in Huijbregts et al., (2016):

$$GWP_{x,100} = \frac{AGWP_{x,100}}{AGWP_{CO_2,100}} \tag{4-23}$$

where x is the $AGWP_{x,100}$ is the GHG with a 100-year time horizon and $AGWP_{CO_2\,,100}$ is the CO_2 with a 100-year time horizon. The results yield a time-horizon-specific GWP with units of kg CO_2 equivalents/kg GHG (Huijbregts et al., 2016). The GWPs for 100 years are directly provided by the 2013 IPCC report (Stocker et al., 2013).

4.5.2.2 Stratospheric Ozone Depletion

Emissions of ozone depleting substances (ODS) can ultimately lead to damage to human health because of the resultant increase of UVB-radiation (Huijbregts et al., 2016). Chemicals that deplete ozone are relatively persistent and have chlorine and bromine groups in their molecules that mainly interact with ozone in the stratosphere. After an emission of ODS, the tropospheric concentrations of all ODS increase and, in time, causes the stratospheric concentrations to also increase. The increase in ozone depletion potential leads to a decrease in the atmospheric ozone concentration, which causes a larger portion of UVD-radiation to hit the earth. This radiation negatively affects human health and can increase the incidence of skin cancer and cataracts (Huijbregts et al., 2016).

The ozone depletion potential (ODP) expressed in unis of kg CFC-11 equivalents, quantifies the amount of ozone a substance can deplete relative to CFC-11 for a specific time horizon. It is largely related to the molecular structure of the ozone depleting substance, especially to the number of chlorine or bromine groups in the molecule and the atmospheric lifetime of the chemical. OPDs are calculated in a semi-empirical fashion by the World Meteorological Organization and ReCiPe 2016 uses the 2010 values (Huijbregts et al., 2016).

4.5.2.3 Ionizing Radiation

Anthropogenic emissions of radionuclides are generated in the nuclear cycle (e.g., mining, processing, and waste disposal) and other human activities (e.g., coal burning, phosphate rock extraction). Exposure to the ionizing radiation caused by these radionuclides can lead to damaged DNA molecules (Huijbregts et al., 2016). During a fate analysis, the environmental fate of an emitted radionuclide can be assessed. The exposure analysis is used to estimate the collective exposure dose (units of Man Sievert) caused by the emission of a radionuclide. The unit of Man Sievert represents the total average exposure in J/kg body weight multiplied by the number of people in a population (assumed to be 10 billion for the next 100,000 years) integrated over time. The ionizing radiation potential (IRP) can be calculated as (Huijbregts et al., 2016):

$$IRP_{x,air} = \frac{CD_{x,air}}{CD_{Co_{60},air}} \tag{4-24}$$

where $CD_{x,air}$ is the collective dose of substance x released to air and $CD_{Co_{60},air}$ is the collective dose of the reference unit (Cobalt-60) released to air. The $IRP_{x,air}$ represents the ionizing radiation potential (in units of 1 kBq) of a substance emitted to air (Huijbregts et al., 2016).

4.5.2.4 Fine Particulate Matter Formation

Air pollution that causes primary and secondary aerosols in the atmosphere can have a substantial negative impact on human health, ranging from respiratory symptoms to hospital admissions and death (Huijbregts et al., 2016). Fine particulate matter is defined of having a diameter less that 2.5 μm (PM2.5). These particulates are composed of a mixture of organic and inorganic substances.

PM2.5 aerosols are formed in air from emissions of sulfur dioxide, ammonia, and nitrogen oxides, as well as other elements (Huijbregts et al., 2016). The intake of a pollutant plays an important role in determining the fine particulate matter formation potential. The intake fraction (*iF)* of fine particulate matter due to emissions to a region *i* is determined by precursor *x*. Particulate matter formation potentials (PMFP) can be expressed as (Huijbregts et al., 2016):

$$PMFP_{x,i} = \frac{iF_{x,i}}{iF_{PM2.5,world}} \tag{4-25}$$

where $iF_{PM2.5,world}$ is the emission-weighted world average intake fraction of PM2.5.

4.5.2.5 Photochemical Ozone Formation

Air pollution that causes primary and secondary aerosols in the atmosphere can have substantial negative impacts on human health (Huijbregts et al., 2016). Ozone is not directly emitted into the atmosphere but is formed because of photochemical reactions of NO_x and non-methane volatile organic compounds (NM-VOCs). Ozone formation is more intense in the summer months. Ozone is a health hazard to humans because it can inflame airways and damage lungs. Ozone concentrations lead to an increased frequency and severity of respiratory distress in humans (e.g., asthma and chronic obstructive pulmonary disease. Ozone can also have a negative impact (e.g., reduction in seed growth, acceleration of leaf senescence, reduced ability to withstand stressors) on the terrestrial environment. Ozone formation is a non-linear process that depends on meteorological conditions and background concentrations (Huijbregts et al., 2016).

4.5.2.6 Terrestrial Acidification

A change in acidity in the soil can come from atmospheric deposition of inorganic substances (e.g., sulphates, nitrates, and phosphates) (Huijbregts et al., 2016). For nearly all plant species, there is a clearly defined optimum level of acidity and acidification occurs when a serious deviation from this optimum level becomes harmful for that kind of species.

The fate of a pollutant in the atmosphere and the soil are important for the midpoint characterization factors of terrestrial ecosystem damage due to acidifying emissions. The acidification potential (AP), expressed in kg SO_2 equivalents, can be calculated as (Huijbregts et al., 2016):

$$AP_{x,i} = \frac{FF_{x,i}}{FF_{SO_2,world\ average}} \tag{4-26}$$

where $FF_{x,i}$ is the fate factor due to emissions in the grid i by precursor x and $FF_{SO_2,world\ average}$ is the emission-weighted world average fate factor of SO_2.

The fate factors are determined through atmospheric fate factors and a soil sensitivity fate factor. The atmospheric fate factors represent the climatic conditions and deposition mechanisms between the source and a reception location in a single fraction. The soil sensitivity can be determined as the receptor change in soil properties over a certain area due to a certain deposition in a single fraction (Huijbregts et al., 2016).

4.5.2.7 Freshwater Eutrophication

Freshwater eutrophication occurs due to the discharge of nutrients into soil or into freshwater bodies and leads to a subsequent rise in nutrient levels (i.e., phosphorus and nitrogen) (Huijbregts et al., 2016). Environmental impacts related to freshwater eutrophication follow a sequence of ecological impacts offset by increasing nutrient emissions into fresh water. This, in turn, increases nutrient uptake by autotrophic organisms (e.g., cyanobacteria and algae) and heterotrophic species (e.g., fish and invertebrates). Consequently, this leads to a relative loss of species (Huijbregts et al., 2016).

The new global fate model on a half-degree grid resolution is used to derive the fate factors for phosphorus emissions to fresh water. The fate factor represents the net residence time in the freshwater compartment (in years). The freshwater eutrophication potential (FEP), expressed in kg P to freshwater equivalents, can be define as (Huijbregts et al., 2016):

$$FEP_{x,c,i} = \frac{FF_{x,c,i}}{FF_{P,fw,world\ average}} \tag{4-27}$$

where $FF_{x,c,i}$ is the fate factor of substance x emitted to compartment c in grid cell i and $FF_{P,fw,world\ average}$ is the world average fate factor of phosphorus emission to freshwater.

4.5.2.8 Toxicity

The characterization factor human toxicity and ecotoxicity accounts for the environmental persistence (fate), accumulation in the human food chain (exposure), and toxicity (effect) of a chemical (Huijbregts et al., 2016). The toxicity potential, expressed in kg 1,4-dichlorombenzene equivalents (1,4-DCB eq.) is used to characterize the midpoint level for human toxicity, freshwater ecotoxicity, marine ecotoxicity, and terrestrial ecotoxicity. The ecotoxicological midpoint characterization factor can be determined through (Huijbregts et al., 2016):

$$ETP_{x,i,j,c} = \sum \frac{FF_{x,i,j,g,c} \times EF_{x,j,c}}{FF_{DCB,ref,j,g,c} \times EF_{DCB,j,c}} \tag{4-28}$$

where $ETP_{x,i,j,c}$ is the ecological toxicity potential for receiving compartment j (freshwater, marine, or terrestrial) of chemical x emitted to compartment i, transported to receiving compartment j, related to cultural perspective c (kg 1,4-DCB eq. to freshwater for freshwater ecotoxicity, to seawater for marine ecotoxicity, and to industrial soil for terrestrial ecotoxicity), $FF_{x,i,j,c}$ is the fate factor (the marginal change in the steady state mass of substance x in an environmental compartment j at scale g due to a marginal emission in compartment i for cultural perspective c, and $EF_{x,j,c}$ is the effect factor representing the change of potential disappeared fraction of species due to a change in the environmental concentration of substance x in receiving compartment j for cultural perspective c.

The human toxicological midpoint characterization factor can be determined through (Huijbregts et al., 2016):

$$HTP_{i,x,c/nc,c} = \sum_{r} \sum_{g} \frac{iF_{x,i,r,g,c} \times EF_{x,r,c/nc,c}}{iF_{DCB,ua,r,g,c} \times EF_{DCB,r,c/nc,c}} \tag{4-29}$$

where $HTP_{i,x,c/nc,c}$ is the human characterization factor at midpoint level for carcinogenic or non-carcinogenic effects of substance x to emission compartment i for cultural perspective c (kg 1,4-DCB to urban air equivalents), $iF_{x,i,r,g,c}$ is the human population intake fraction of substance x at geographical scale g via intake route r emitted to compartment i for cultural perspective c, and $EF_{x,r,c/nc,c}$ is the carcinogenic or non-carcinogenic effect factor of substance x for intake route r

related to cultural perspective c reflecting the change in lifetime disease incidence due to a change in intake of the substance and intake route of interest.

4.5.2.9 Water Use

Water consumption is the use of water so that the water is evaporated, incorporated into products, transferred to other watersheds, or disposed into the sea (Huijbregts et al., 2016). The characterization factor at midpoint level is the cubic meters of water consumed per cubic meter of water extracted. Water extraction is the withdrawal of water from surface water bodies or the abstraction of groundwater from aquifers. Water consumption is the amount of water that the watershed of origin is losing (Huijbregts et al., 2016).

4.5.2.10 Land Use

Land use includes the direct, local impact of land use on terrestrial species via change of land cover and the actual use of new land. The change of land cover directly affects the original habitat and the original species composition (Huijbregts et al., 2016). Agricultural and urban activities disqualifies the land as a suitable habitat for many species. There are three steps in determining the land use. The first, the transformation phase, is when the land is made more suitable for its new function. The second phase, occupation, is when the land is used for a certain period. The first two phases cover the characterization factors (CFs) for land occupation and are expressed in potentially disappeared fraction of species (PDF) per annual crop equivalent. The third phase, relaxation, is when the land is no longer being used and the land is allowed to return to a semi-natural state. During this stage, land still has some negative impact on species richness. CFs for land relaxation are usually provided separately (Huijbregts et al., 2016).

The midpoint characterization factor ($CF_{m_{occ,x}}$), expressed in annual crop equivalents, for land transformation/occupation is defined as (Huijbregts et al., 2016):

$$CF_{m_{occ,x}} = \frac{S_{rel,x}}{S_{rel,annual\ crop}} \tag{4-30}$$

where $S_{rel,x}$ is the relative species loss cause by land type x and $S_{rel,annual\ crop}$ is the relative loss resulting from annual crop production. $S_{rel,x}$ can be calculated using (Huijbregts et al., 2016):

$$S_{rel,x} = 1 - \frac{S_{LU,x,i}}{S_{ref,i}} \tag{4-31}$$

where $S_{LU,x,i}$ is the observed species richness under land use type x and $S_{ref,i}$ is the observed species richness of the reference land cover in region i.

The midpoint characterization factor for land relaxation to semi-natural state ($CF_{relax,x}$) can be define as (Huijbregts et al., 2016):

$$CF_{relax,x} = CF_{occ,x} \times 0.5 \times t_{rel} \tag{4-32}$$

where t_{rel} is the recovery time for species richness.

4.5.2.11 Mineral Resource Scarcity

The primary extraction of a mineral resource will lead to an overall decrease in ore grade which will increase the ore produced per kilogram of resource extracted (Huijbregts et al., 2016). When combined with the expected future extraction of that mineral resource it created an average surplus ore potential (SOP). An increase in surplus ore potential will then lead to a surplus cost potential (Huijbregts et al., 2016).

SOP expresses the average extra amount of ore to be produced in the future and can be defined as (Huijbregts et al., 2016):

$$SOP_{x,R} = \frac{ASOP_{x,R}}{ASOP_{Cu,R}} \tag{4-33}$$

where $ASOP_{x,R}$ is the absolute surplus ore potential for the extraction of 1 kg of a mineral resource x considering all future production (R) of that mineral resource and $ASOP_{Cu,R}$ is the absolute surplus ore potential for the average extra amount of ore produced in the future due to the extract of 1 kg of copper.

4.5.2.12 Fossil Resource Scarcity

The fossil fuel potential of fossil resource x, expressed in units of kg oil equivalents per unit of resource, is defined as (Huijbregts et al., 2016):

$$FFP_x = \frac{HHV_x}{HHV_{oil}} \tag{4-34}$$

where HHV_x is the energy content of fossil resource x and HHV_{oil} is the energy content of crude oil.

4.6 Assumptions

Several assumptions were required to complete the analyses. They are listed in the following section.

4.6.1 Missing LCI information

In the case a particular chemical was missing from LCI information, the closest proxy-chemical was used rather than omitting it from the analysis. It is important that this substitution is done with a good understanding of the manufacturing routes of the proxy-chemicals being used and those of the one that is being replaced. In most cases, the closest proxy-chemical used is direct precursor to the chemicals mixing LCI information (Parvatker et al., 2019). In this study, three chemicals required the use of a proxy chemical: 2-methyl tetrahydrofuran (2-MeTHF), N-methylmorpholine (NMM), and 2-Chloro-4,6-dimethoxy-1,3,5-triazine (CMDT).

2-MeTHF synthesis route uses glucose from corn, rice, and sugarcane to create hydroxymethylfurfural (HMF). The HMF then converts to levulinic acid before reacting with formic acid to produce 2-methyl tetrahydrofuran. Both levulinic and furfural (an alternative synthesis route) are not present in Ecoinvent's database. According to a study conducted by Khoo et al. (2015), 10.46, 8.01, and 10.14 kg of corn stover, sugarcane bagasse, and rice straw, respectively, are required to produce 1 kg of 2-MeTHF. Therefore, these values will be used to create a database entry for 2-MeTHF.

NMM is produced from a reaction of methyl amine and diethylene glycol. Diethylene glycol was used as the proxy-chemical since it contains inventory information from Ecoinvent. CMDT is produced from cyanuric chloride and sodium methoxide. Cyanuric chloride was used as the proxy-chemical since it contains inventory information from Ecoinvent.

4.6.2 Scaling Up Lab-Scale Processes

Several assumptions were required to scale up the lab scale processes to industrial scale. No loss of mass was assumed between the transfer of liquids from one unit to another via a pump. For reactions with mixing, heating, or cooling, catalysts were not included in the inventory analysis (Parvatker et al., 2019). In distillation, if not specified in the process, the 99% of the light key product was recovered in the distillate. Further, the relative volatility was estimated based on the temperature difference of the mixture components and only reboiler energy and heating requirements were considered for distillation unit operations (Parvatker et al., 2019). It was assumed that 10% of the API was lost as uncrystallized material in the solution post-filtration. After filtration, it was assumed that 20% of the solvent from the crystallization and filtration step reached the dryer and 100% of the solvent in the dryer is evaporated. For the dryer, only the specific heat capacity of the solvent is considered. The sensible heat for heating the product is ignored (Parvatker et al., 2019). Further, the heat lost is incorporated in the dryer efficiency along with heat lost to the environment (Parvatker et al., 2019). The vacuum dryer was operated at -29 inHg and 50ºC. The efficiency of the distillation column and dryer were assumed to be 85% (Parvatker et al., 2019).

Chapter 5: Results

Several analyses were conducted, and the results are shown in the following sections. Life Cycle Impacts were assessed by crystallization type, solvent, and solvent class. Further, the major contributors to the LCI were examined for each process.

5.1 Classification of Processes

There are four main crystallization process types that were examined in this project. Please refer to section 3.1.12to understand how the processes were categorized by crystallization type. The breakdown of crystallization types can be seen in Figure 5-1. Reactive crystallization processes were most common (21 processes – 38.9%), followed by antisolvent processes (14 processes – 25.9%), followed by evaporative 10 (18.5%), and then cooling and 9 (16.7%).

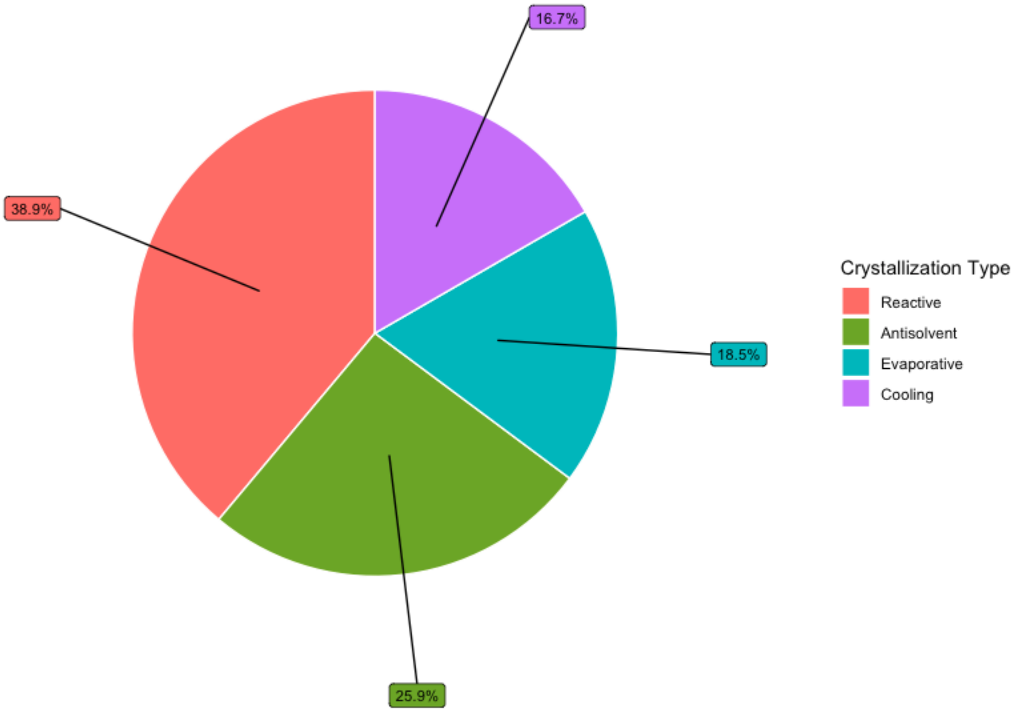

Figure 5-1. Breakdown of crystallization types used in this project.

5.2 Mass of Solvents

5.2.1 Total Solvent Mass

Total solvent masses from all crystallization processes were collected to determine which solvents were more prevalent. This is represented in Figure 5-2. A total of 1250 kg of solvent was used in all 54 crystallization processes. Water was the most solvent used most frequently in API crystallization processes (used 22.6% of the time), and accounts for 279 kg of the total mass. Dichloromethane, a class 2 solvent, accounted for 140 kg (11.3%) of the total mass. Heptane, a common antisolvent, accounted for 99 kg (8%) of the total mass. Other commonly used solvents included acetone (110 kg), ethyl acetate (92 kg), methanol (88 kg), ethanol (83 kg), isopropyl alcohol (76 kg), and tetrahydrofuran (59 kg). It was found that class 3 solvents were used most of the time (74.1%), while class 2 solvents were only used 25.9% of the time.

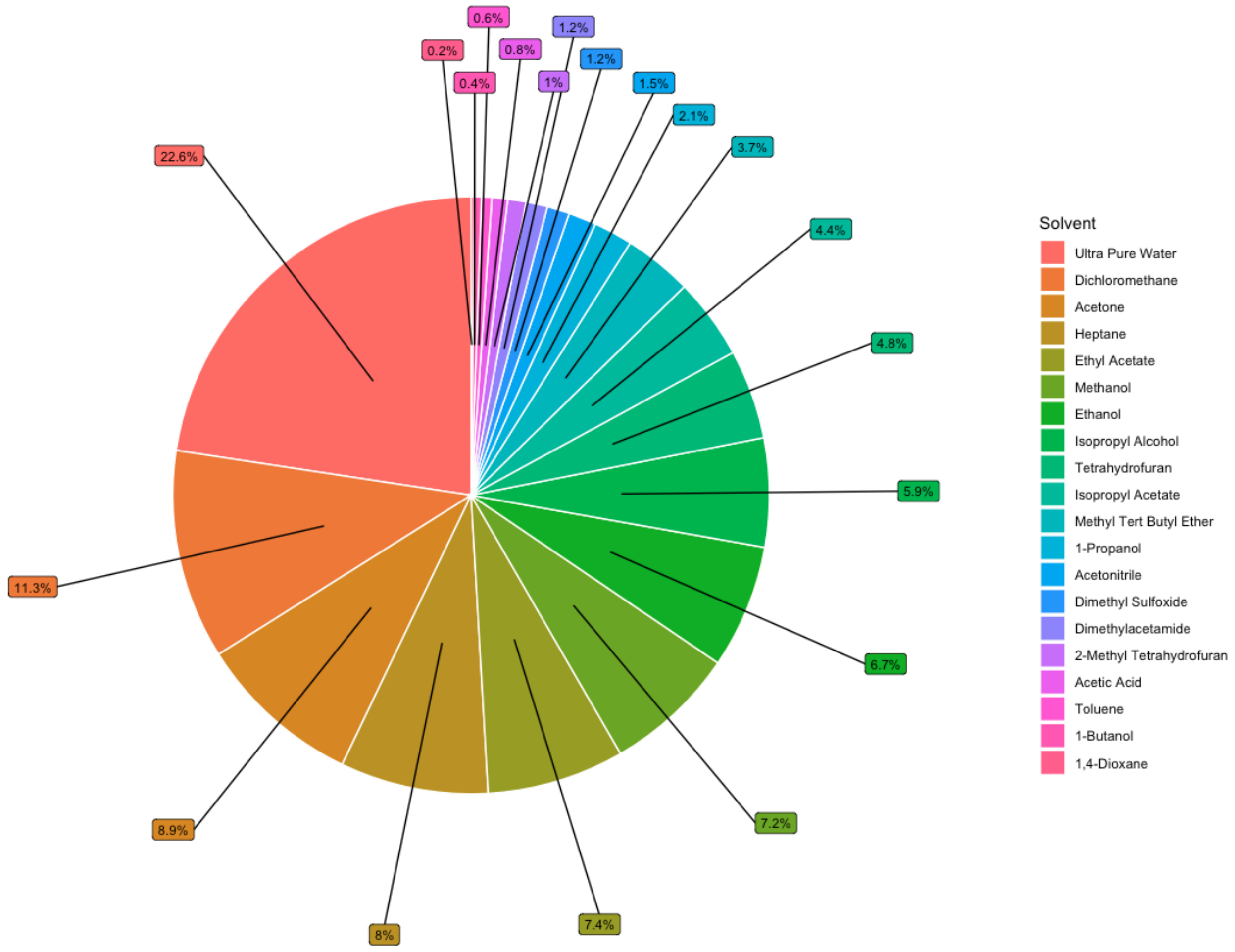

Figure 5-2. Typical breakdown of solvents used in API crystallization processes.

5.2.2 Solvent Mass by Process ID

The total mass of solvent can also be examined by process ID and crystallization type. This is represented in Figure 5-3. Class 2 solvents were most used in reactive crystallization processes. Reactive and evaporative crystallization processes tended to contain elevated amounts of solvents when compared to the other two crystallization types. However, some reactive processes (e.g., P06, P29, P38A, P38B, P38, and P45) contained lower amounts of solvents, like the amounts in the cooling processes. Cooling had the lowest solvent usage compared with the other three crystallization types. Antisolvent processes had slightly higher usage of solvents from cooling processes, but lower than evaporative processes. Reactive process P32 contained the highest amount of solvent usage (105 kg). This process also contained elevated amounts of class 2 solvent (dichloromethane). Therefore, P32 encompasses 75% of the total amount of dichloromethane used in all processes.

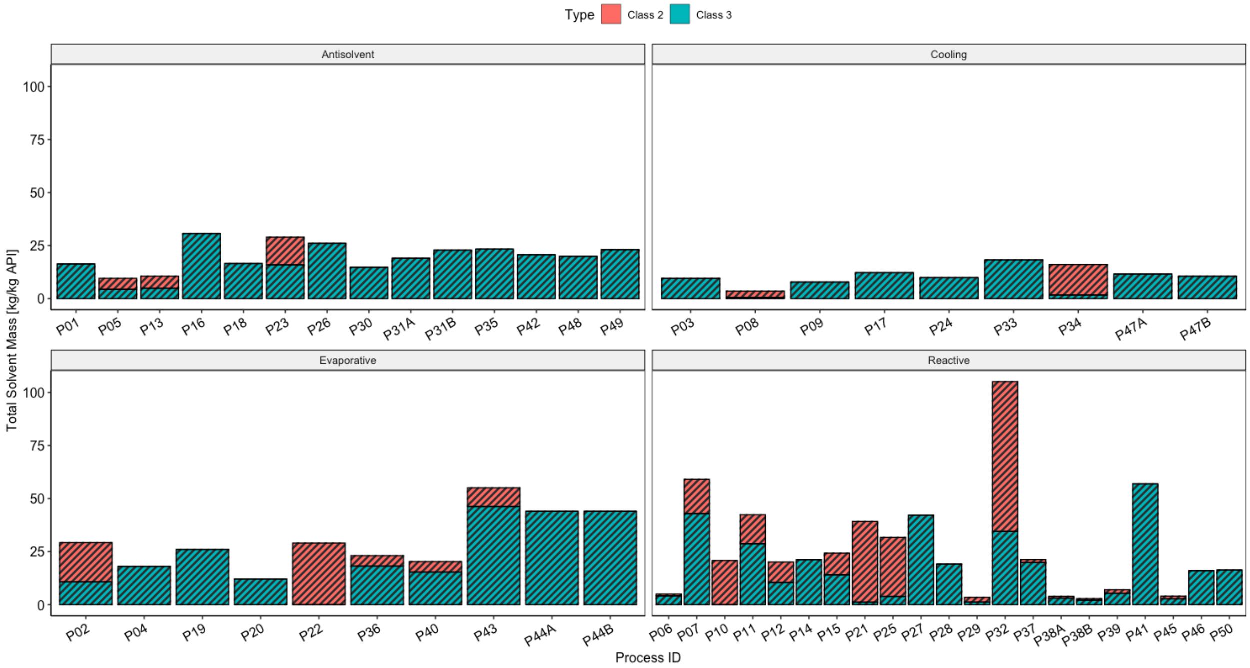

Figure 5-3. Total solvent mass per crystallization process categorized by residual solvent class and organized by crystallization type.

5.3 Process E-Factors

E-factor is an important metric in determining amount of waste associated to final product production. Figure 5-4 breaks down the E-factors for all processes categorized by crystallization type. These values exclude the mass of water from the calculation, as water is the “safest” solvent. Approximate E-factors containing water, are listed in Figure 5-3. Those values would contain all inputs (starting API, reactants, and solvents). Since we are assuming 100% conversion during reactive processes and that all solvents end up in waste streams, the only additional mass from the E-factor equation is the amount of starting API.

E-factors were determined to be highest in evaporative and reactive processes. As mentioned previously, P32 contained very large amounts of dichloromethane, giving it the largest E-factor of all 54 processes. It is important to note that several reactive processes had very low E-factors, because these processes tended to use water as one of their main solvents. Evaporative processes had higher E-factors overall because organic solvents tended to be used since, they usually have lower boiling points than water. Antisolvent process E-Factors were higher than those of the cooling process because of the addition of an antisolvent (typically heptane) to the process.

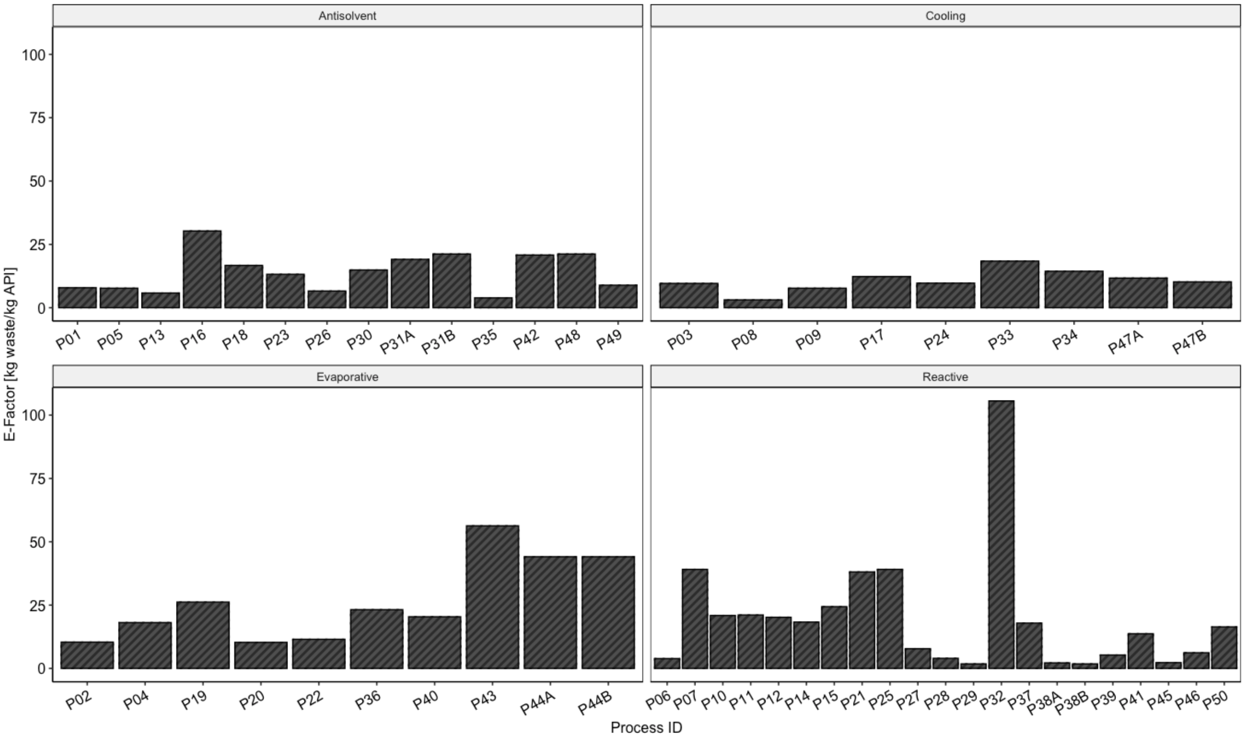

Figure 5-4. E-Factors for each crystallization process organized by crystallization type. It is important to note that E-Factors have been calculated by excluding the mass of water. E-Factor values containing water would be similar to those in Figure 5-3.

5.4 Environmental Impacts by Crystallization Type

Eighteen different environmental impact categories were investigated in the life cycle assessment. This section contains the results from the LCIAs conducted on all 54 processes.

5.4.1 Terrestrial Acidification Potential (TAP) by Crystallization Type

The terrestrial acidification potential (TAP) results can be found in Figure 5-5 for both incineration and recovery options. The cooling and antisolvent processes had the lowest impacts when compared to evaporative and reactive. Further, the solvent recovery option had lower impacts than incineration for all processes except P16, P18, P26, and P27. The specific contributions towards these elevated impacts will be examined in more detail in Section 5.6 For the antisolvent processes, the mean terrestrial acidification impacts were 0.130 ± 0.025 and 0.143 ± 0.063 kg SO_2 equivalents for incineration and recovery, respectively. For the cooling processes, the means were 0.106 ± 0.021 and 0.040 ± 0.005 kg SO_2 equivalents for incineration and recovery, respectively. For the evaporative processes, the means were 0.399 ± 0.145 and 0.166 ± 0.071 kg SO_2 equivalents for incineration and recovery, respectively. For the reactive processes, the means were 0.302 ± 0.079 and 0.0824 ± 0.015 kg SO_2 equivalents for incineration and recovery, respectively.

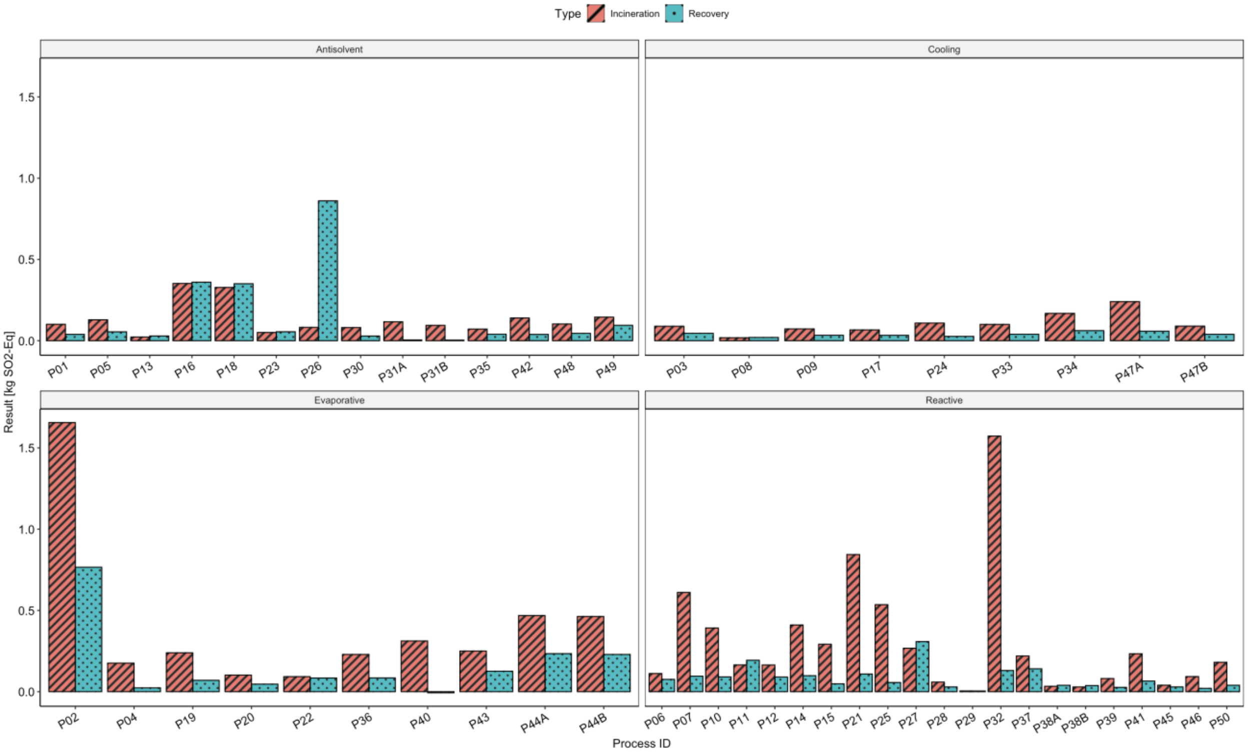

Figure 5-5. Terrestrial acidification potential (TAP) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.4.2 Global Warming Potential (GWP100) by Crystallization Type

The global warming potential (GWP100) results can be found in Figure 5-6 for both incineration and recovery options. Impacts were lowest in the cooling and antisolvent processes when compared to the evaporative and reactive processes. All processes containing solvent recovery had lower impacts than those with incineration (except for P26). For the antisolvent processes, the mean global warming potential impacts were 67.9 ± 8.4 and 30.9 ± 12.9 kg CO_2 equivalents for incineration and recovery, respectively. The range of GWP100 impacts for antisolvent processes were from 23.5 to 74.3 and from 0.65 to 98.7 kg CO_2 equivalents for incineration and recovery, respectively. For the cooling processes, the means were 48.9 ± 7.9 and 10.6 ± 1.7 kg CO_2 equivalents for incineration and recovery, respectively. The range of GWP100 impacts for cooling processes were from 10.7 to 59.5 and from 4.2 to 14.7 kg CO_2 equivalents for incineration and recovery, respectively. For the evaporative processes, the means were 142.0 ± 22.4 and 32.9 ± 9.8 kg CO_2 equivalents for incineration and recovery, respectively. The range of GWP100 impacts for evaporative processes were from 53.1 to 180.0 and from -3.8 to 92.5 kg CO_2 equivalents for incineration and recovery, respectively. For the reactive processes, the means were 117.0 ± 26.8 and 17.0 ± 2.4 kg CO_2 equivalents for incineration and recovery, respectively. The range of GWP100 impacts for reactive processes were from 13.34 to 316.3 and from 1.1 to 31.2 kg CO_2 equivalents for incineration and recovery, respectively. Impact ranges excluded outliers that were more than three times the standard deviations of each crystallization type.

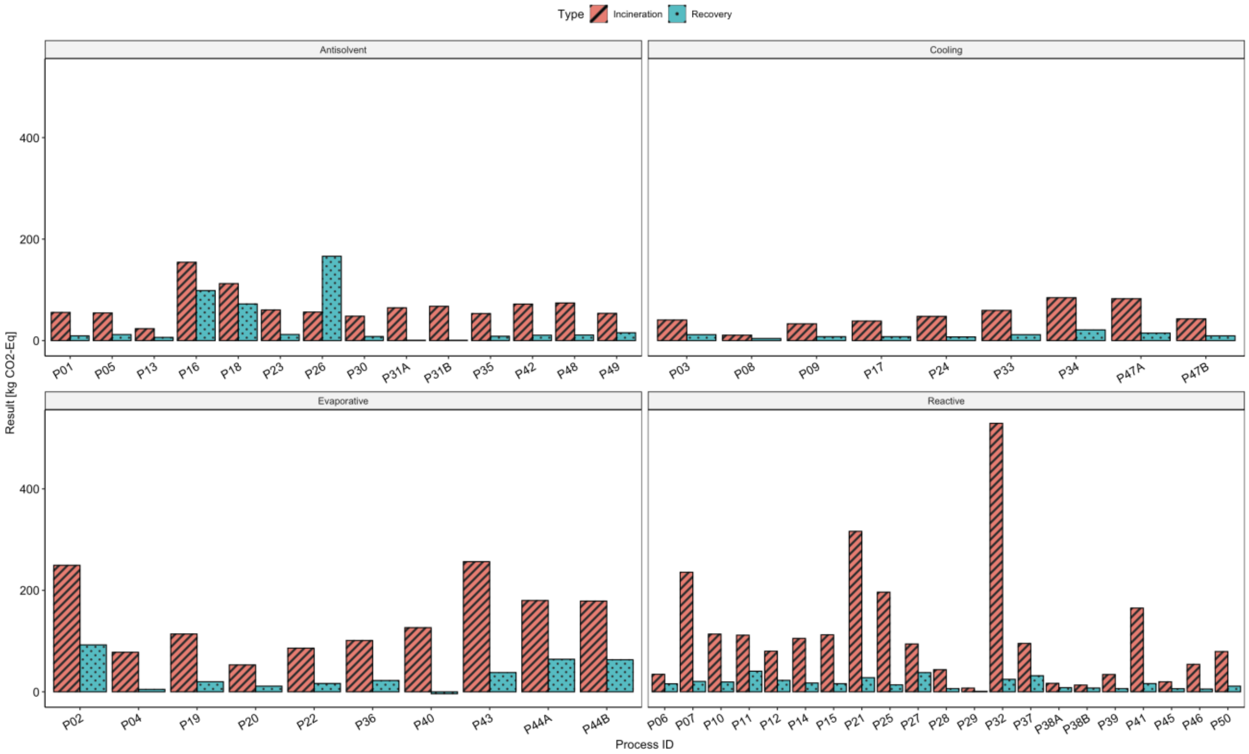

Figure 5-6. Global warming potential (GWP100) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.4.3 Freshwater Ecotoxicity Potential (FETP) by Crystallization Type

The freshwater ecotoxicity potential (FETP) results can be found in Figure 5-7 for both incineration and recovery options. Impacts were lowest in the cooling and antisolvent processes when compared to the evaporative and reactive processes. All processes involving solvent recovery (except P26) had lower impacts than those with incineration (except for P26). For the antisolvent processes, the mean freshwater ecotoxicity potential impacts were 1.22 ± 0.26 and 0.73 ± 0.29 kg 1,4-DCB equivalents for incineration and recovery, respectively. For the cooling processes, the means were 1.10 ± 0.21 and 0.31 ± 0.06 kg 1,4-DCB equivalents for incineration and recovery, respectively. For the evaporative processes, the means were 3.03 ± 0.55 and 1.00 ± 0.31 kg 1,4-DCB equivalents for incineration and recovery, respectively. For the reactive processes, the means were 1.85 ± 0.43 and 0.42 ± 0.06 kg 1,4-DCB equivalents for incineration and recovery, respectively.

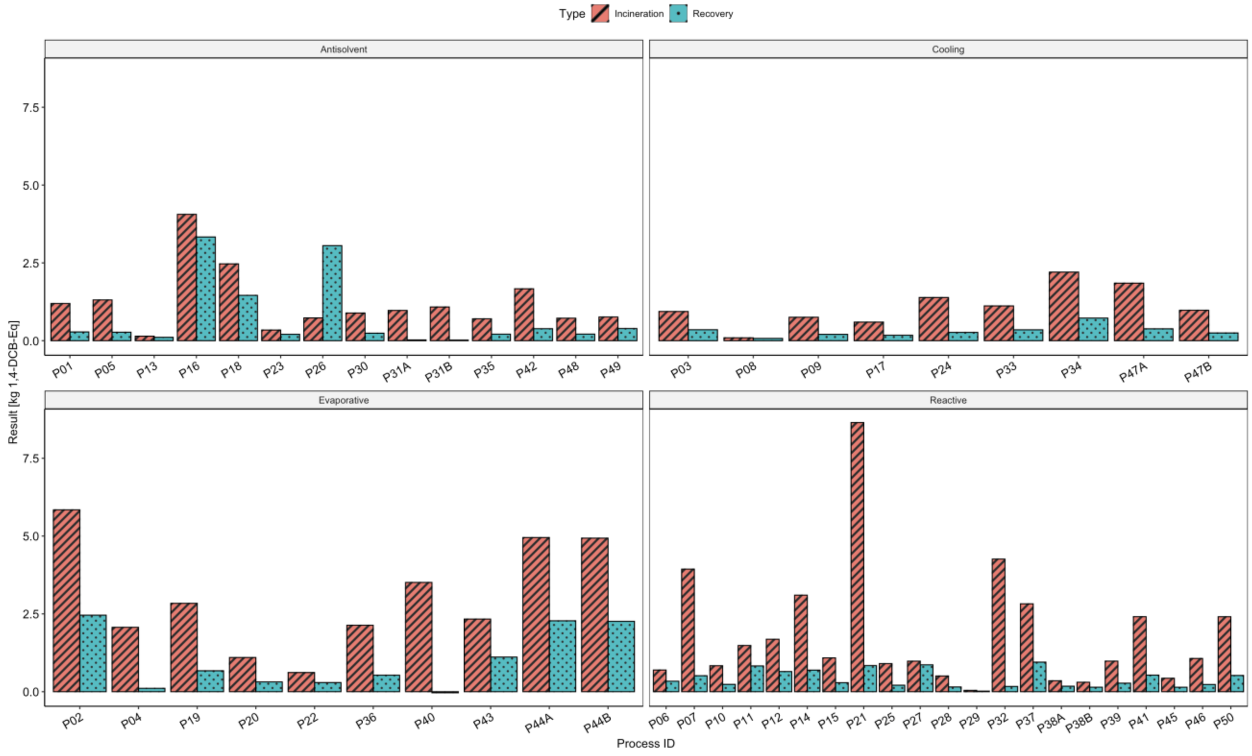

Figure 5-7. Freshwater ecotoxicity potential (FETP) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.4.4 Marine Ecotoxicity Potential (METP) by Crystallization Type

The marine ecotoxicity potential (METP) results can be found in Figure 5-8 for both incineration and recovery. Overall, the cooling and antisolvent processes had lower impacts than the evaporative and most reactive processes. All processes with the recovery option (except P26) had lower impacts that those with the incineration option. For the antisolvent processes, the mean freshwater ecotoxicity potential impacts were 1.62 ± 0.35 and 0.99 ± 0.40 kg 1,4-DCB equivalents for incineration and recovery, respectively. For the cooling processes, the means were 1.45 ± 0.28 and 0.41 ± 0.08 kg 1,4-DCB equivalents for incineration and recovery, respectively. For the evaporative processes, the means were 3.93 ± 0.67 and 1.29 ± 0.39 kg 1,4-DCB equivalents for incineration and recovery, respectively. For the reactive processes, the means were 2.46 ± 0.57 and 0.56 ± 0.08 kg 1,4-DCB equivalents for incineration and recovery, respectively.

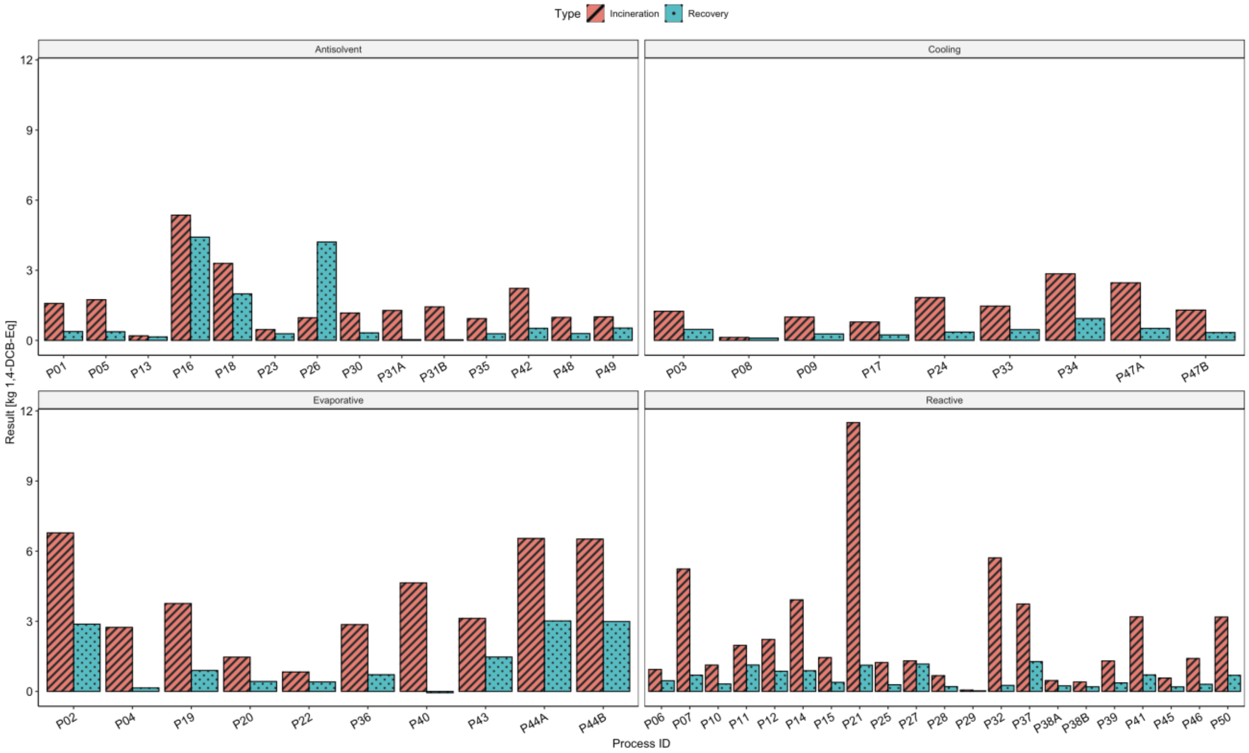

Figure 5-8. Marine ecotoxicity potential (METP) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.4.5 Terrestrial Ecotoxicity Potential (TETP) by Crystallization Type

Terrestrial ecotoxicity potential (TETP) results can be found in Figure 5-9. Overall, the cooling and antisolvent processes had lower results than the antisolvent and most reactive processes. The processes with the recovery option always had lower impacts than those of the incineration option, except P26. For the antisolvent processes, the mean terrestrial ecotoxicity potential impacts were 114.0 ± 24.7 and 47.0 ± 21.2 kg 1,4-DCB equivalents for incineration and recovery, respectively. For the cooling processes, the means were 103.0 ± 30.9 and 25.1 ± 5.47 kg 1,4-DCB equivalents for incineration and recovery, respectively. For the evaporative processes, the means were 269.0 ± 42.1 and 74.2 ± 23.5 kg 1,4-DCB equivalents for incineration and recovery, respectively. For the reactive processes, the means were 170.0 ± 42.6 and 29.3 ± 5.6 kg 1,4-DCB equivalents for incineration and recovery, respectively.

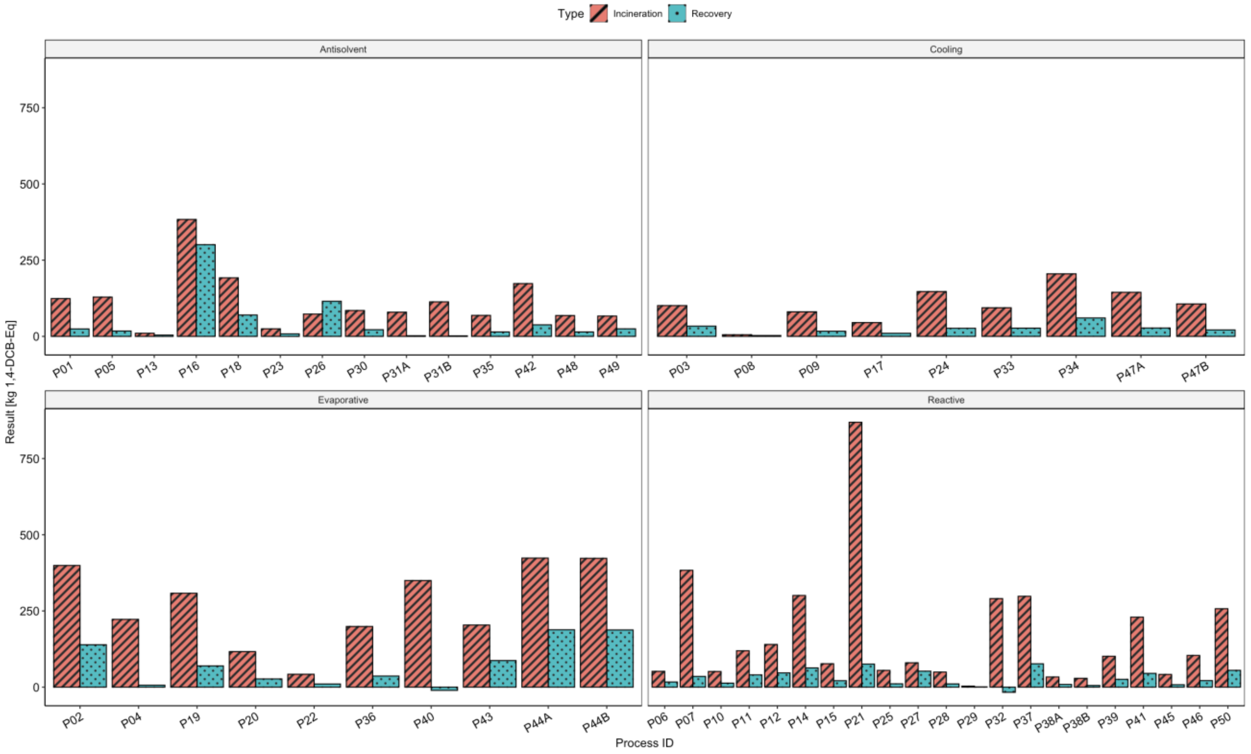

Figure 5-9. Terrestrial ecotoxicity potential (TETP) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.4.6 Fossil Fuel Potential (FFP) by Crystallization Type

Fossil fuel potential (FFP) results can be found in Figure 5-10. In general, the cooling and antisolvent processes showed lower impacts than the evaporative and most reactive processes. Processes with the incineration option had higher impacts than those with the recovery option, except for P26. For the antisolvent processes, the mean fossil fuel potential impacts were 19.1 ± 3.3 and 10.7 ± 4.0 kg oil equivalents for incineration and recovery, respectively. For the cooling processes, the means were 16.9 ± 2.6 and 4.9 ± 0.9 kg oil equivalents for incineration and recovery, respectively. For the evaporative processes, the means were 44.8 ± 5.8 and 14.9 ± 3.9 kg oil equivalents for incineration and recovery, respectively. For the reactive processes, the means were 26.7 ± 0.4 and 5.9 ± 0.8 kg oil equivalents for incineration and recovery, respectively.

Figure 5-10. Fossil fuel potential (FFP) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.4.7 Freshwater Eutrophication Potential (FEP) by Crystallization Type

Freshwater eutrophication potential (FEP) results can be found in Figure 5-11. Cooling and antisolvent processes, in general, had lower impacts than antisolvent and most reactive processes. All processes with the recovery option, except P26, had lower impacts than those with the incineration option. The recovery option of P40 had a negative impact, meaning that the recovery option was able to improve freshwater eutrophication. However, all values for freshwater eutrophication were quite low and near-zero. For the antisolvent processes, the mean freshwater eutrophication potential impacts were 0.014 ± 0.002 and 0.012 ± 0.005 kg phosphorus equivalents for incineration and recovery, respectively. For the cooling processes, the means were 0.010 ± 0.002 and 0.003 ± 0.000 kg phosphorus equivalents for incineration and recovery, respectively. For the evaporative processes, the means were 0.029 ± 0.000 and 0.010 ± 0.003 kg phosphorus equivalents for incineration and recovery, respectively. For the reactive processes, the means were 0.020 ± 0.005 and 0.006 ± 0.001 kg phosphorus equivalents for incineration and recovery, respectively.

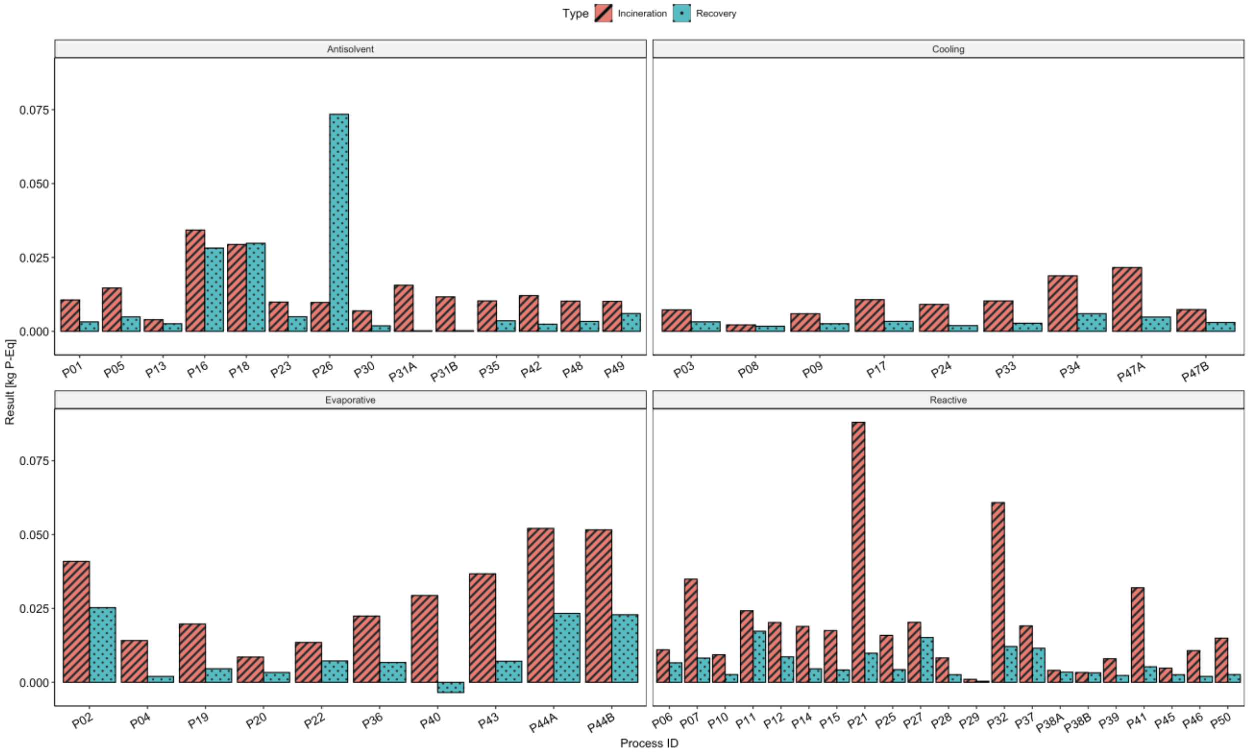

Figure 5-11. Freshwater eutrophication potential (FEP) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.4.8 Marine Eutrophication Potential (MEP) by Crystallization Type

Marine eutrophication potential (MEP) results can be found in Figure 5-12. The results for all processes except for P02, P14, P34 have near-zero values. For the antisolvent processes, the mean marine eutrophication potential impacts were 0.0015 ± 0.0002 and 0.0008 ± 0.0003 kg nitrogen equivalents for incineration and recovery, respectively. For the cooling processes, the means were 0.0050 ± 0.0041 and 0.0015 ± 0.0013 kg nitrogen equivalents for incineration and recovery, respectively. For the evaporative processes, the means were 0.0346 ± 0.0315 and 0.0119 ± 0.0106 kg nitrogen equivalents for incineration and recovery, respectively. For the reactive processes, the means were 0.0042 ± 0.0009 and 0.0009 ± 0.0004 kg nitrogen equivalents for incineration and recovery, respectively.

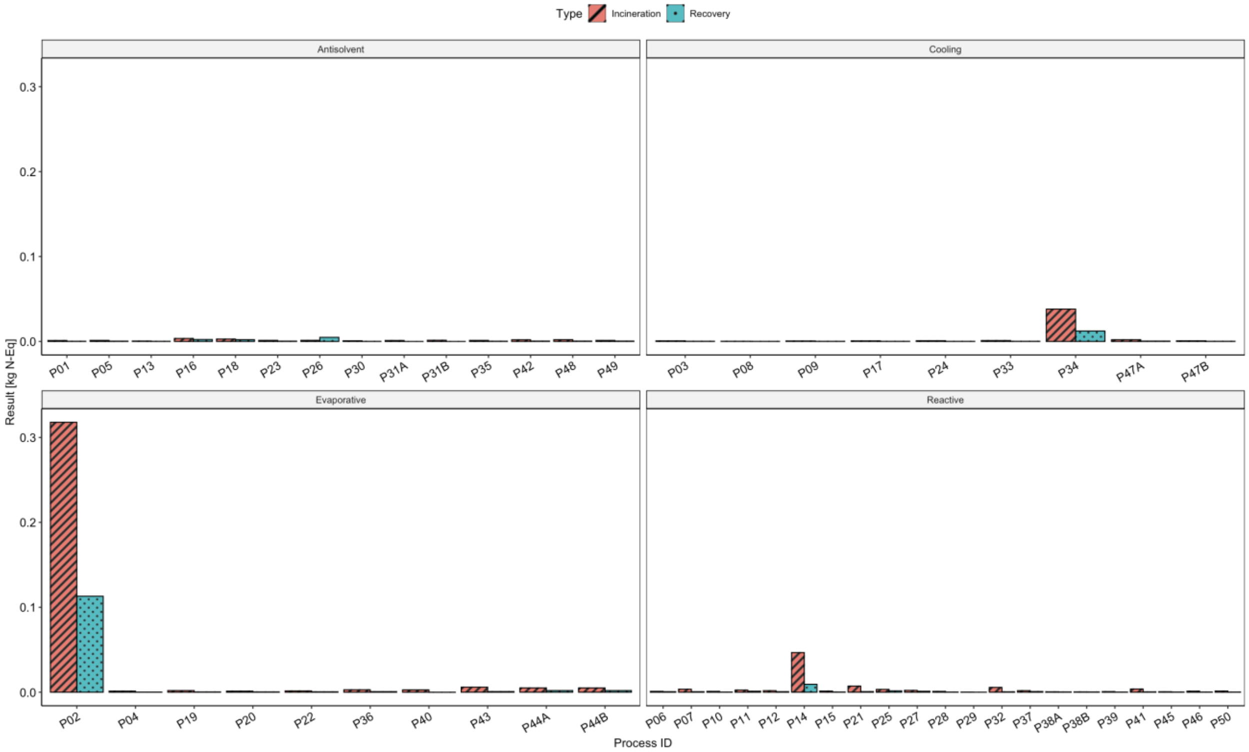

Figure 5-12. Marine eutrophication potential (MEP) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.4.9 Human Toxicity potential – Carcinogenic (HTPc) by Crystallization Type

Human toxicity potential – carcinogenic (HTPc) results are show in Figure 5-13. Results demonstrate that, in general, values for cooling and antisolvent processes are lower than those for evaporative and most reactive processes. All processes with recovery option (except P26) are lower than those with the incineration option. P40's recovery option showed negative impact results and signify that this option can positively affect human toxicity. For the antisolvent processes, the mean human toxicity potential impacts were 1.69 ± 0.34 and 1.40 ± 0.59 kg 1,4-DCB equivalents for incineration and recovery, respectively. For the cooling processes, the means were 1.42 ± 0.31 and 0.46 ± 0.08 kg 1,4-DCB equivalents for incineration and recovery, respectively. For the evaporative processes, the means were 4.04 ± 0.70 and 1.44 ± 0.44 kg 1,4-DCB equivalents for incineration and recovery, respectively. For the reactive processes, the means were 3.16 ± 0.17 and 0.76 ± 0.11 kg 1,4-DCB equivalents for incineration and recovery, respectively.

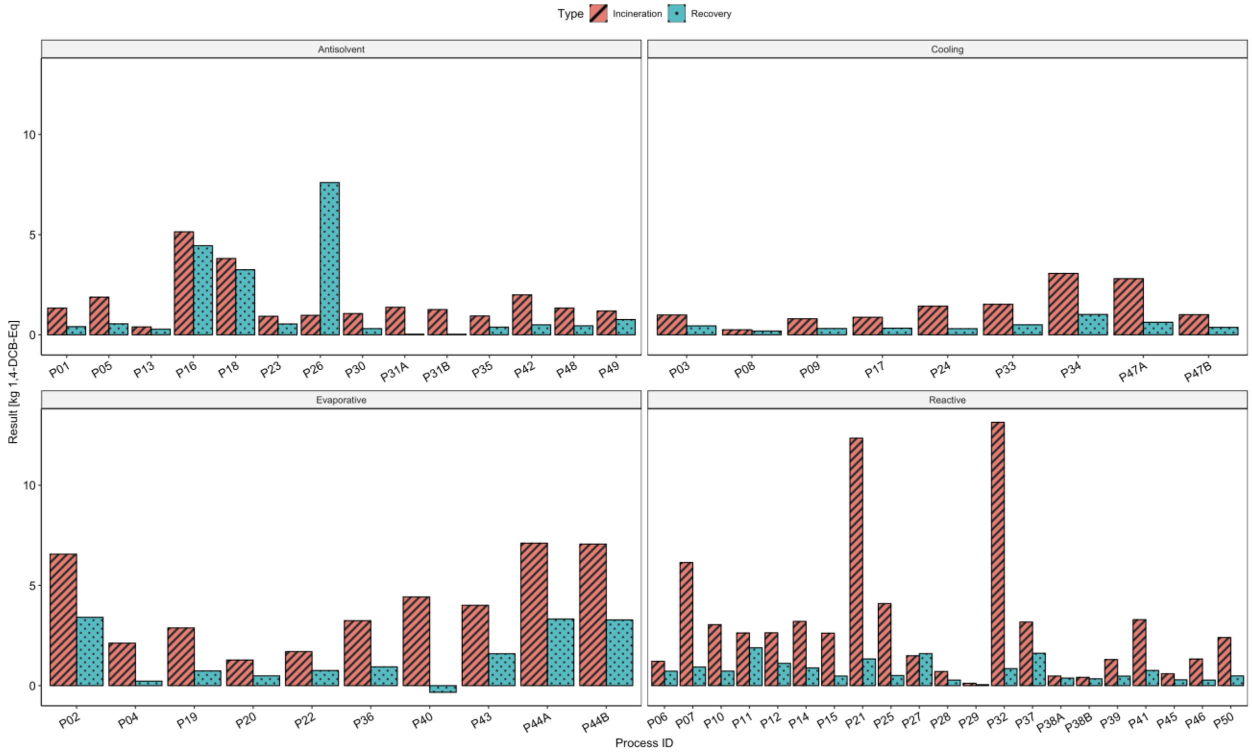

Figure 5-13. Human toxicity potential – carcinogenic (HTPc) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.4.10 Human Toxicity Potential – Non-Carcinogenic (HTPnc) by Crystallization Type

Human toxicity potential – non-carcinogenic (HTPnc) results are shown in Figure 5-14. In general, the cooling and antisolvent processes had smaller impacts than the evaporative and most reactive processes. Results were higher in processes with the incineration option (except for P26) than those with the recovery option. For the antisolvent processes, the mean freshwater eutrophication potential impacts were 26.6 ± 5.9 and 23.1 ± 9.8 kg 1,4-DCB equivalents for incineration and recovery, respectively. For the cooling processes, the means were 23.8 ± 4.7 and 7.7 ± 1.2 kg 1,4-DCB equivalents for incineration and recovery, respectively. For the evaporative processes, the means were 52.4 ± 12.4 and 18.5 ± 6.1 kg 1,4-DCB equivalents for incineration and recovery, respectively. For the reactive processes, the means were 40.5 ± 9.6 and 12.1 ± 1.8 kg 1,4-DCB equivalents for incineration and recovery, respectively.

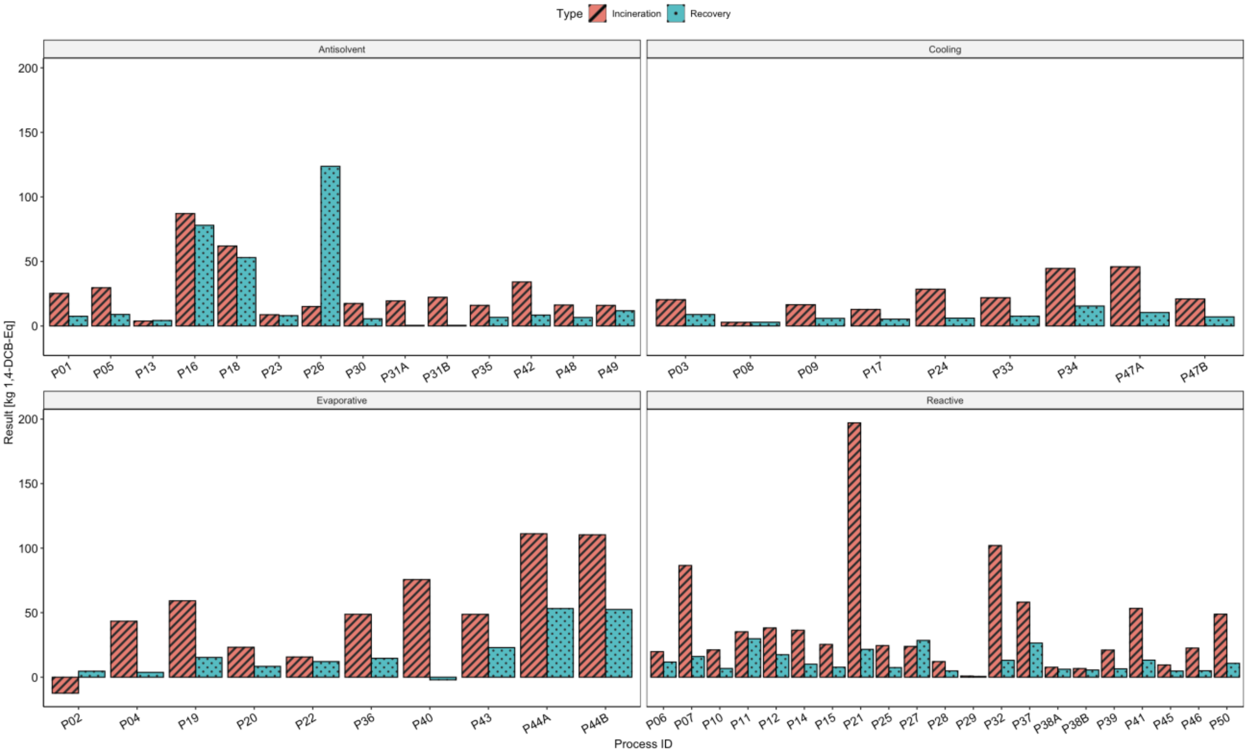

Figure 5-14. Human toxicity potential – non-carcinogenic (HTPnc) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.4.11 Ionising Radiation Potential (IRP) by Crystallization Type

Ionising radiation potential (IRP) results can be found in Figure 5-15. Overall, results for cooling and antisolvent processes were lower than those for evaporative and most reactive processes. All processes with the recovery option (except P26) were lower than those for incineration. Further, the P40 recycle option had negative ionising radiation potential and therefore produces a positive effect for this environmental impact category. For the antisolvent processes, the mean freshwater eutrophication potential impacts were 1.13 ± 0.36 and 0.39 ± 0.21 kBq Cobalt-60 equivalents for incineration and recovery, respectively. For the cooling processes, the means were 0.95 ± 0.37 and 0.23 ± 0.11 kBq Cobalt-60 equivalents for incineration and recovery, respectively. For the evaporative processes, the means were 2.43 ± 0.58 and 0.43 ± 0.37 kBq Cobalt-60 equivalents for incineration and recovery, respectively. For the reactive processes, the means were 1.88 ± 0.84 and 0.22 ± 0.09 kBq Cobalt-60 equivalents for incineration and recovery, respectively.

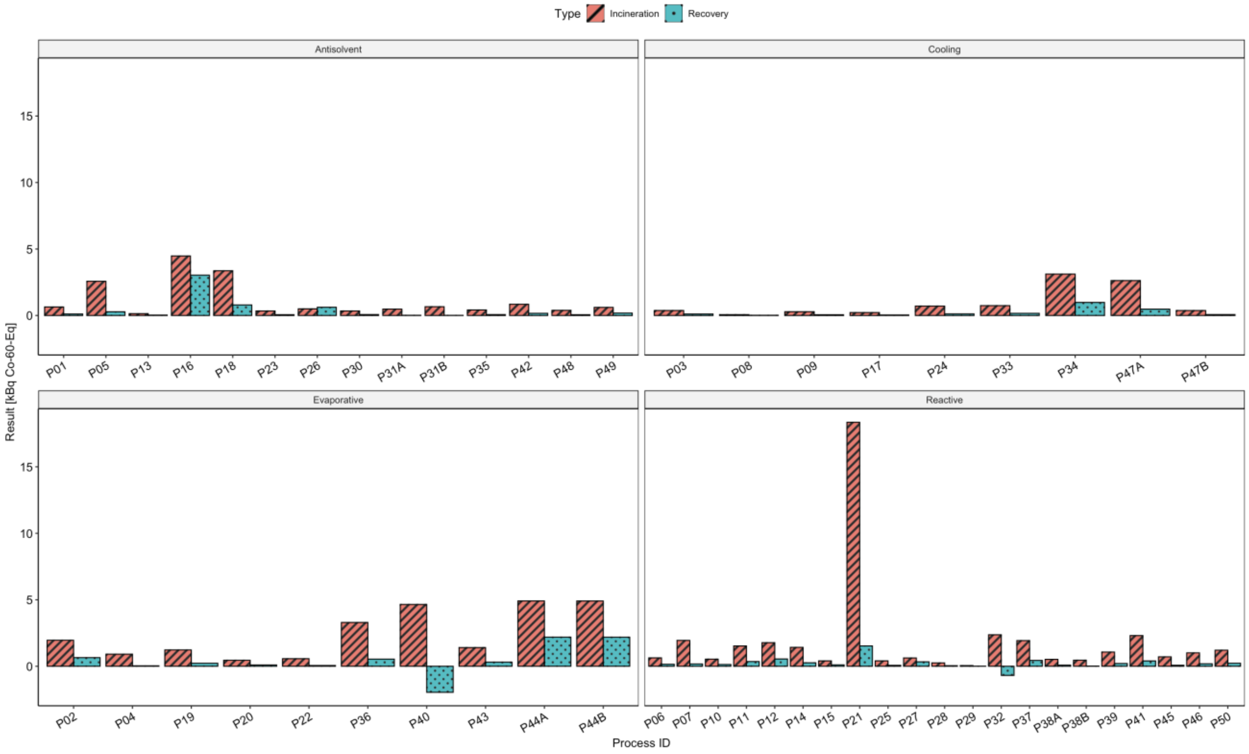

Figure 5-15. Ionising radiation potential (IRP) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.4.12 Agricultural Land Occupation (LOP) by Crystallization Type

Agricultural land occupation (LOP) results can be found in Figure 5-16. All processes except for P02, P14, and P21 have near-zero results. For the antisolvent processes, the mean agricultural land occupation impacts were 0.58 ± 0.16 and 0.19 ± 0.02 kBq Cobalt-60 equivalents for incineration and recovery, respectively. For the cooling processes, the means were 16.40 ± 15.9 and 7.07 ± 6.93 kBq Cobalt-60 equivalents for incineration and recovery, respectively. For the evaporative processes, the means were 2.21 ± 2.00 and 0.64 ± 0.40 kBq Cobalt-60 equivalents for incineration and recovery, respectively. For the reactive processes, the means were 1.88 ± 0.84 and 0.22 ± 0.09 kBq Cobalt-60 equivalents for incineration and recovery, respectively.

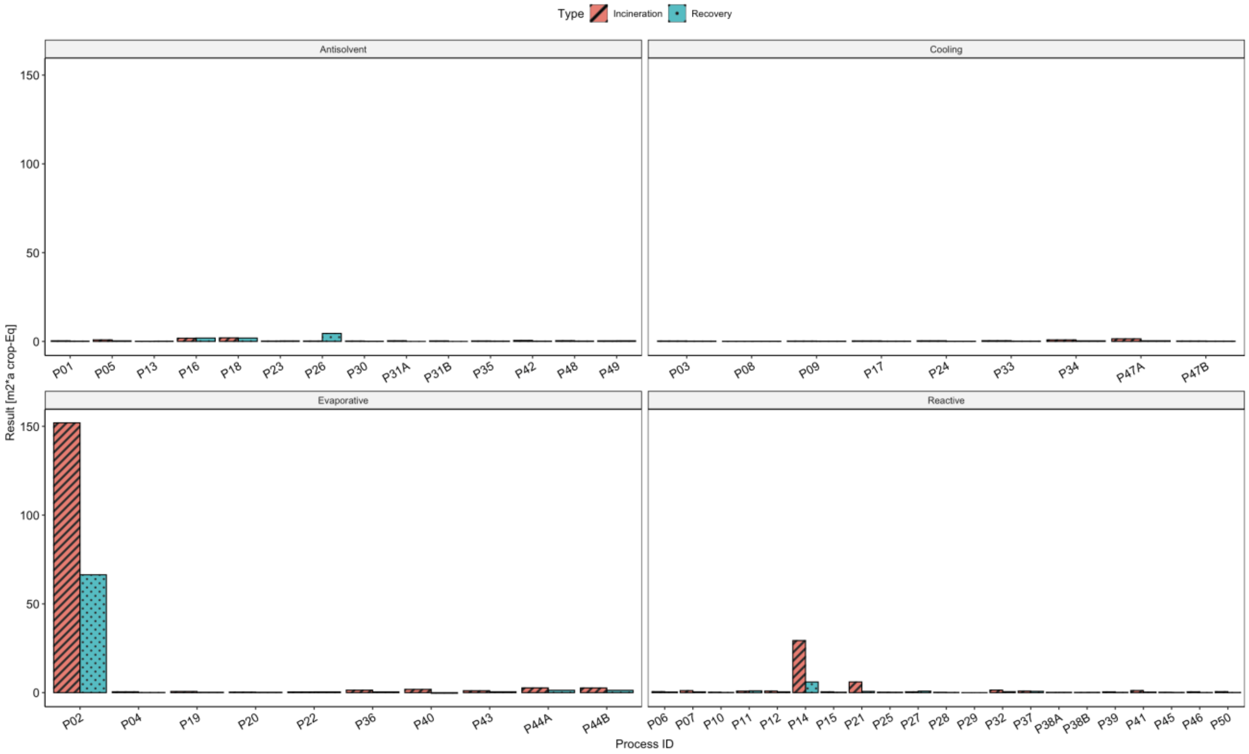

Figure 5-16. Agricultural land occupation (LOP) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.4.13 Surplus Ore Potential (SOP) by Crystallization Type

Surplus ore potential (SOP) results can be found in Figure 5-17. Results showed that, in general, cooling and antisolvent processes showed smaller impacts than did the evaporative and most reactive processes. The processes with the recovery option showed lower impacts than processes with the incineration option. For the antisolvent processes, the mean surplus ore potential were 0.50 ± 0.07 and 0.15 ± 0.06 kBq Cobalt-60 equivalents for incineration and recovery, respectively. For the cooling processes, the means were 0.37 ± 0.07 and 0.07 ± 0.02 kBq Cobalt-60 equivalents for incineration and recovery, respectively. For the evaporative processes, the means were 1.24 ± 0.21 and 0.30 ± 0.11 kBq Cobalt-60 equivalents for incineration and recovery, respectively. For the reactive processes, the means were 0.70 ± 0.14 and 0.10 ± 0.02 kBq Cobalt-60 equivalents for incineration and recovery, respectively.

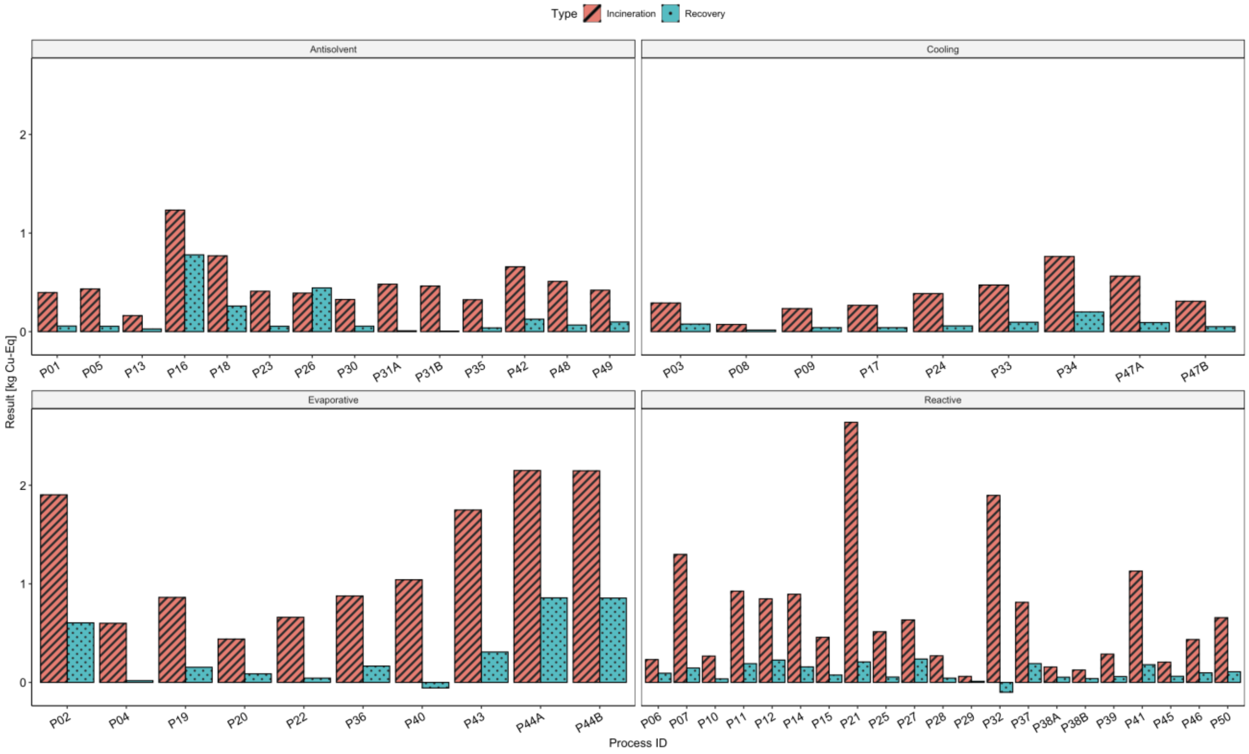

Figure 5-17. Surplus ore potential (SOP) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.4.14 Ozone Depletion Potential ($ODP_{infinite}$) by Crystallization Type

Ozone depletion potential ($ODP_{potential}$) results can be found in Figure 5-18. Most processes were near zero (below 0.005 kg CFC-11 equivalents). For the antisolvent processes, the mean ozone depletion potential were $1.5 \times 10^{-5} \pm 0.2 \times 10^{-5}$ and $0.6 \times 10^{-5} \pm 0.3 \times 10^{-5}$ kg CFC-11 equivalents for incineration and recovery, respectively. For the cooling processes, the means were $1.0 \times 10^{-5} \pm 0.2 \times 10^{-5}$ and $0.2 \times 10^{-5} \pm 0.0 \times 10^{-5}$ kg CFC-11 equivalents for incineration and recovery, respectively. For the evaporative processes, the means were $9.7 \times 10^{-5} \pm 0.2 \times 10^{-5}$ and $3.5 \times 10^{-5} \pm 3.0 \times 10^{-5}$ kg CFC-11 equivalents for incineration and recovery, respectively. For the reactive processes, the means were $46.5 \times 10^{-5} \pm 23.1 \times 10^{-5}$ and $2.6 \times 10^{-5} \pm 1.3 \times 10^{-5}$ kg CFC-11 equivalents for incineration and recovery, respectively.

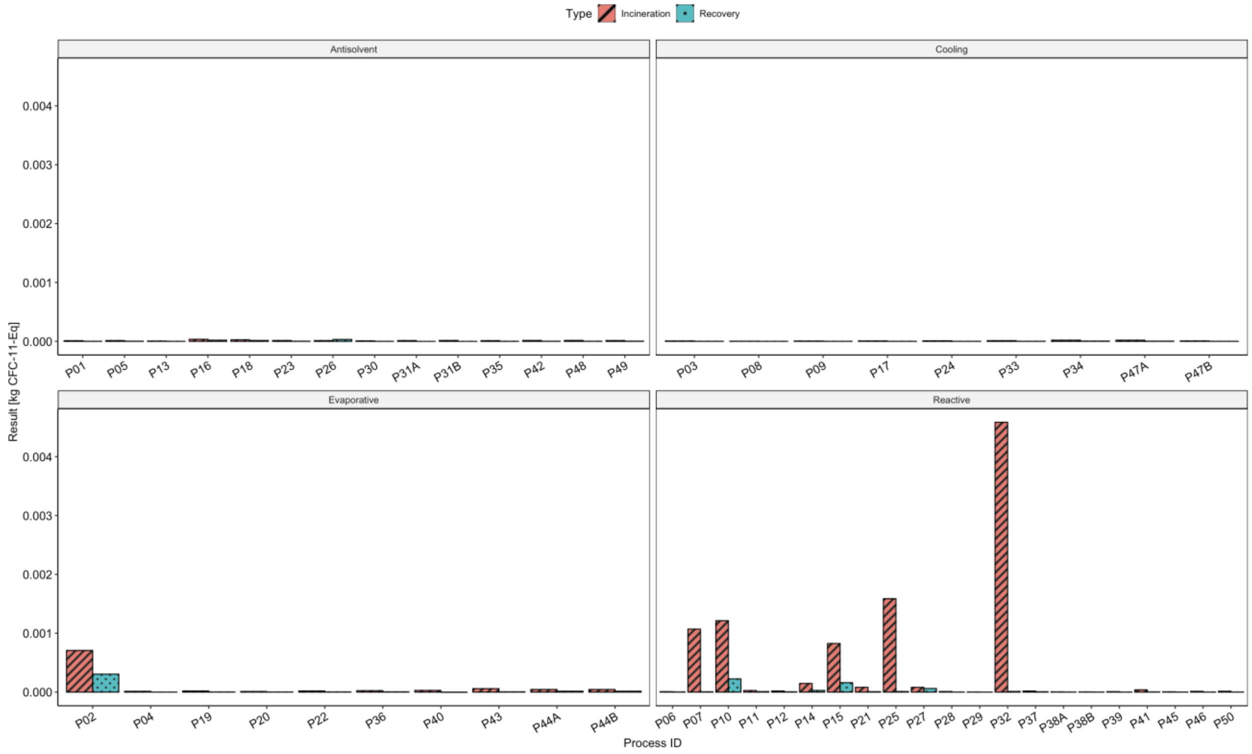

Figure 5-18. Ozone depletion potential ($ODP_{infinite}$) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.4.15 Particulate Matter Formation Potential (PMFP) by Crystallization Type

Particulate matter formation potential (PMFP) results can be found in Figure 5-19. Overall, results were lowest for cooling and most antisolvent processes when compared to evaporative and reactive processes. Results for processes with the incineration option were higher than all processes with the recovery option (except for P26). For the antisolvent processes, the mean particulate matter formation potential were 0.053 ± 0.012 and 0.048 ± 0.020 kg $PM_{2.5}$ equivalents for incineration and recovery, respectively. For the cooling processes, the means were 0.044 ± 0.011 and 0.015 ± 0.002 kg $PM_{2.5}$ equivalents for incineration and recovery, respectively. For the evaporative processes, the means were 0.129 ± 0.029 and 0.049 ± 0.017 kg $PM_{2.5}$ equivalents for incineration and recovery, respectively. For the reactive processes, the means were 0.115 ± 0.031 and 0.027 ± 0.005 $PM_{2.5}$ equivalents for incineration and recovery, respectively.

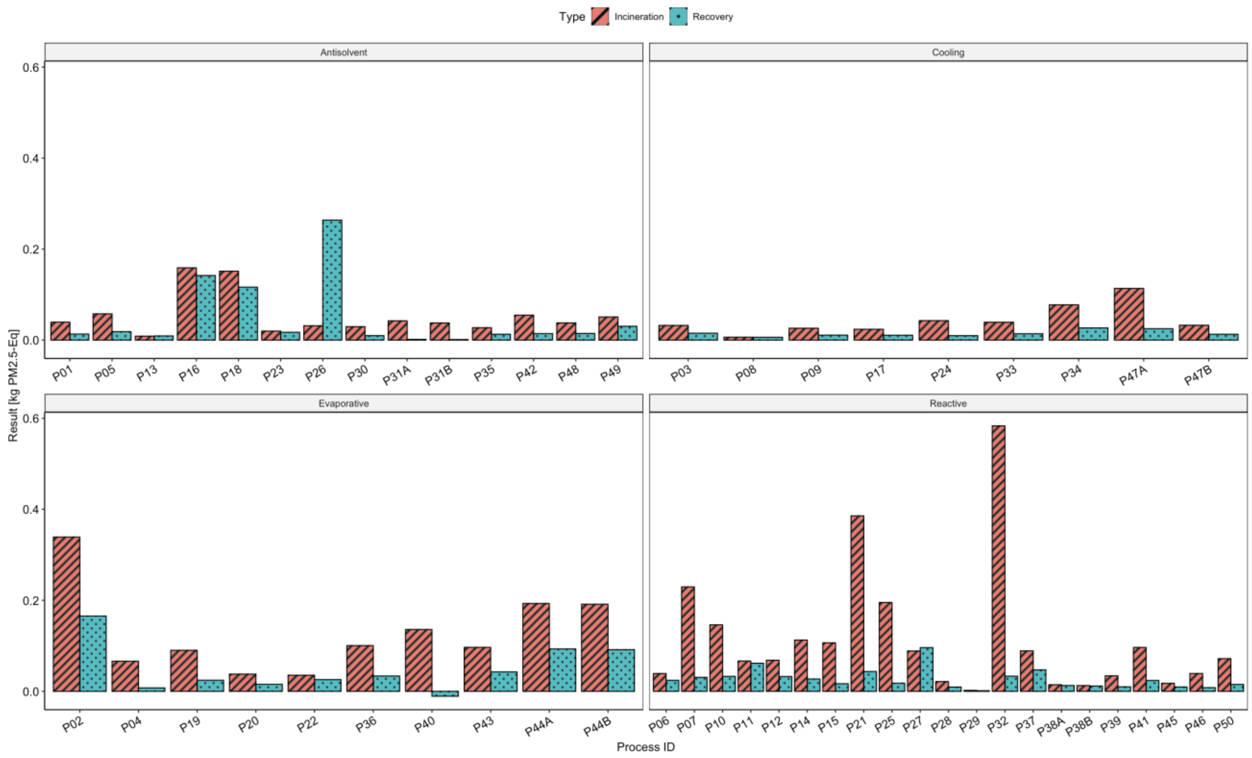

Figure 5-19. Particulate matter formation potential (PMFP) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.4.16 Photochemical Oxidant Formation Potential – Humans (HOFP) by Crystallization Type

Photochemical oxidant formation potential – humans (HOFP) results can be found in Figure 5-19. Results were lowest in cooling and antisolvent processes when compared to evaporative and most reactive processes. All processes with the incineration option (except P26) had greater impacts than those with the recovery option. For the antisolvent processes, the mean particulate matter formation potential were 0.104 ± 0.022 and 0.067 ± 0.026 kg NO_x equivalents for incineration and recovery, respectively. For the cooling processes, the means were 0.086 ± 0.021 and 0.024 ± 0.004 kg NO_x equivalents for incineration and recovery, respectively. For the evaporative processes, the means were 0.232 ± 0.039 and 0.077 ± 0.023 kg NO_x equivalents for incineration and recovery, respectively. For the reactive processes, the means were 0.239 ± 0.063 and 0.049 ± 0.015 NO_x equivalents for incineration and recovery, respectively.

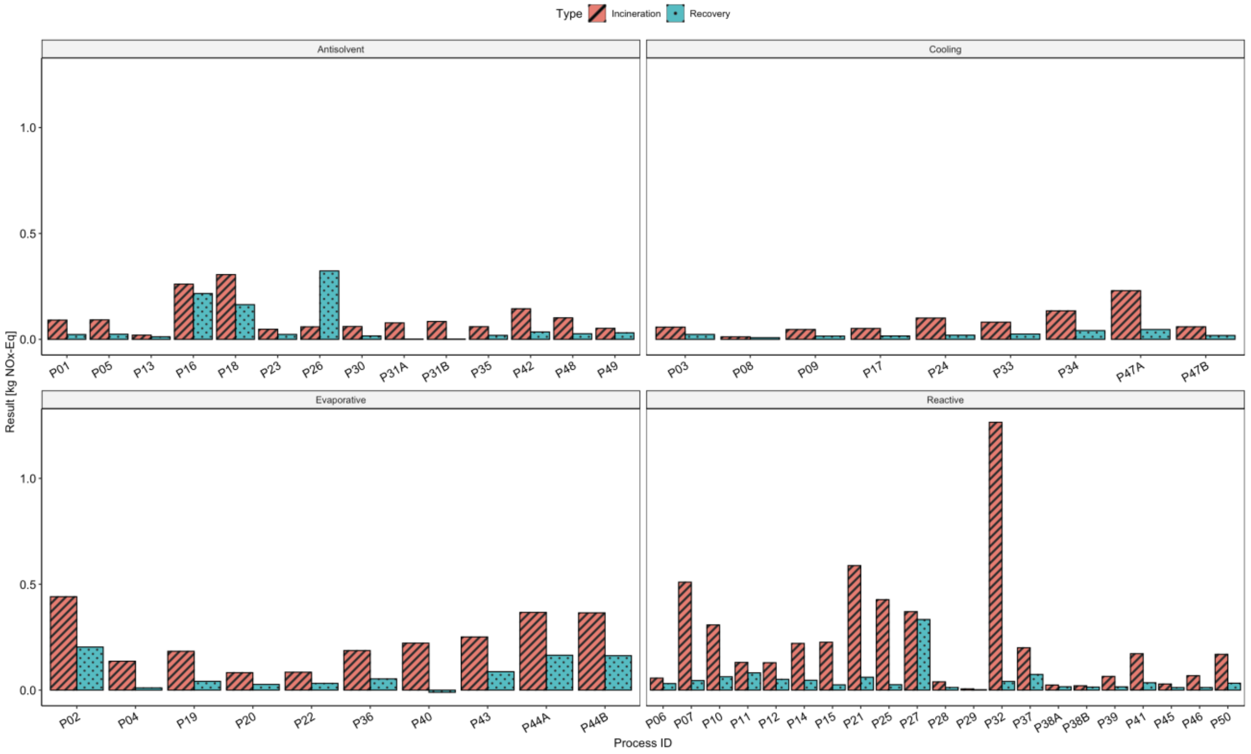

Figure 5-20. Photochemical oxidant formation potential – humans (HOFP) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.4.17 Photochemical Oxidant Formation Potential – Ecosystems (EOFP) by Crystallization Type

Photochemical oxidant formation potential ecosystems (EOFP) results can be found in Figure 5-21. Cooling and most antisolvent processes had smaller impacts that the majority of the evaporative and reactive processes. Additionally, all processes with the recovery option (except P26) had smaller impacts than those with the incineration option. For the antisolvent processes, the mean particulate matter formation potential were 0.121 ± 0.025 and 0.070 ± 0.027 kg NO_x equivalents for incineration and recovery, respectively. For the cooling processes, the means were 0.099 ± 0.026 and 0.027 ± 0.005 kg NO_x equivalents for incineration and recovery, respectively. For the evaporative processes, the means were 0.259 ± 0.041 and 0.084 ± 0.025 kg NO_x equivalents for incineration and recovery, respectively. For the reactive processes, the means were 0.256 ± 0.065 and 0.052 ± 0.015 NO_x equivalents for incineration and recovery, respectively.

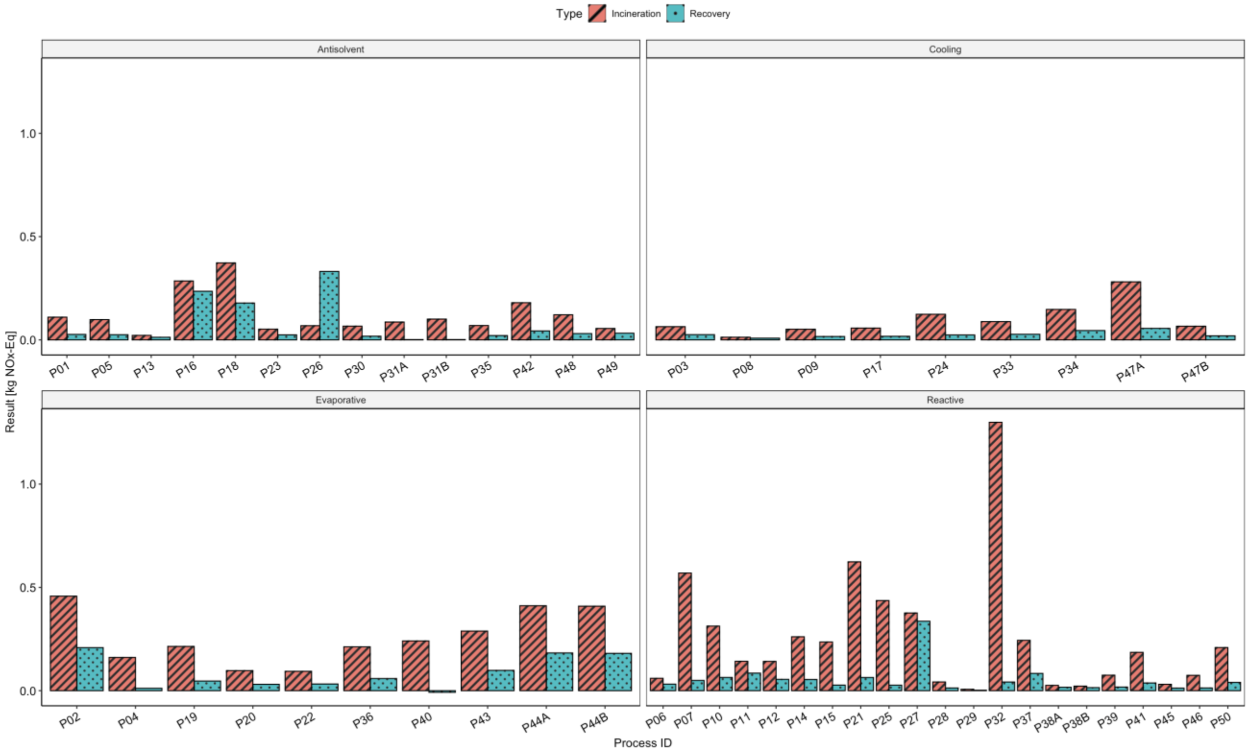

Figure 5-21. Photochemical oxidant formation potential – ecosystems (EOFP) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.4.18 Water Consumption Potential (WCP) by Crystallization Type

Water consumption potential (WCP) results are found in Figure 5-22. All processes had near-zero values (below 0.3 m^3) except for P02, P14, and P21. All results for the processes with the incineration option (except P26) had greater impacts than those with the recovery option. For the antisolvent processes, the mean water consumption potential were 0.523 ± 0.161 and 0.206 ± 0.089 m^3 for incineration and recovery, respectively. For the cooling processes, the means were 0.358 ± 0.125 and 0.091 ± 0.032 m^3 for incineration and recovery, respectively. For the evaporative processes, the means were 4.790 ± 3.700 and 1.660 ± 1.625 m^3 for incineration and recovery, respectively. For the reactive processes, the means were 1.450 ± 0.644 and 0.212 ± 0.080 m^3 for incineration and recovery, respectively.

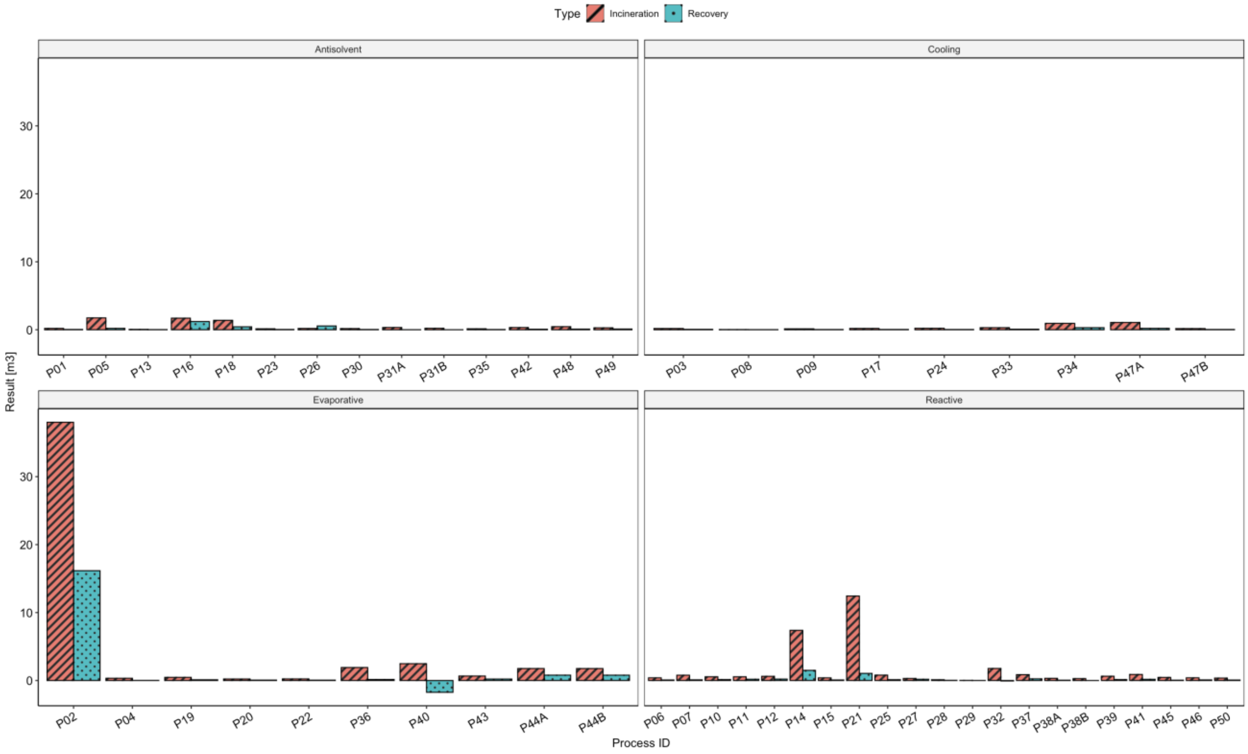

Figure 5-22. Water consumption potential (WCP) by process ID for incineration and solvent recovery options categorized by crystallization type.

5.5 Environmental Impacts of Solvents

Environmental impacts for all solvents involved in the 54 processes were examined in more detail. Their LCIA results for the 18 impact categories are found in the following sub-sections. The analysis was conducted on a basis of 1 kg of solvent produced for a cradle-to-cradle perspective.

5.5.1 Terrestrial Acidification Potential (TAP) per 1 kg of Solvent

Terrestrial acidification potential (TAP) results for each solvent can be found in Figure 5-23. The results showed that 2-MeTHF demonstrated the greatest impacts. This is likely due to the amount of crop area required to produce corn, sugarcane, and rice. Water, methanol, toluene, ethanol, and heptane showed the lowest results when compared to the other solvents. When analysed, there was no significant different between class 2 and class 3 solvents for this impact category.

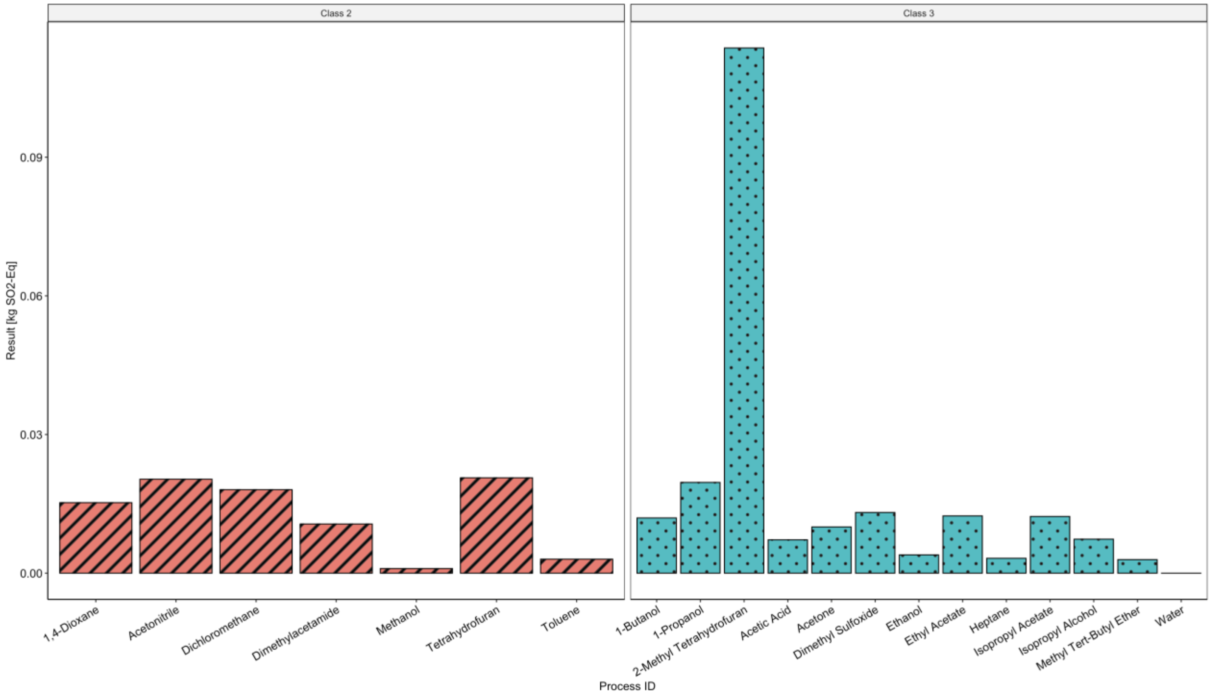

Figure 5-23. Terrestrial acidification potential (TAP) for 1 kg of solvent categorized by residual solvent class.

5.5.2 Global Warming Potential (GWP100) per 1 kg of Solvent

Global warming potential results for each solvent can be found in Figure 5-24. Results showed that the highest impacts came from 2-MeTHF and then from tetrahydrofuran. Water and methanol showed the lowest impacts. In general, class 3 solvents had a slightly lower global warming potential than class 2 solvents.

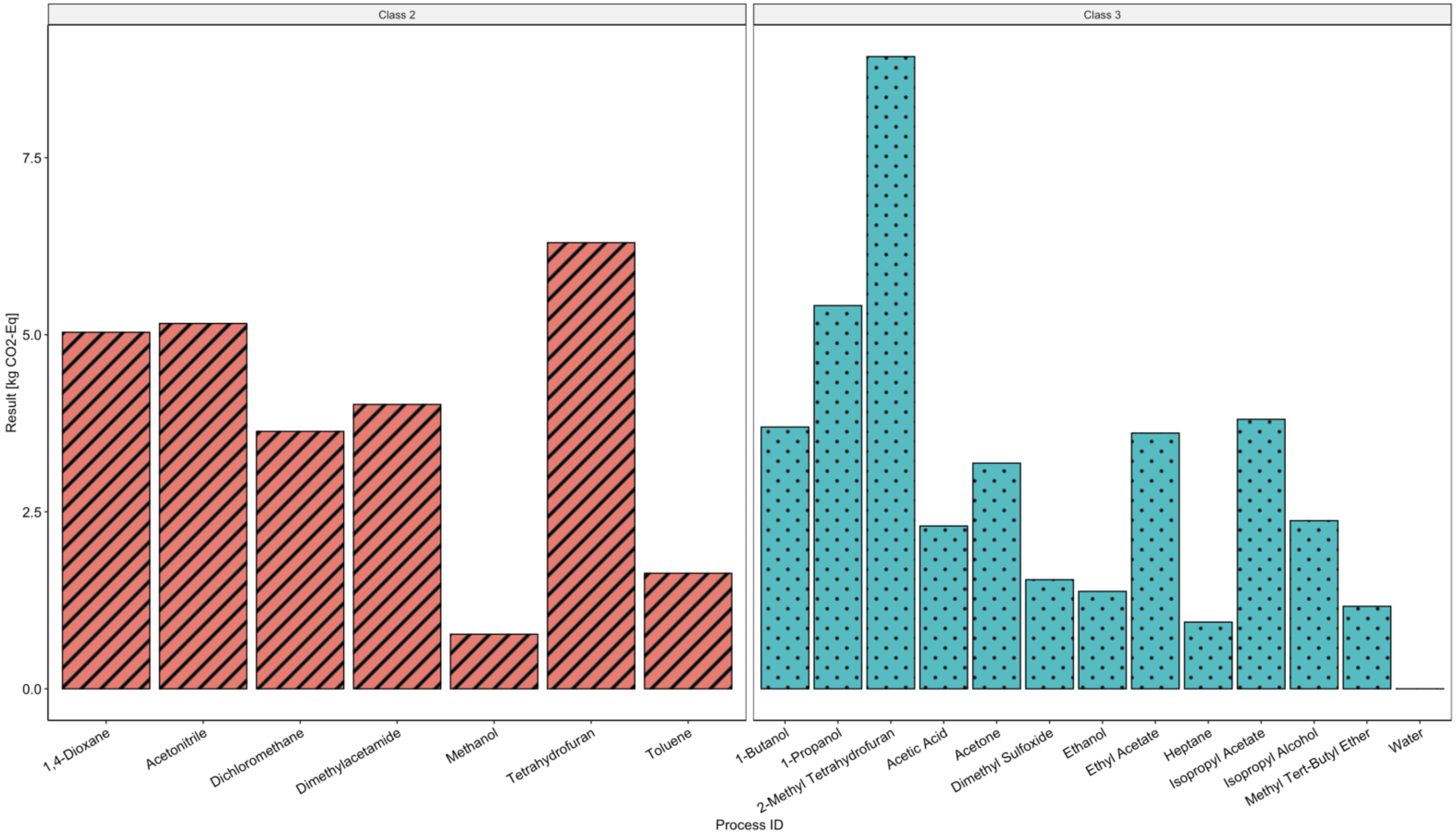

Figure 5-24. Global warming potential (GWP100) for 1 kg of solvent categorized by residual solvent class.

5.5.3 Freshwater Ecotoxicity Potential (FETP) per 1 kg of Solvent

Freshwater ecotoxicity potential (FETP) results for each solvent can be found in Figure 5-25. The solvent having the largest impacts were 2-MeTHF and tetrahydrofuran. Water, toluene, methanol, and dichloromethane showed the smallest impacts. The remaining class 3 solvents showed similar or lower results than the remaining class 2 solvents.

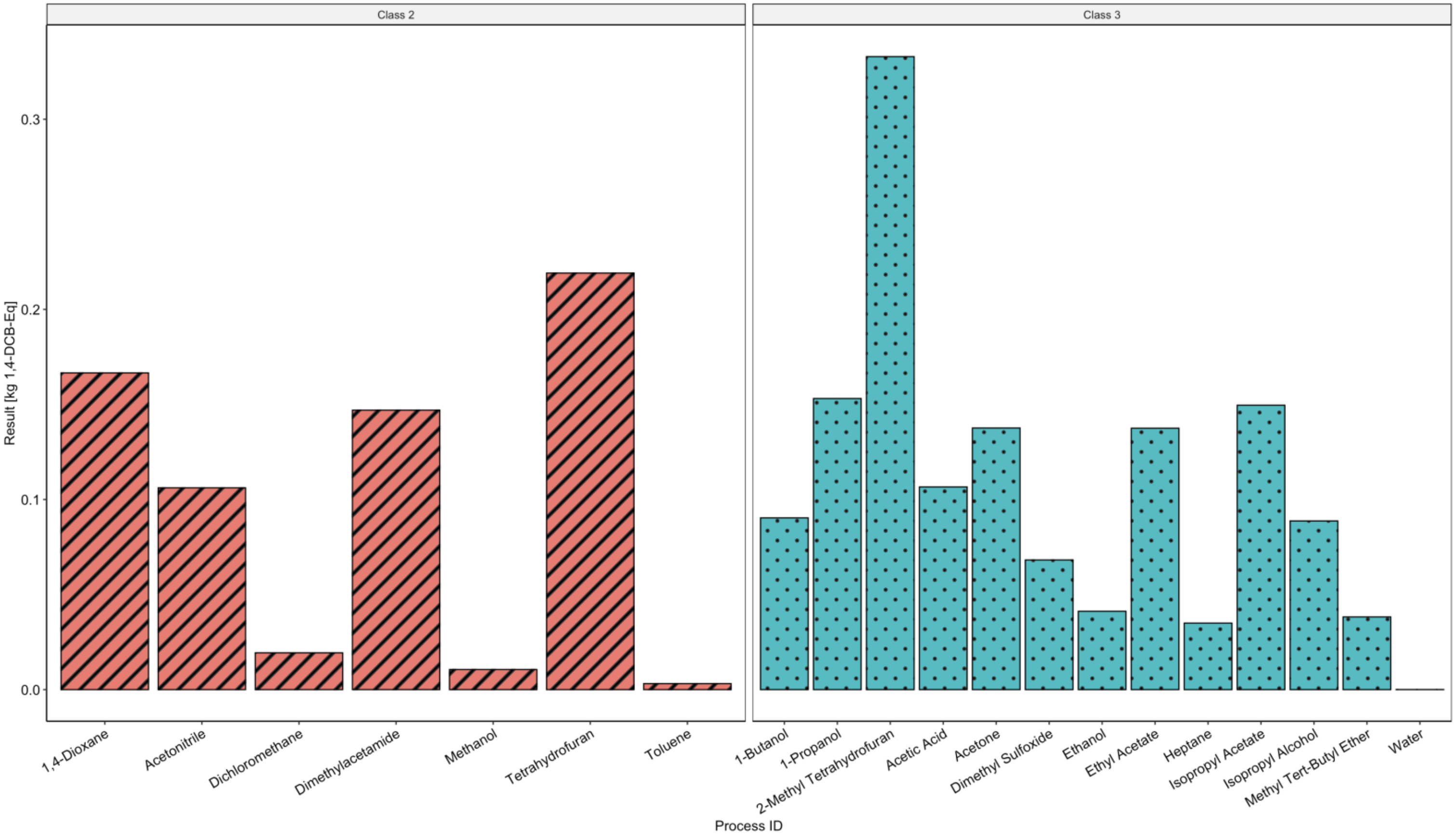

Figure 5-25. Freshwater ecotoxicity potential (FETP) for 1 kg of solvent categorized by residual solvent class.

5.5.4 Marine Ecotoxicity Potential (METP) per 1 kg of Solvent

Marine ecotoxicity potential (METP) results for each solvent can be found in Figure 5-26. Results showed similarities to the freshwater ecotoxicity potential: 2-MeTHF and tetrahydrofuran had the largest impacts while water, toluene, methanol, and dichloromethane had the smallest impacts. No significant different between class 2 and class 3 solvents could be observed.

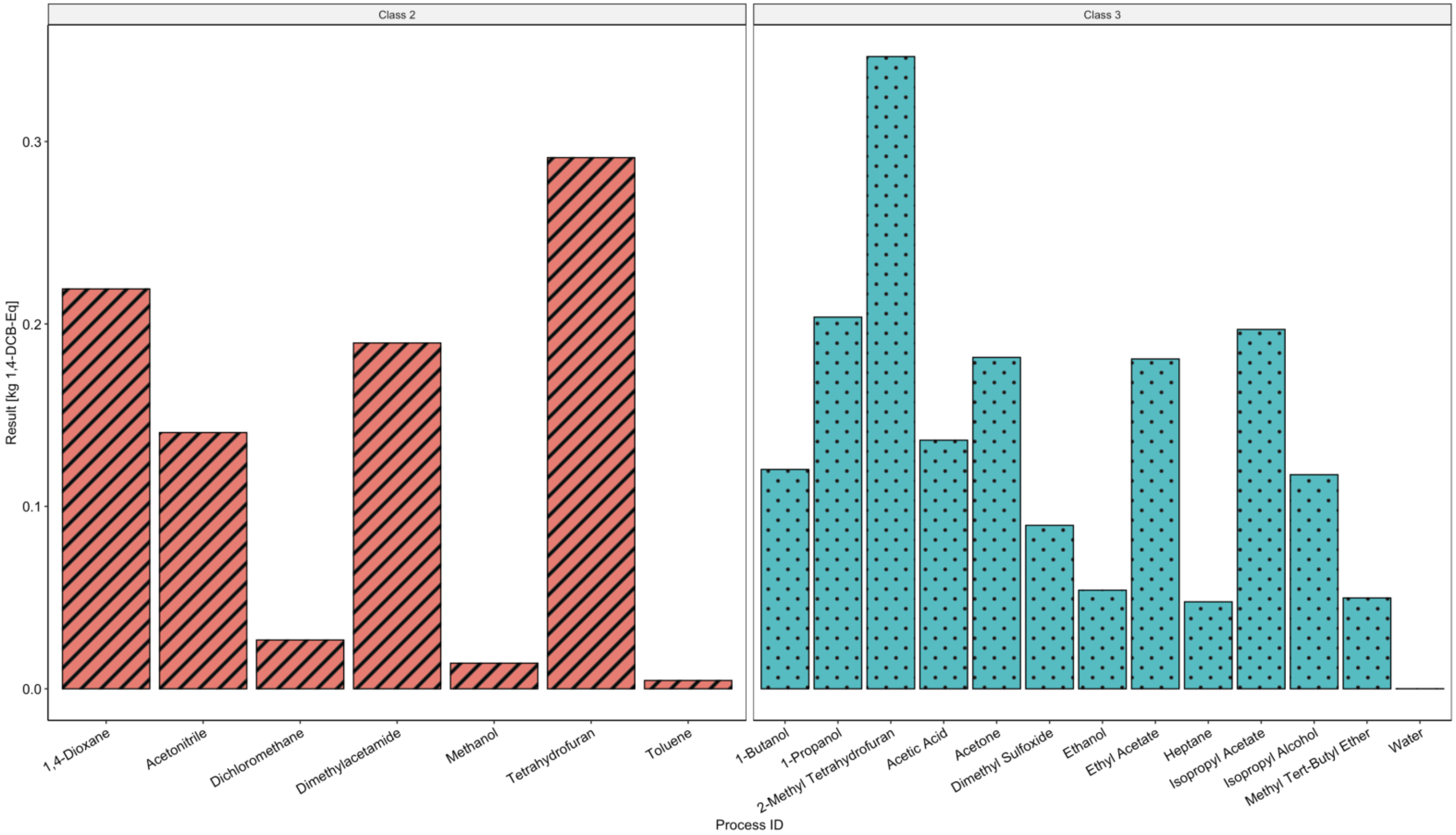

Figure 5-26. Marine ecotoxicity potential (METP) for 1 kg of solvent categorized by residual solvent class.

5.5.5 Terrestrial Ecotoxicity Potential (TETP) per 1 kg of Solvent

Terrestrial ecotoxicity potential results for each solvent can be found in Figure 5-27. Similar to the marine and freshwater ecotoxicity potentials, terrestrial ecotoxicity potential showed 2-MeTHF and tetrahydrofuran having the largest impacts and water, toluene, methanol, and dichloromethane having the lowest results. Some of the remaining class 3 solvents had larger impacts than the remaining class 2 solvents, though not to a significant level.

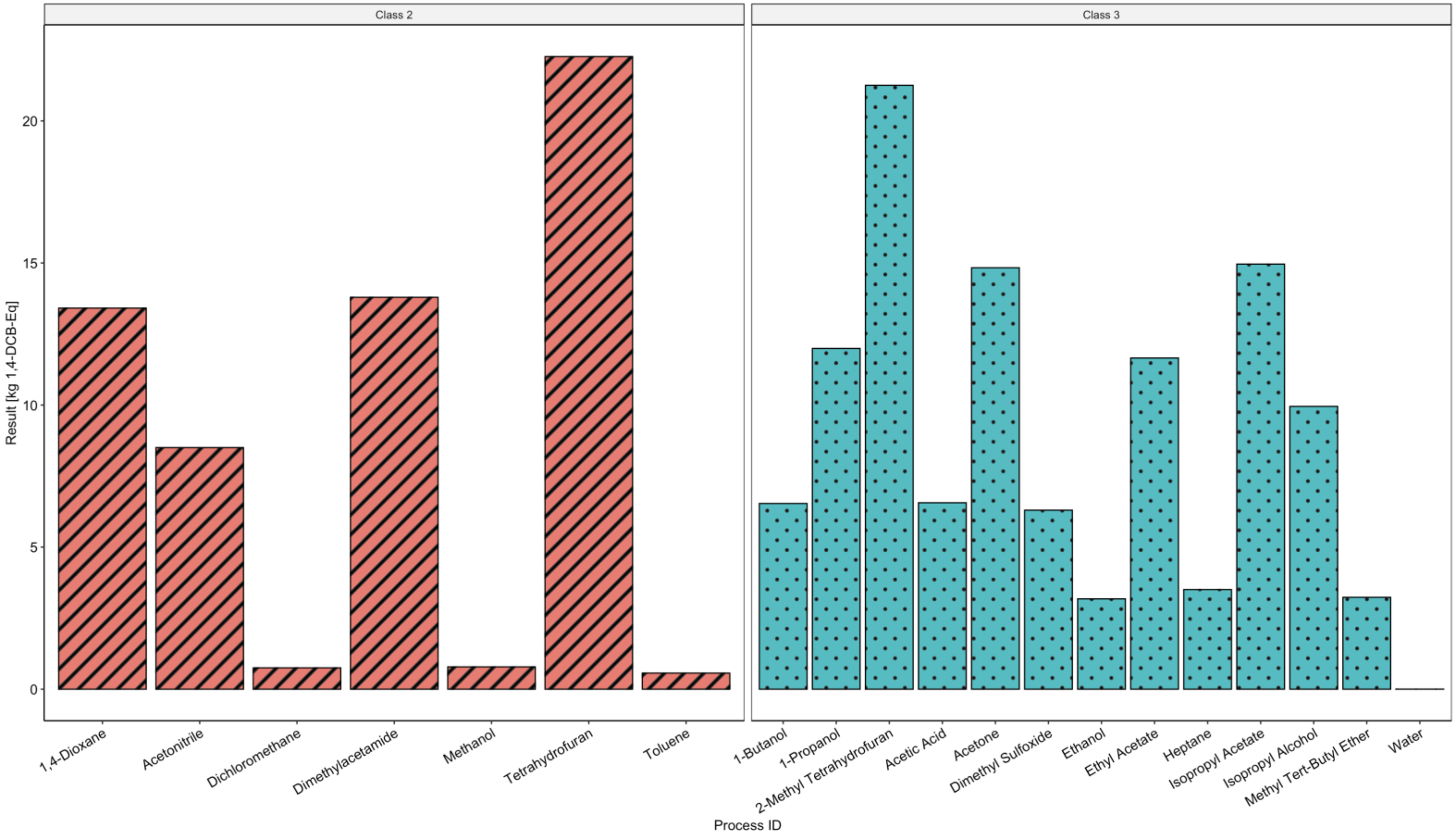

Figure 5-27. Terrestrial ecotoxicity potential (TETP) for 1 kg of solvent categorized by residual solvent class.

5.5.6 Fossil Fuel Potential (FFP) per 1 kg of Solvent

Fossil fuel potential (FFP) results for each solvent can be found in Figure 5-28. Impacts were highest in 1,4-dioxane, acetonitrile, dichloromethane, tetrahydrofuran, 1-butanol, 1-propanol, acetone, ethyl acetate, and isopropyl acetate. Impacts were near-zero for water and all other solvents were between 0.5 and 1.5 kg oil equivalents. There was no significant difference observed between class 2 and class 3 solvents.

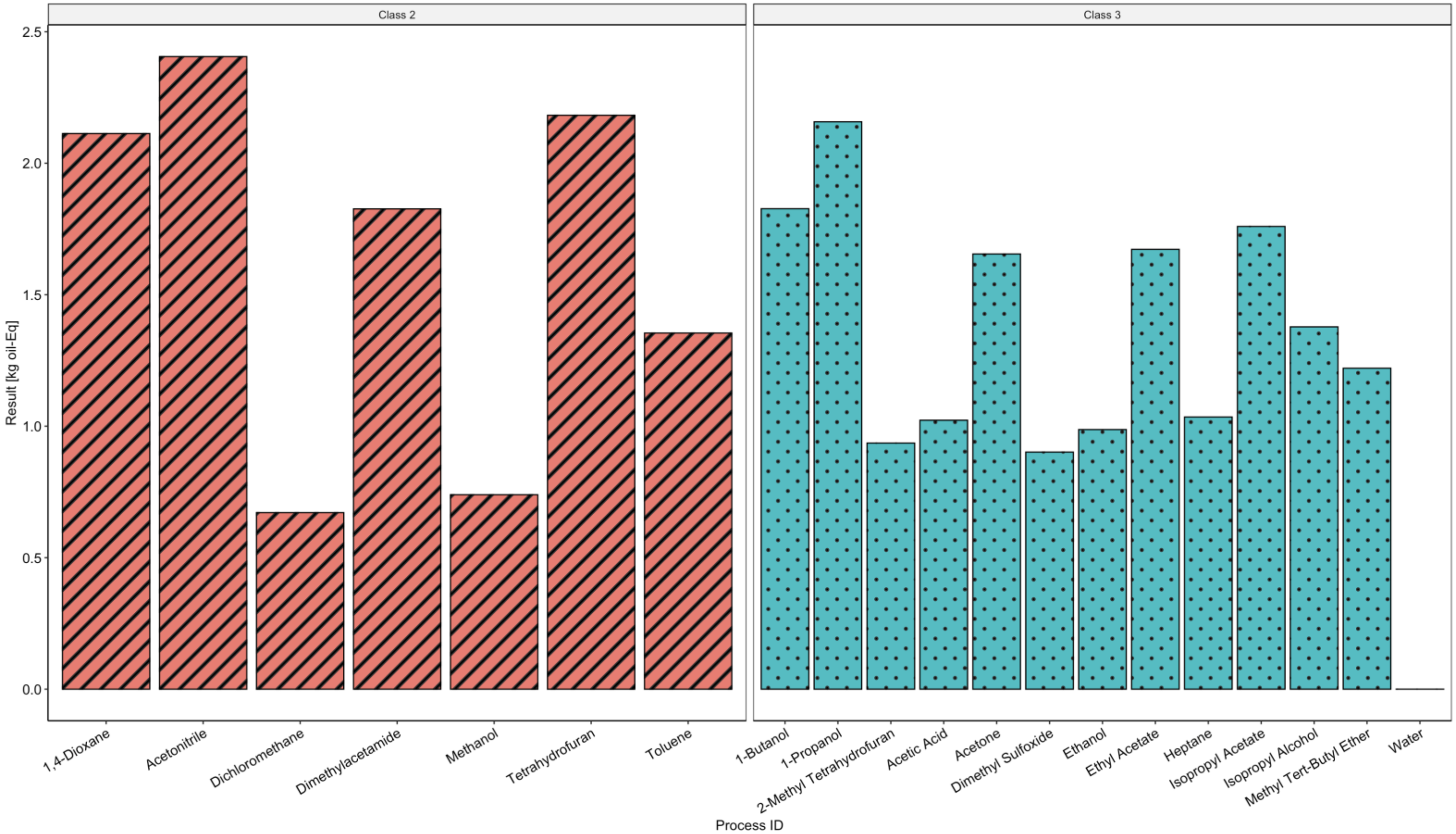

Figure 5-28. Fossil fuel potential (FFP) for 1 kg of solvent categorized by residual solvent class.

5.5.7 Freshwater Eutrophication Potential (FEP) per 1 kg of Solvent

Freshwater eutrophication potential (FEP) results for each solvent can be found in Figure 5-29. Impacts were lowest for water, methyl *tert*-butyl ether, heptane, toluene, methanol, and dichloromethane. Impacts were largest in tetrahydrofuran, 2-MeTHF, ethyl acetate, and 1,4-dioxane. No significant difference between class 2 and class 3 solvents were observed.

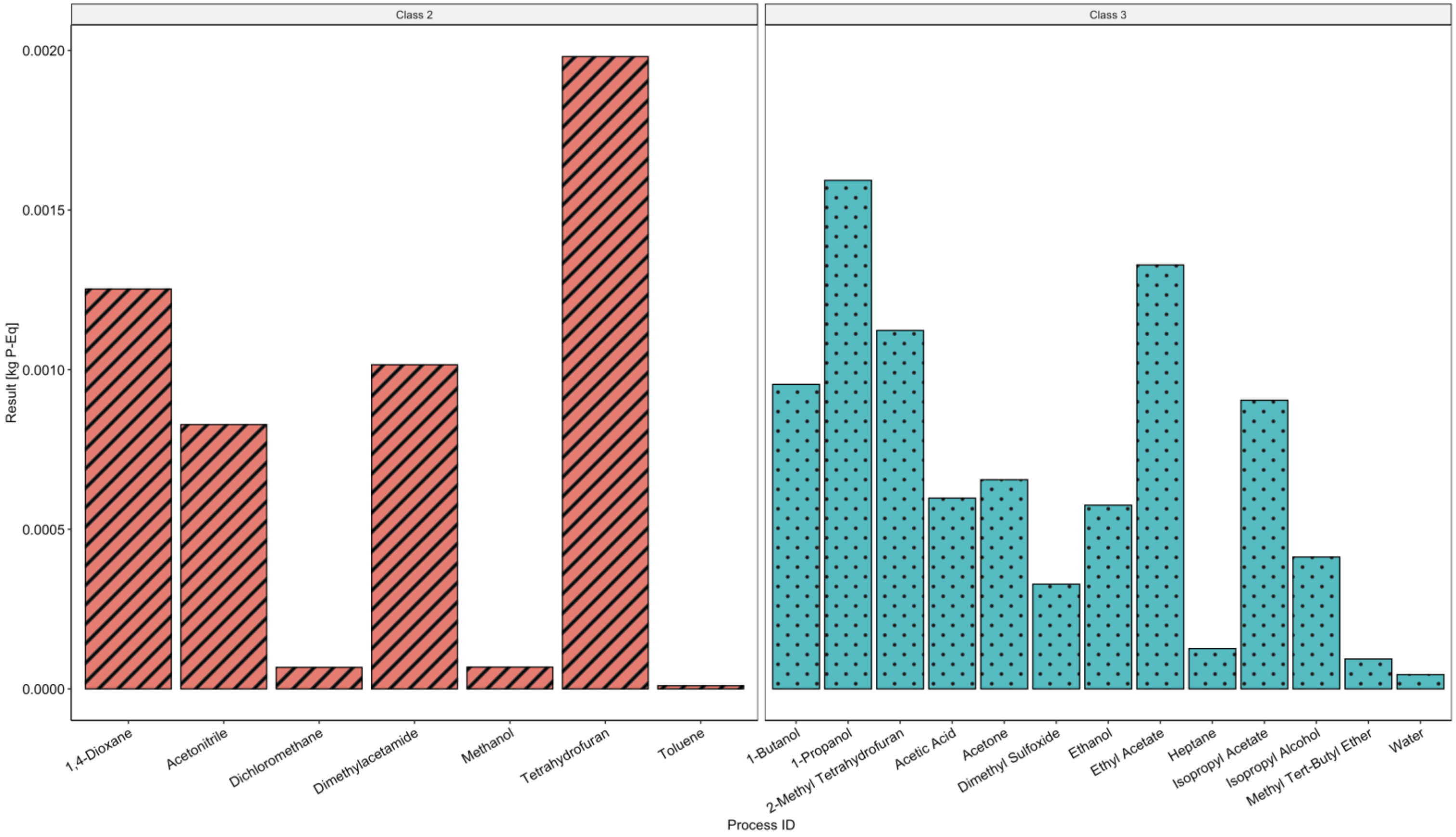

Figure 5-29. Freshwater eutrophication potential (FEP) for 1 kg of solvent categorized by residual solvent class.

5.5.8 Marine Eutrophication Potential (MEP) per 1 kg of Solvent

Marine eutrophication potential (MEP) results for each solvent can be found in Figure 5-30. Impacts were largest for 2-MeTHF and then followed by acetonitrile and dimethylacetamide. All other solvents were near-zero.

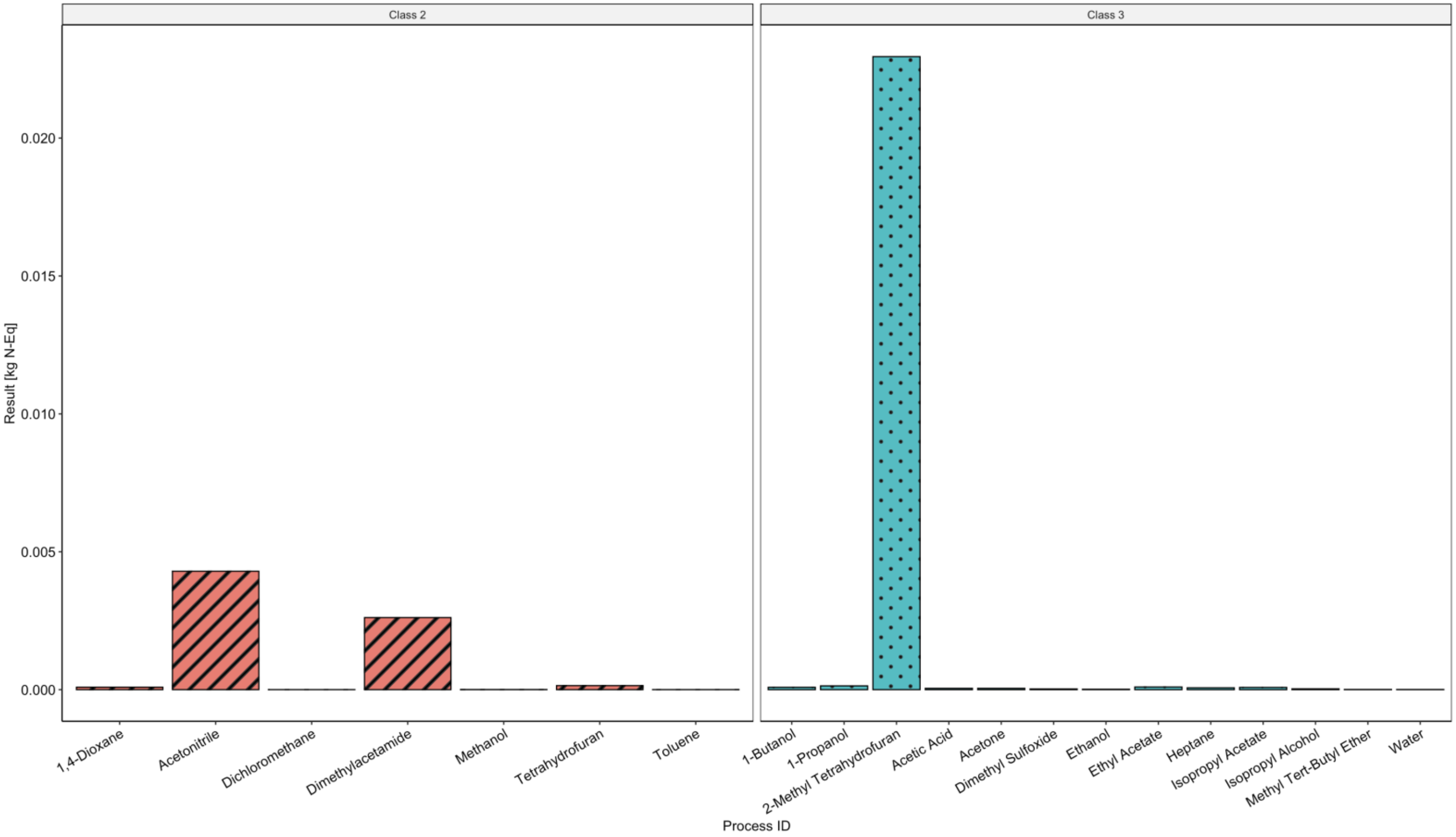

Figure 5-30. Marine eutrophication potential (MEP) for 1 kg of solvent categorized by residual solvent class.

5.5.9 Human Toxicity Potential – Carcinogenic (HTPc) per 1 kg of Solvent

Human toxicity potential – carcinogenic (HTPc) results for each solvent can be found in Figure 5-31. Water had the lowest impact and was then followed by toluene and methanol. Tetrahydrofuran and 2-MeTHF had the largest impacts. Overall, class 3 solvents had a slightly lower impact than class 2 solvents.

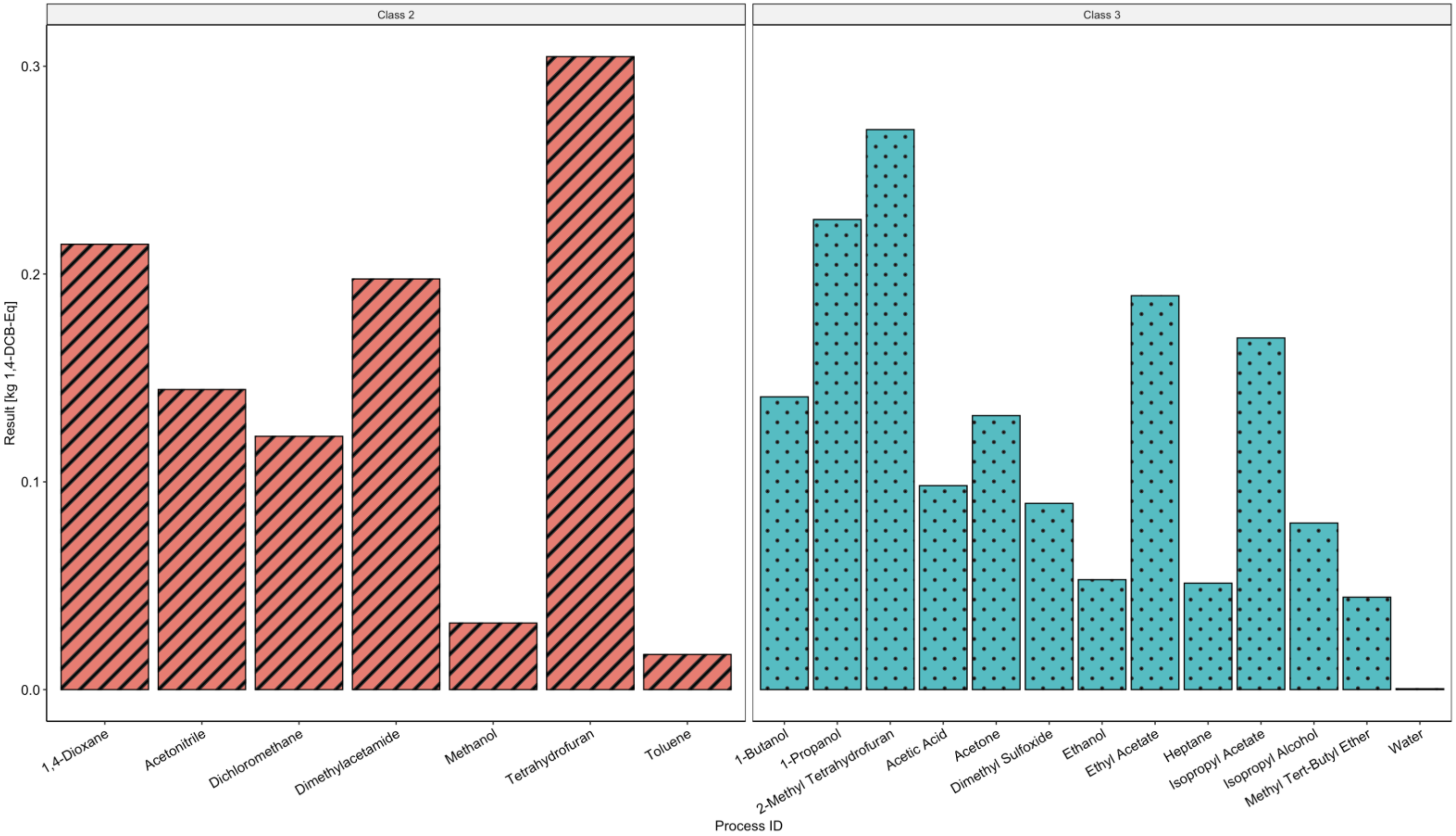

Figure 5-31. Human toxicity potential – carcinogenic (HTPc) for 1 kg of solvent categorized by residual solvent class.

5.5.10 Human Toxicity Potential – Non-Carcinogenic (HTPnc) per 1 kg of Solvent

Human toxicity potential – non-carcinogenic (HTPnc) results for each solvent can be found in Figure 5-32. Water, toluene, methanol, and dichloromethane had the lowest impacts. 2-MeTHF had a negative impact, producing positive outcome for non-carcinogenic human toxicity. This is likely due to 2-MeTHF being sourced from agricultural waste. No significant difference was observed between class 2 and class 3 solvents.

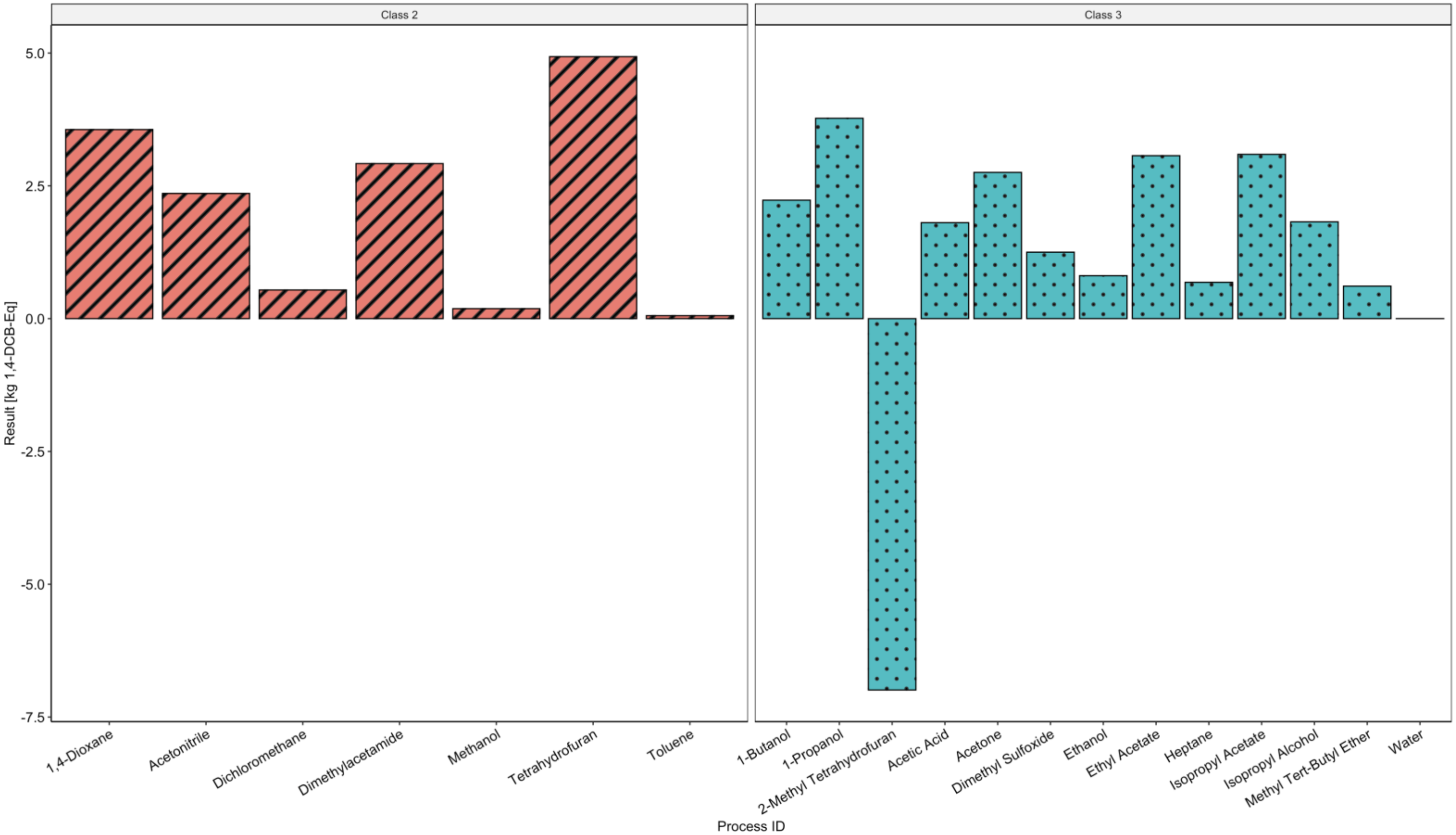

Figure 5-32. Human toxicity potential – non-carcinogenic (HTPnc) for 1 kg of solvent categorized by residual solvent class.

5.5.11 Ionising Radiation Potential (IRP) per 1 kg of Solvent

Ionising radiation potential (IRP) results for each solvent can be found in Figure 5-33. Tetrahydrofuran had the highest results while water, toluene, methanol, ethanol, methyl *tert*-butyl ether, and dichloromethane showed the lowest. No significant difference could be observed between class 2 and class 3 solvents.

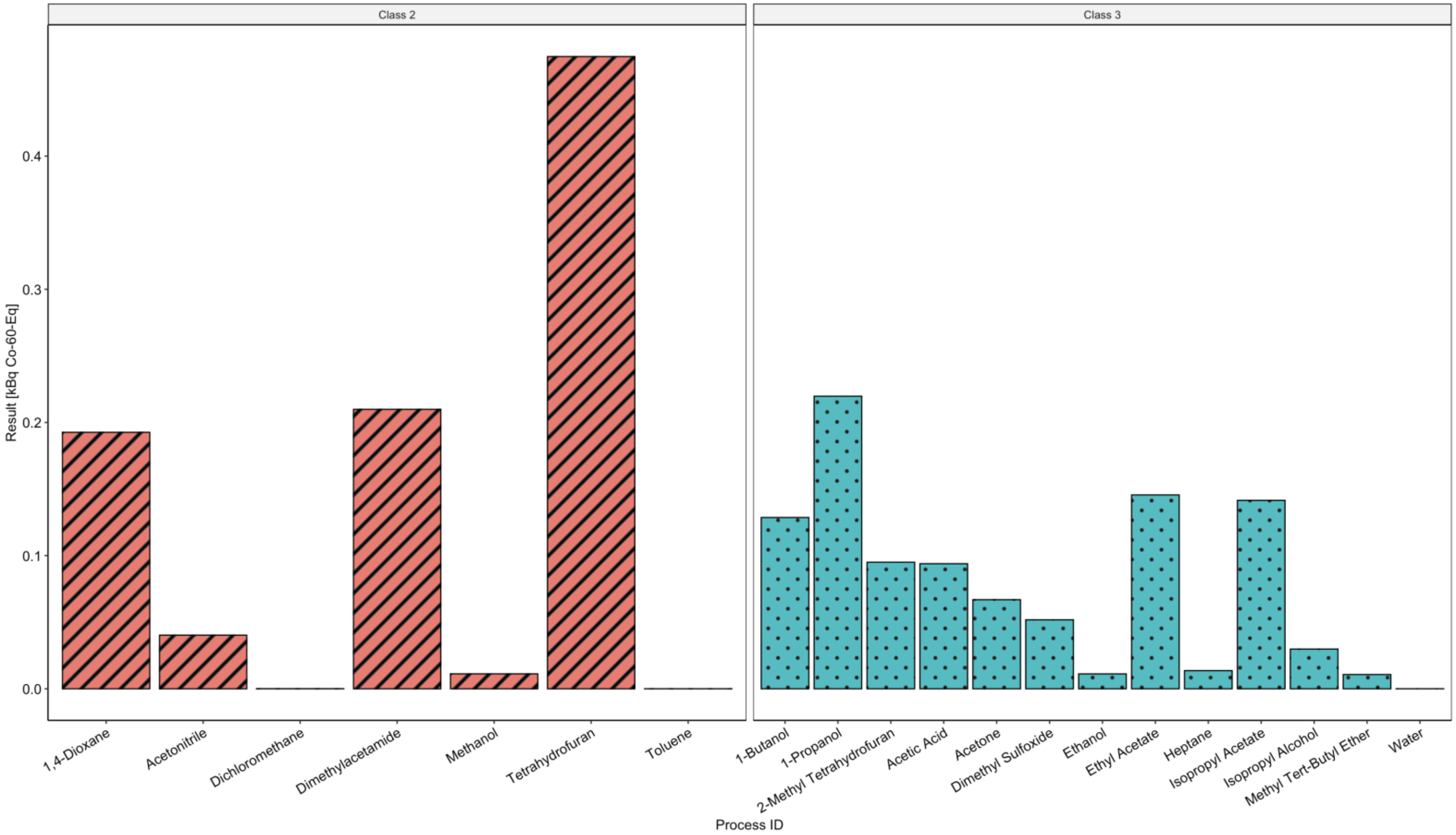

Figure 5-33. Ionising radiation potential (IRP) for 1 kg of solvent categorized by residual solvent class.

5.5.12 Agricultural Land Occupation (LOP) per 1 kg of Solvent

Agricultural land occupation (LOP) results for each solvent can be found in Figure 5-34. 2-MeTHF had the largest impacts due to the large use of agricultural land required for corn, rice, and sugarcane. All other solvents showed low impacts for agricultural land usage.

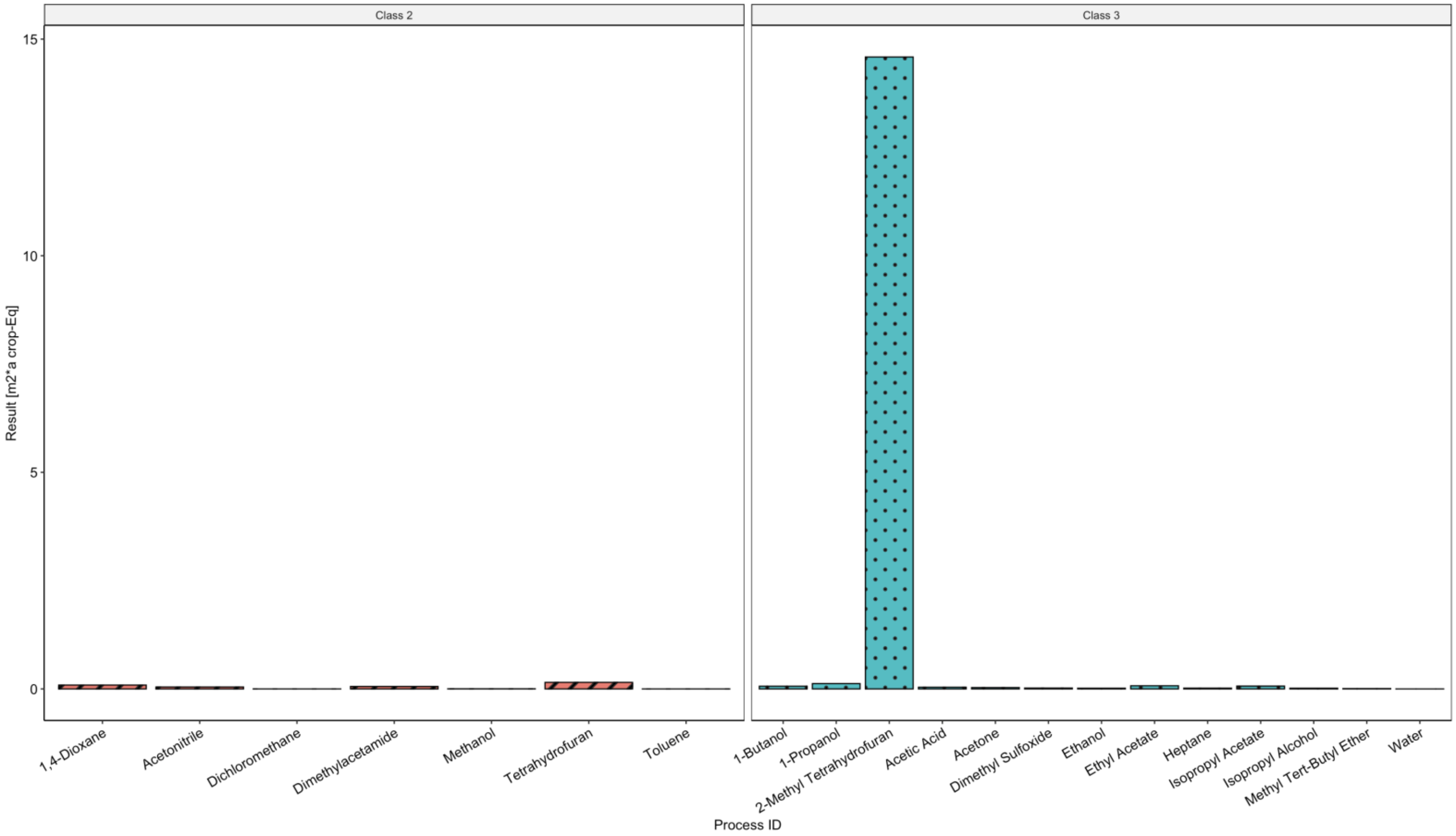

Figure 5-34. Agricultural land occupation (LOP) for 1 kg of solvent categorized by residual solvent class.

5.5.13 Surplus Ore Potential (SOP) per 1 kg of Solvent

Surplus ore potential (SOP) results for each solvent can be found in Figure 5-35. Water, dichloromethane, and toluene showed the smallest impacts, while 2-MeTHF, tetrahydrofuran, and ethyl acetate showed the largest impacts. No significant difference was observed between class 2 and class 3 solvents.

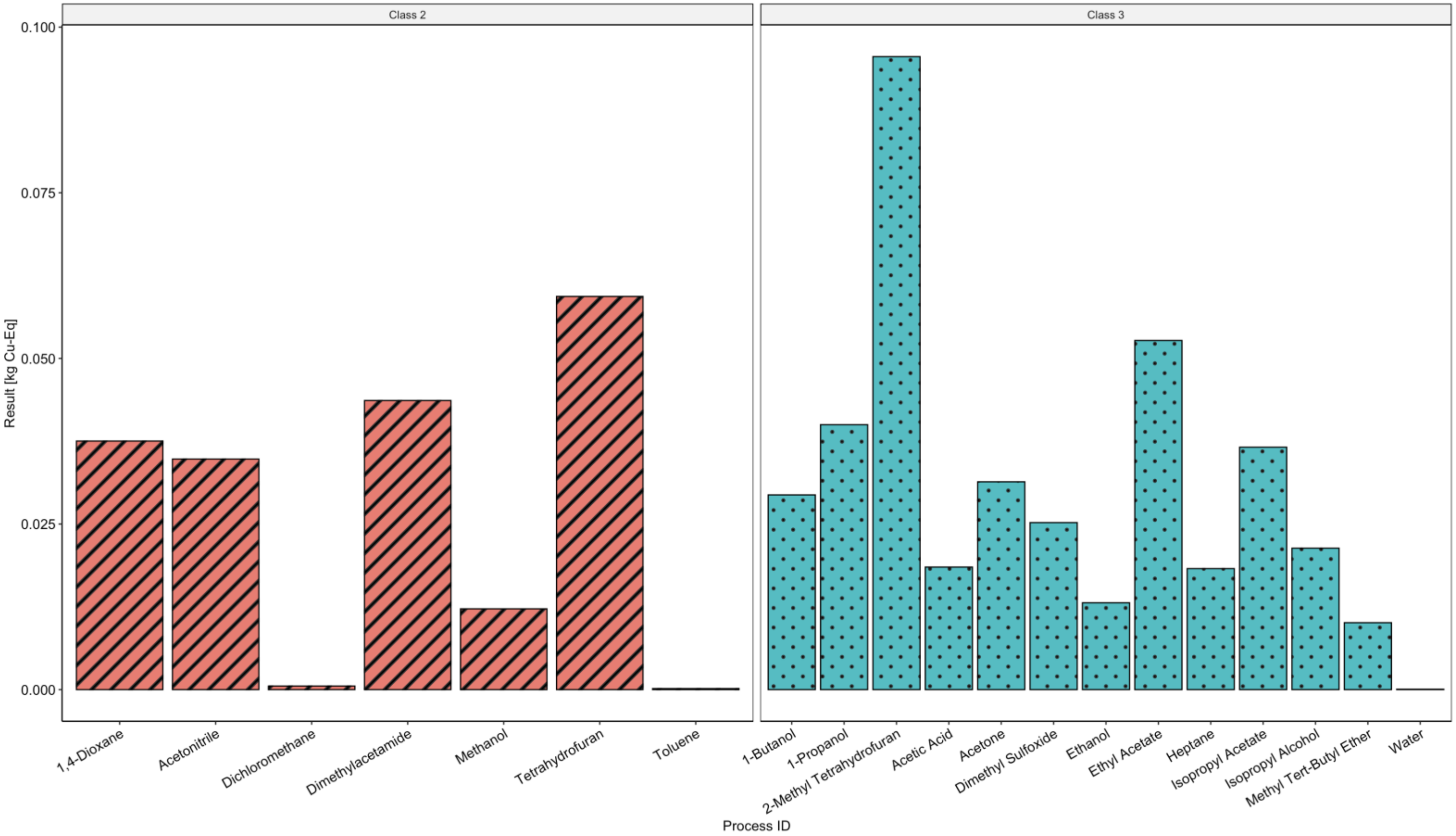

Figure 5-35. Surplus ore potential (SOP) for 1 kg of solvent categorized by residual solvent class.

5.5.14 Ozone Depletion Potential ($ODP_{infinite}$) per 1 kg of Solvent

Ozone depletion potential ($ODP_{infinite}$) results for each solvent can be found in Figure 5-36. Results were highest in 2-MeTHF and dichloromethane. All other solvents were near-zero.

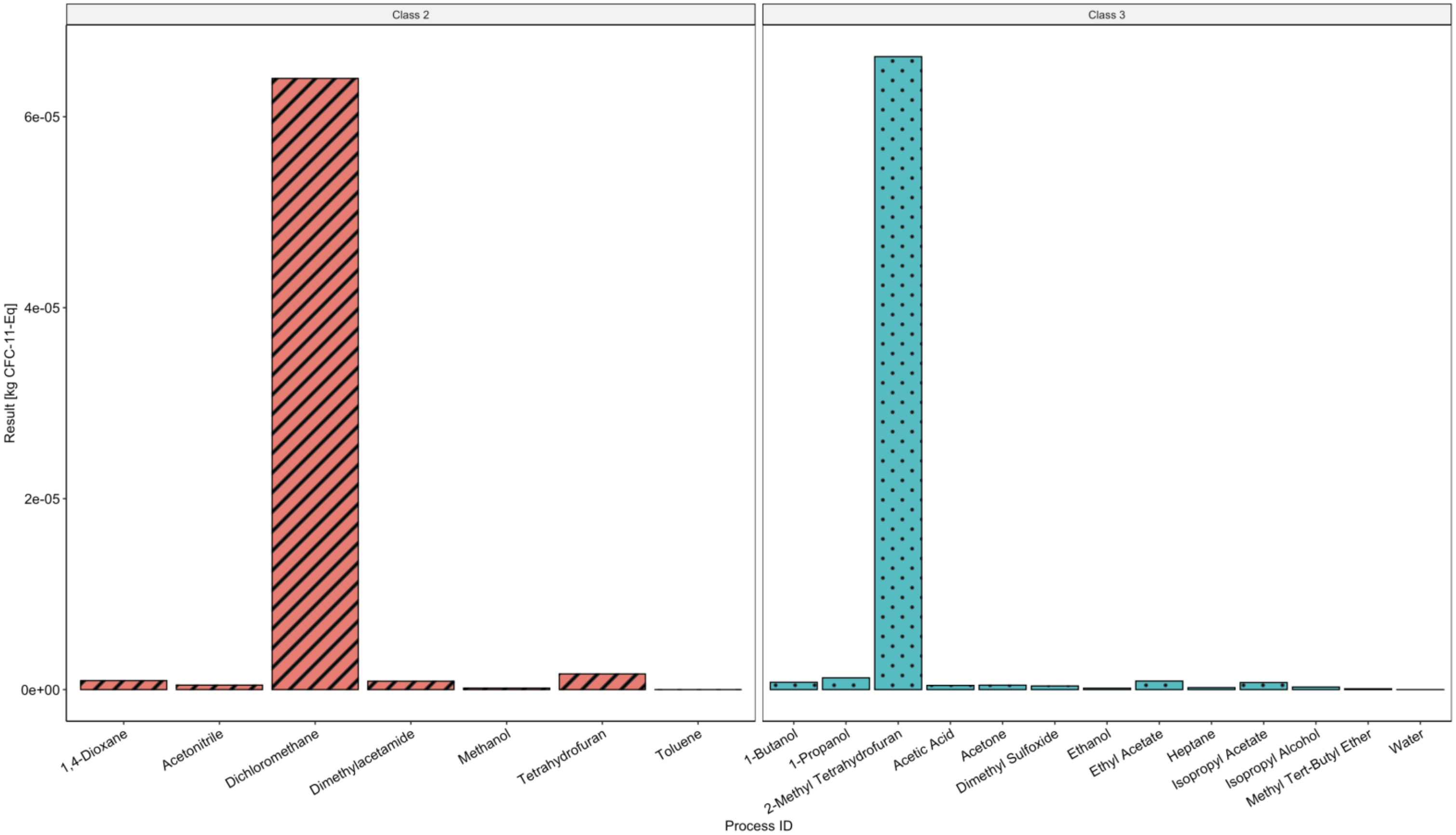

Figure 5-36. Ozone depletion potential ($ODP_{infinite}$) for 1 kg of solvent categorized by residual solvent class.

5.5.15 Particulate Matter Formation Potential (PMFP) per 1 kg of Solvent

Particulate matter formation potential (PMFP) results for each solvent can be found in Figure 5-37. Water, heptane, ethanol, methanol, and toluene showed the smallest impacts while 2-MeTHF showed the largest. No significant difference between class 2 and class 3 solvents were found.

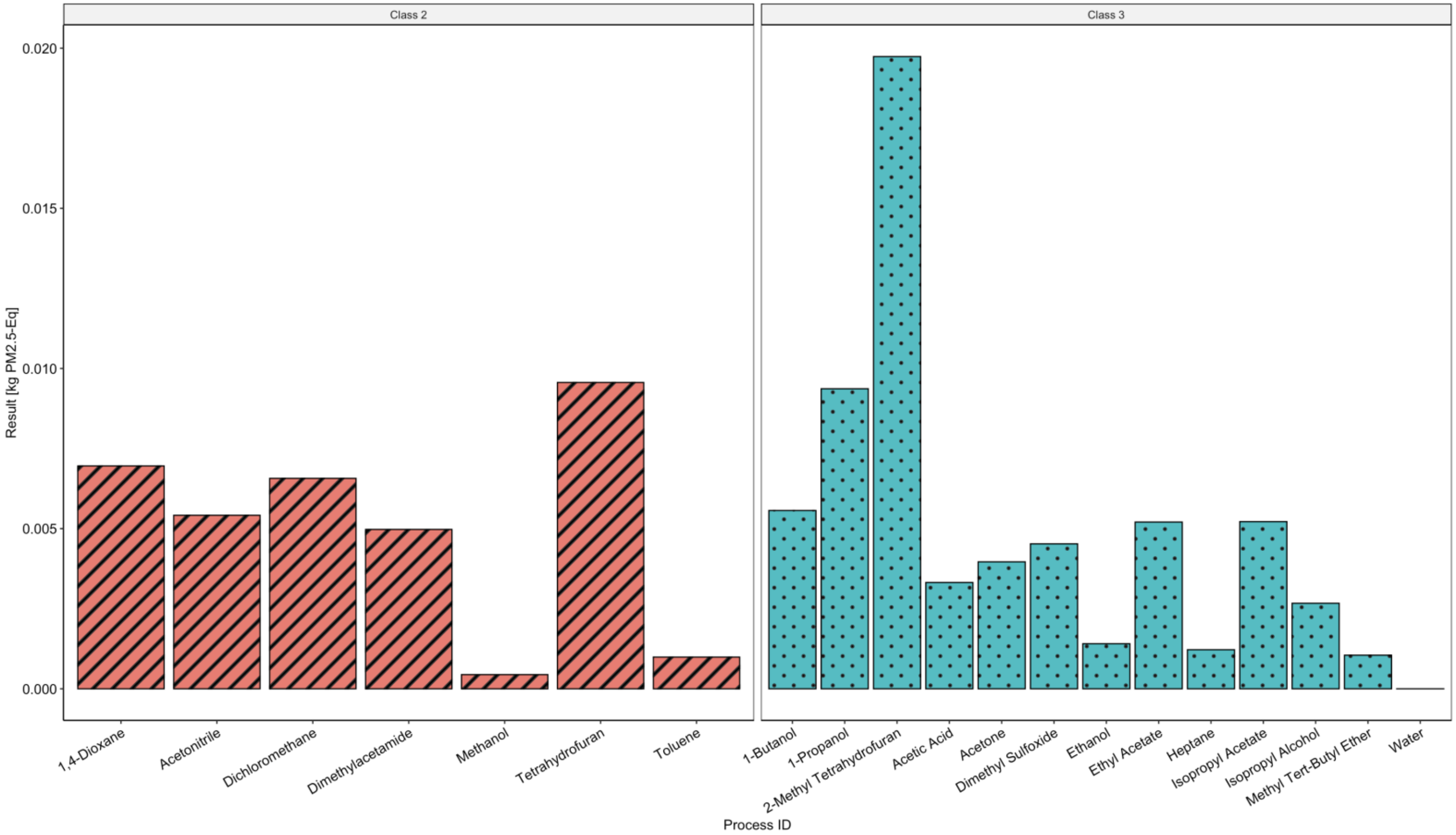

Figure 5-37. Particulate matter formation potential (PMFP) for 1 kg of solvent categorized by residual solvent class.

5.5.16 Photochemical Oxidant Formation Potential – Humans (HOFP) per 1 kg of Solvent

Photochemical oxidant formation potential – humans (HOFP) results can be found in Figure 5-38. Impacts were largest for 2-MeTHF and 1-propanol and smallest for water, methanol, and toluene. No significant difference between class 2 and class 3 solvents was observed.

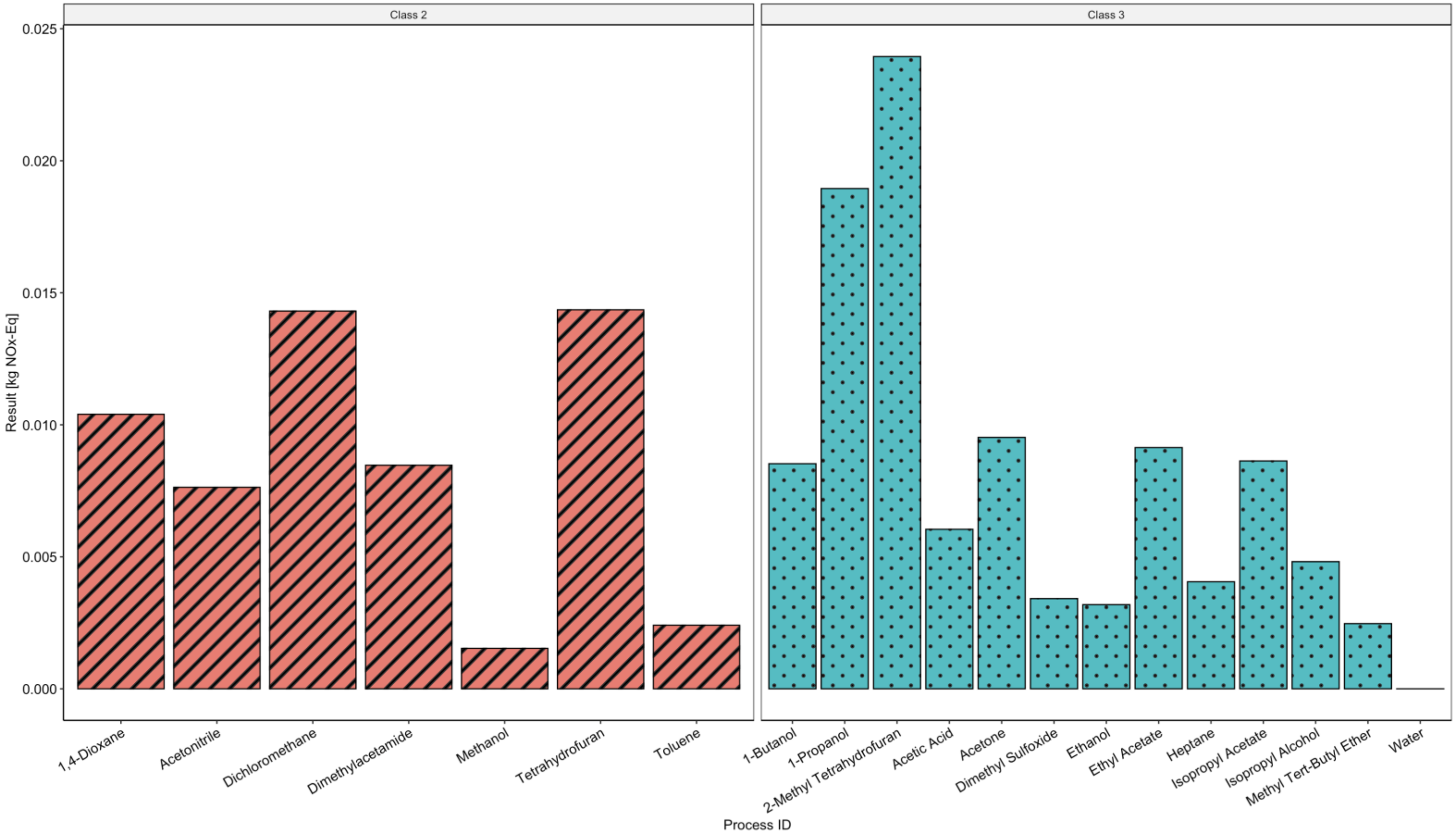

Figure 5-38. Photochemical oxidant formation potential – humans (HOFP) for 1 kg of solvent categorized by residual solvent class.

5.5.17 Photochemical Oxidant Formation Potential – Ecosystems (EOFP) per 1 kg of Solvent

Photochemical oxidant formation potential – ecosystems (EOFP) results for each solvent can be found in Figure 5-38. Similar to HOFP, EOFP's largest impacts are found with 2-MeTHF and 1-propanol and lowest with water, methanol, and toluene. Further, no significant difference was observed between class 2 and class 3 solvents.

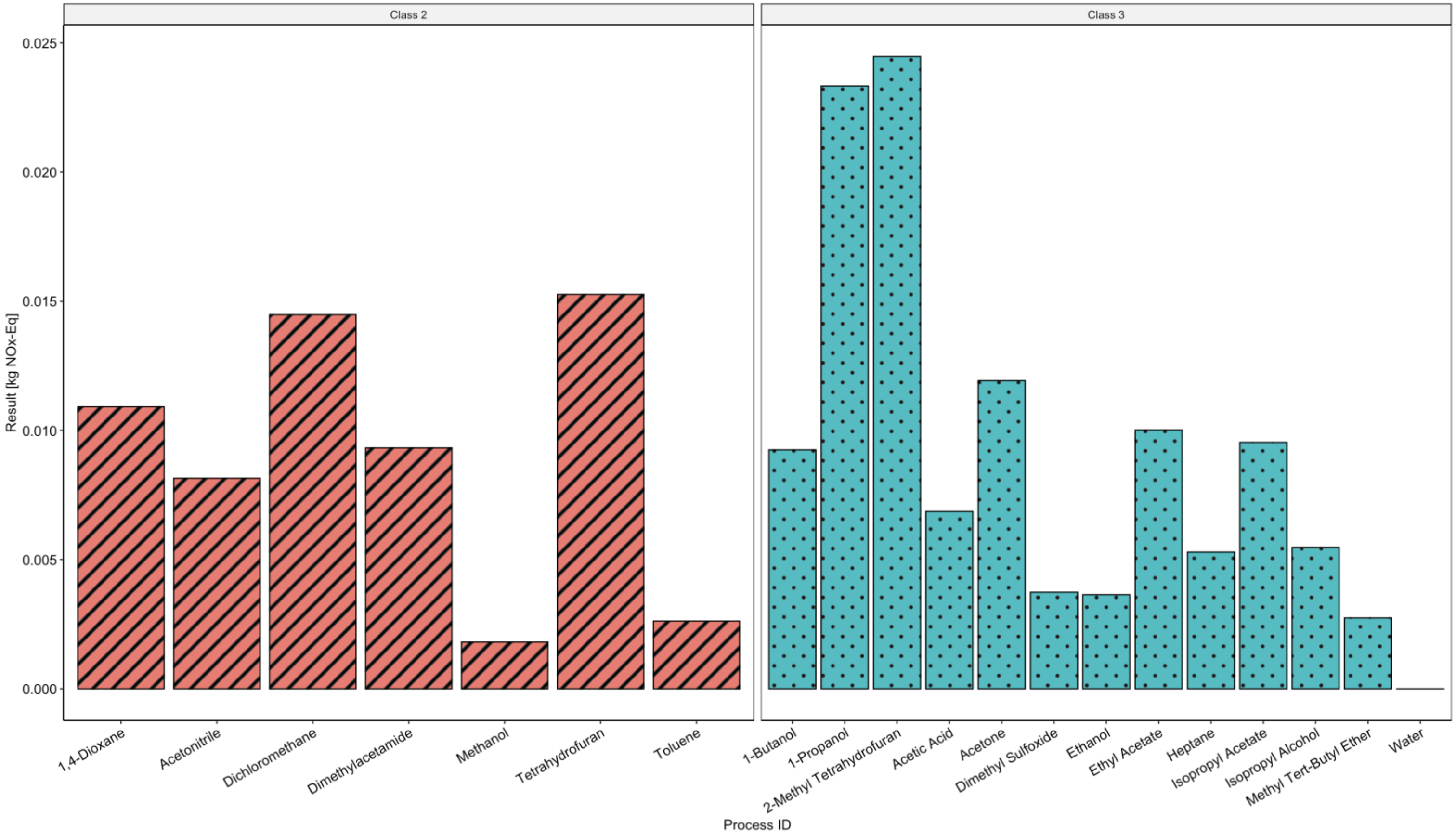

Figure 5-39. Photochemical oxidant formation potential – ecosystems (EOFP) for 1 kg of solvent categorized by residual solvent class.

5.5.18 Water Consumption Potential (WCP) per 1 kg of Solvent

Water consumption potential (WCP) results for each solvent can be found in Figure 5-40. Water consumption was highest for 2-MeTHF likely due to the large amount of water required for agricultural crop growth in the production of the solvent. Tetrahydrofuran was the next largest, but significantly lower than that of 2-MeTHF. All other solvents had relatively small impacts.

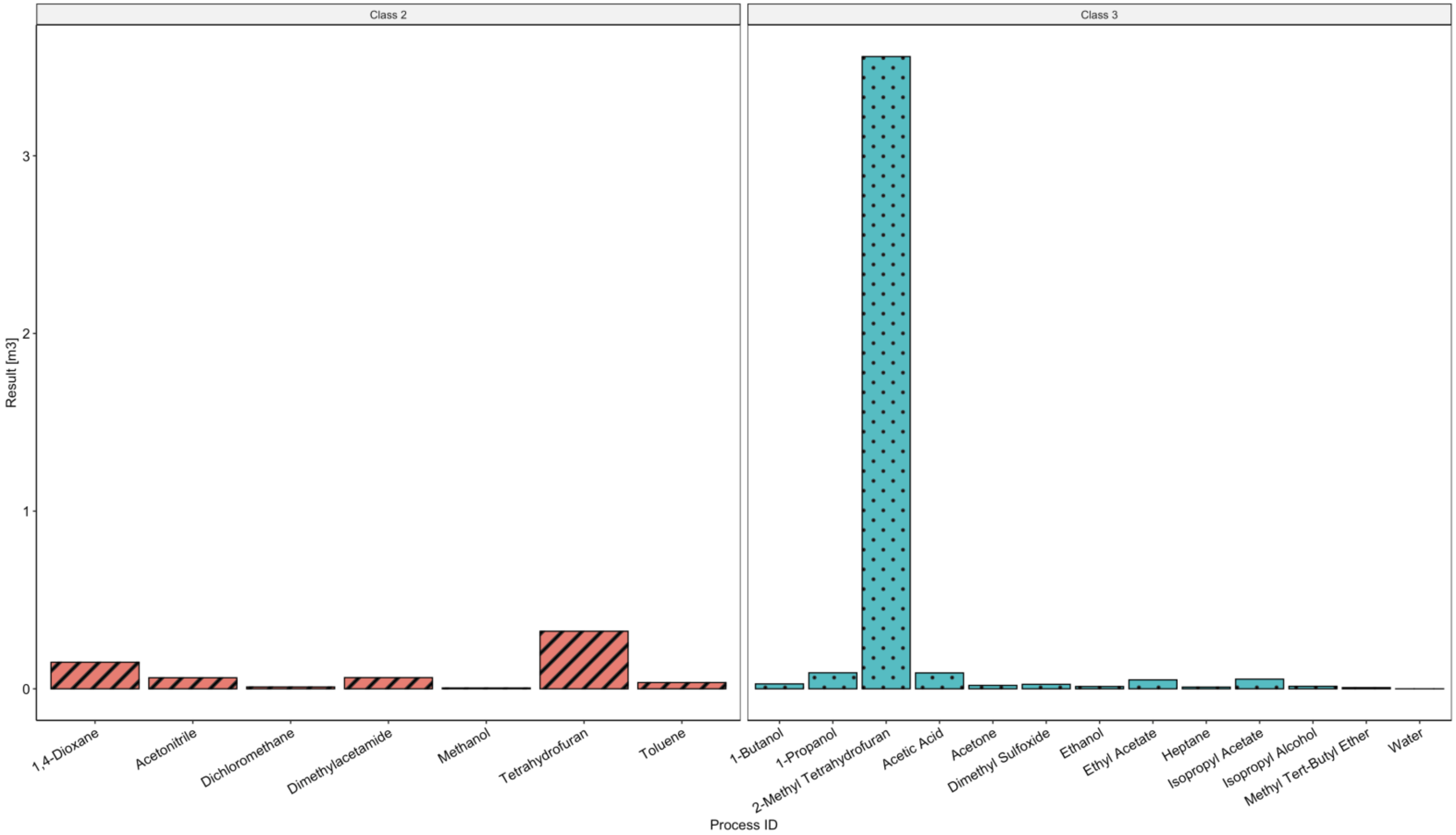

Figure 5-40. Water consumption potential (WCP) for 1 kg of solvent categorized by residual solvent class.

Overall, there were no significant difference between class 2 and class 3 solvents for all impact categories. Water always had the smallest impacts across all impact categories. Methanol and toluene also had relatively small impacts when compared to the remaining solvents. 2-MeTHF had high impacts throughout all categories and this is likely associated to the amount of agricultural crops (corn, rice, and sugarcane) required to produce the solvent. Tetrahydrofuran had elevated impacts for most impact categories.

5.6 Major Environmental Impact Contributors

The major contributors to each environmental impact category for each crystallization process are examined in the following sub-subjects and have been divided by crystallization type.

5.6.1 Major Antisolvent Crystallization Environmental Impact Contributors

The major contributors to the antisolvent crystallization processes for all 18 impact categories can be found below. The major contributors examined are the production of solvent, market for solvent (i.e., transportation), electricity production (i.e., energy requirement for the process equipment), and treatment of spent solvent mixture (i.e., incineration of solvent waste). Since Process 26 had much more elevated results than the other antisolvent processes, throughout all impact categories, it was put in a separate figure.
Terrestrial Acidification Potential (TAP) Contributors for Antisolvent Processes

Terrestrial acidification potential (TAP) major contributors for antisolvent processes can be found in Figure 5-41 and Figure 5-42 (for P26). For the incineration option, solvent production has the greatest impacts throughout all crystallization processes. Electricity production and treatment of spent solvent mixture impacts were similar for the incineration option for most antisolvent processes. For the recovery option, the solvent production impact was significantly reduced, but the electricity production impact was drastically increased due to the additional energy requirement for the solvent recovery system. Treatment of spent solvent mixture was non-existent in the recovery option due to the solvent recovery system.

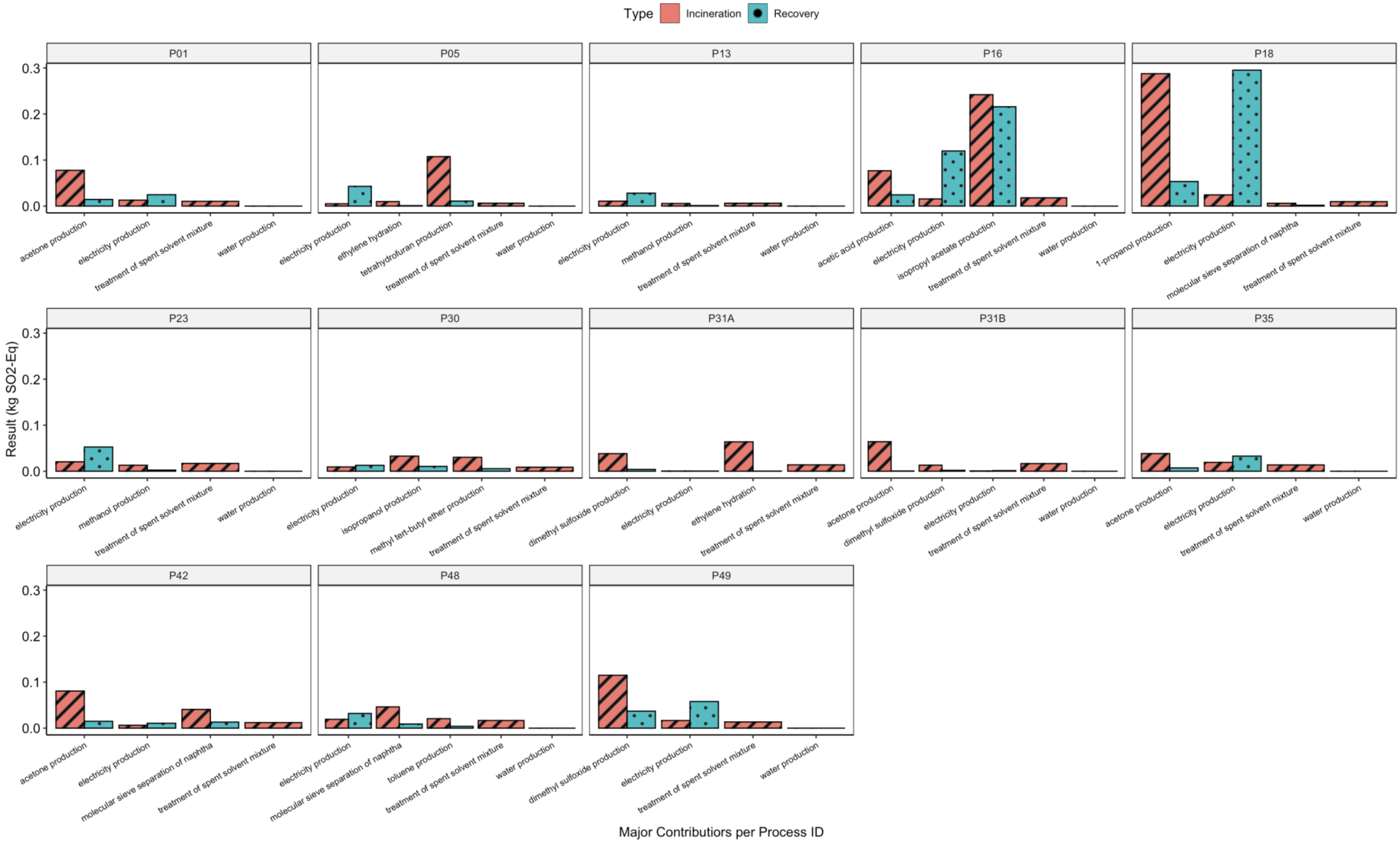

Figure 5-41. Major contributors for each antisolvent crystallization process for terrestrial acidification potential (TAP).

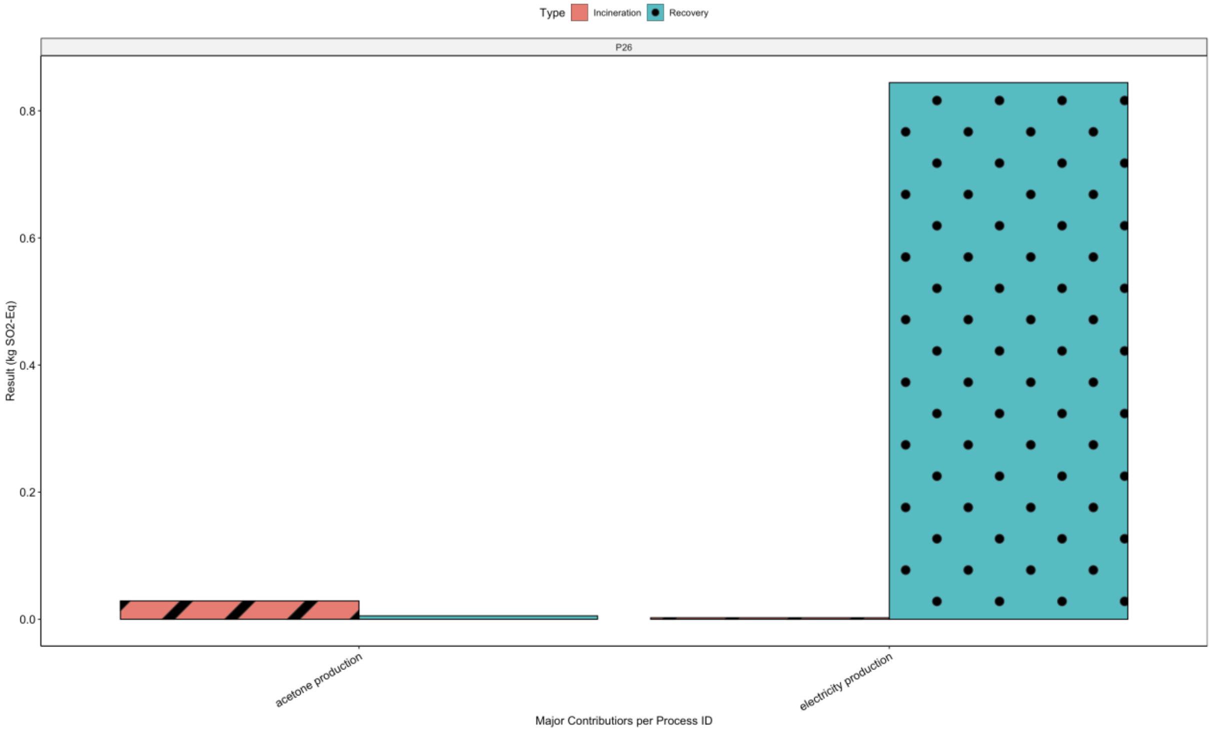

Figure 5-42. Major contributors for Process 26 for terrestrial acidification potential (TAP).

5.6.1.1 Global Warming Potential (GWP100) Contributors for Antisolvent Processes

Global warming potential (GWP100) major contributors for antisolvent processes can be found in Figure 5-43 and Figure 5-44 (for P26). Treatment of spent solvent mixture and solvent production had the greatest impacts in the incineration option. For the recovery option, the impact from treatment of spent solvent mixture was eliminated and the solvent production impact was greatly reduced. However, the electricity production impact was increased due to the additional energy requirement of the solvent recovery system.

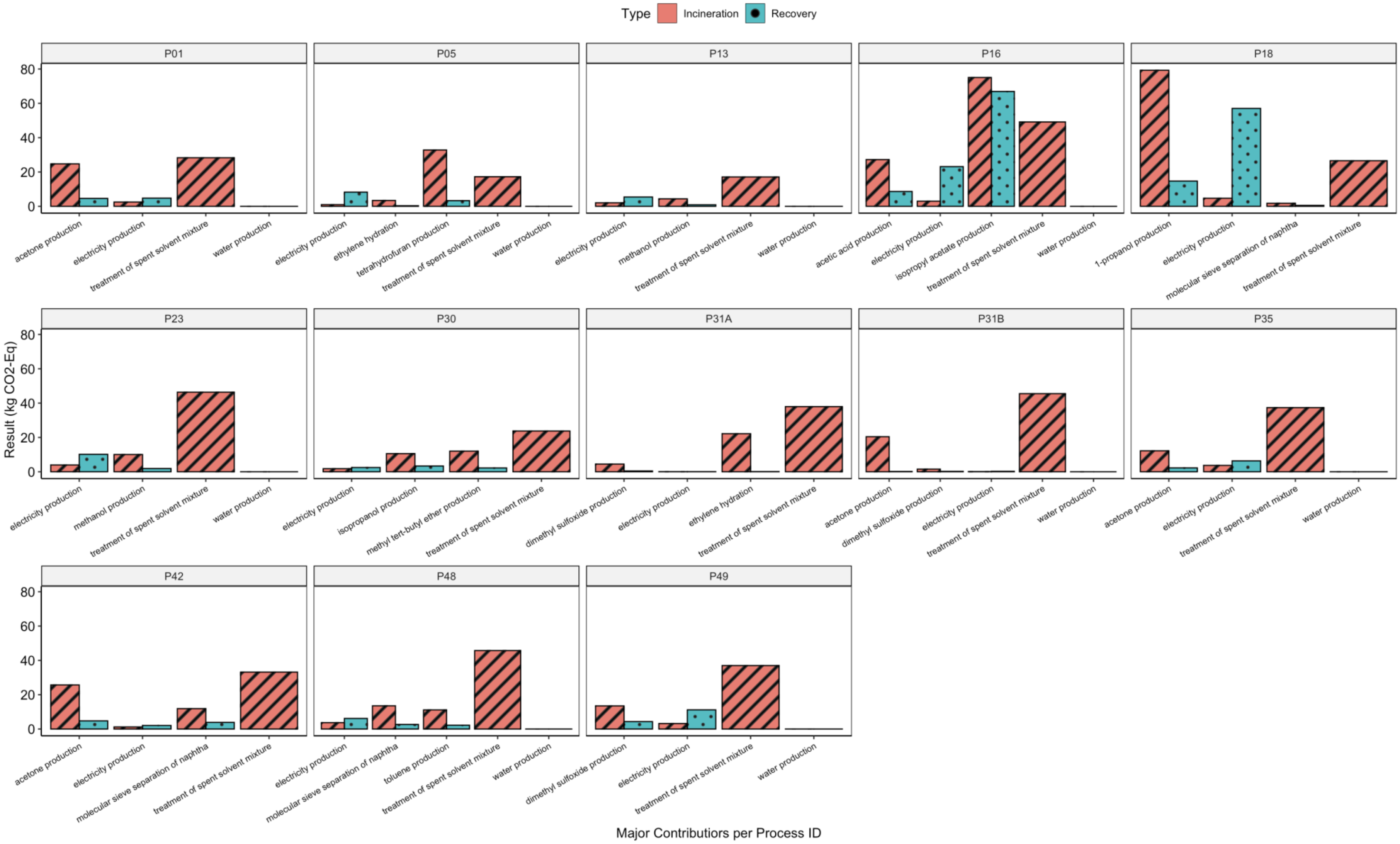

Figure 5-43. Major contributors for each antisolvent crystallization process global warming potential (GWP100).

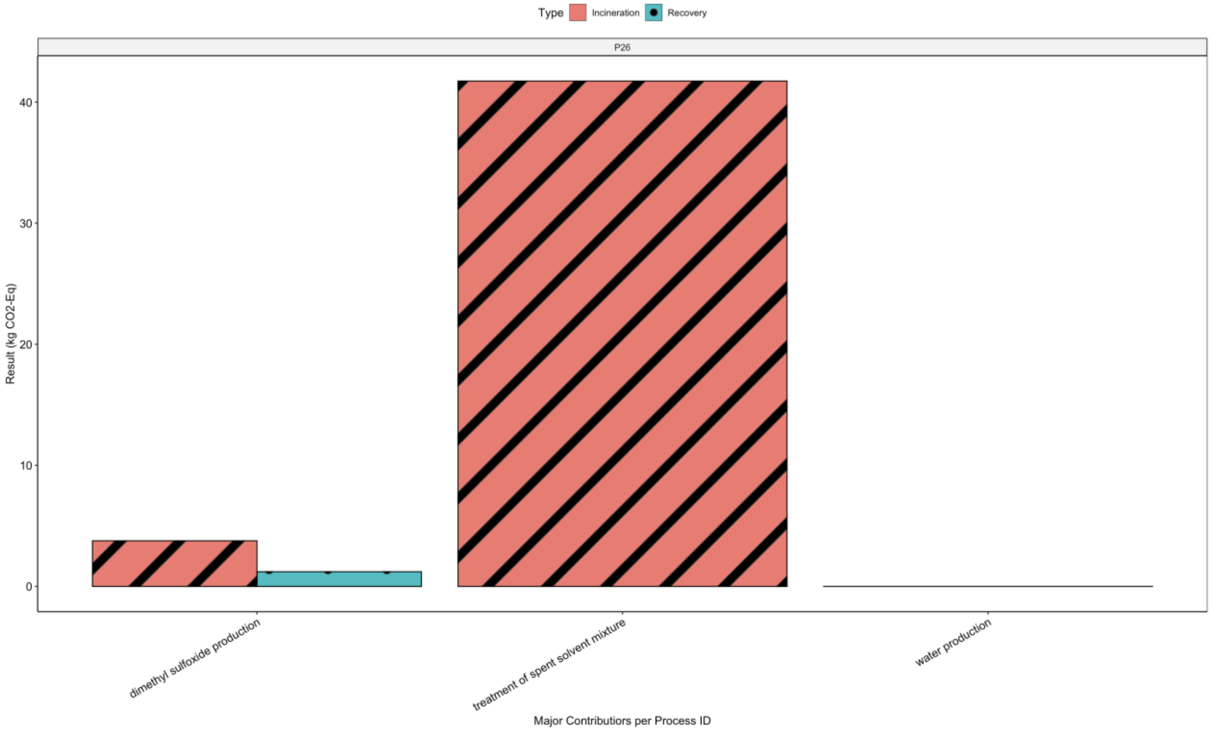

Figure 5-44. Major contributors for Process 26 global warming potential (GWP100).

5.6.1.2 Freshwater Ecotoxicity Potential (FETP) Contributors for Antisolvent Processes

Freshwater ecotoxicity potential (FETP) major contributors for antisolvent processes can be found in Figure 5-45 and Figure 5-46 (for P26). For the incineration option, solvent production had the greatest impacts. Treatment of spent solvent mixture and electricity production showed similar impacts. For the recovery option, solvent production impacts were greatly reduced and the treatment of spent solvent mixture was eliminated. Electricity production impacts were increased due to the addition of the solvent recovery system.

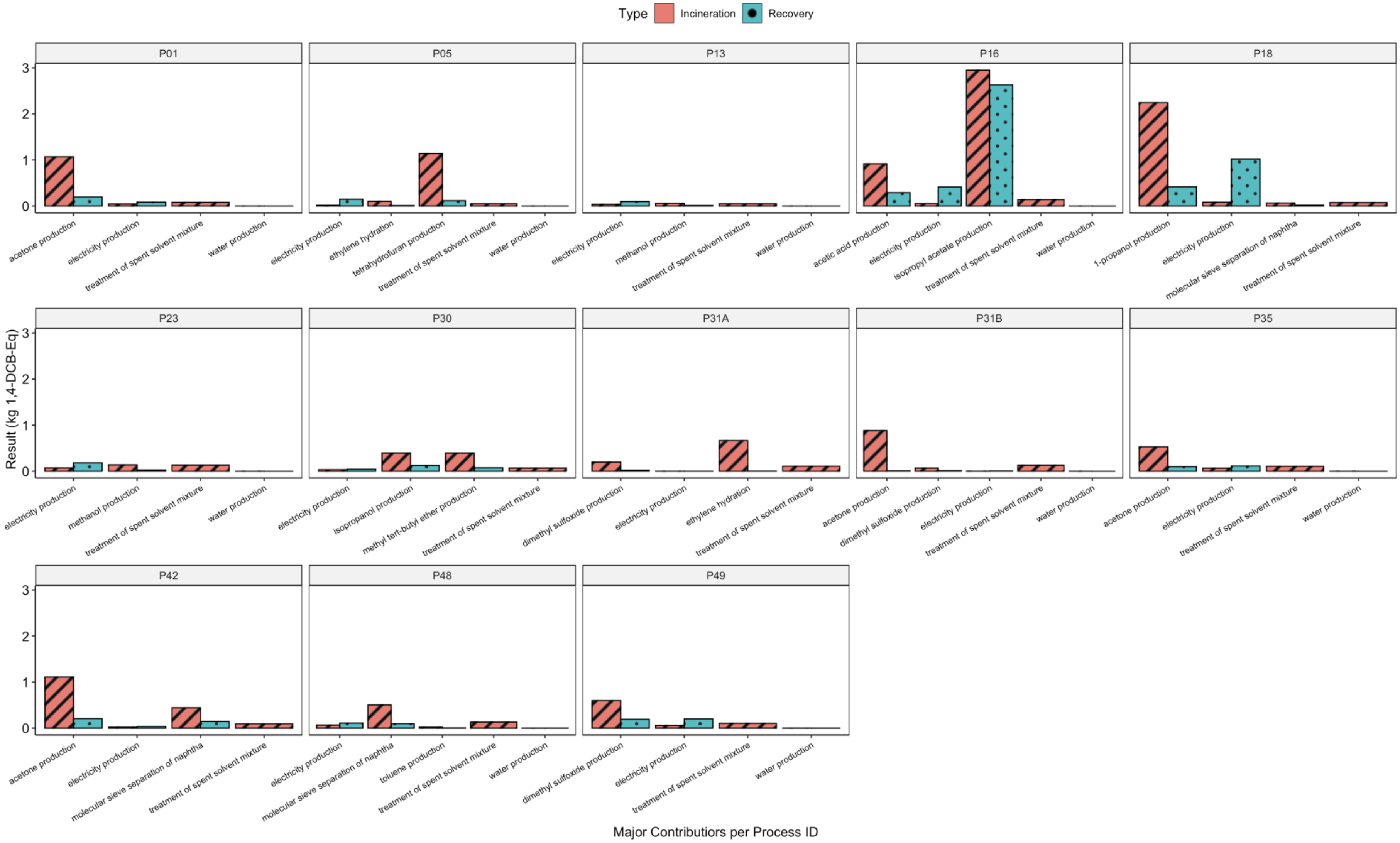

Figure 5-45. Major contributors for each antisolvent crystallization process for freshwater ecotoxicity potential (FETP).

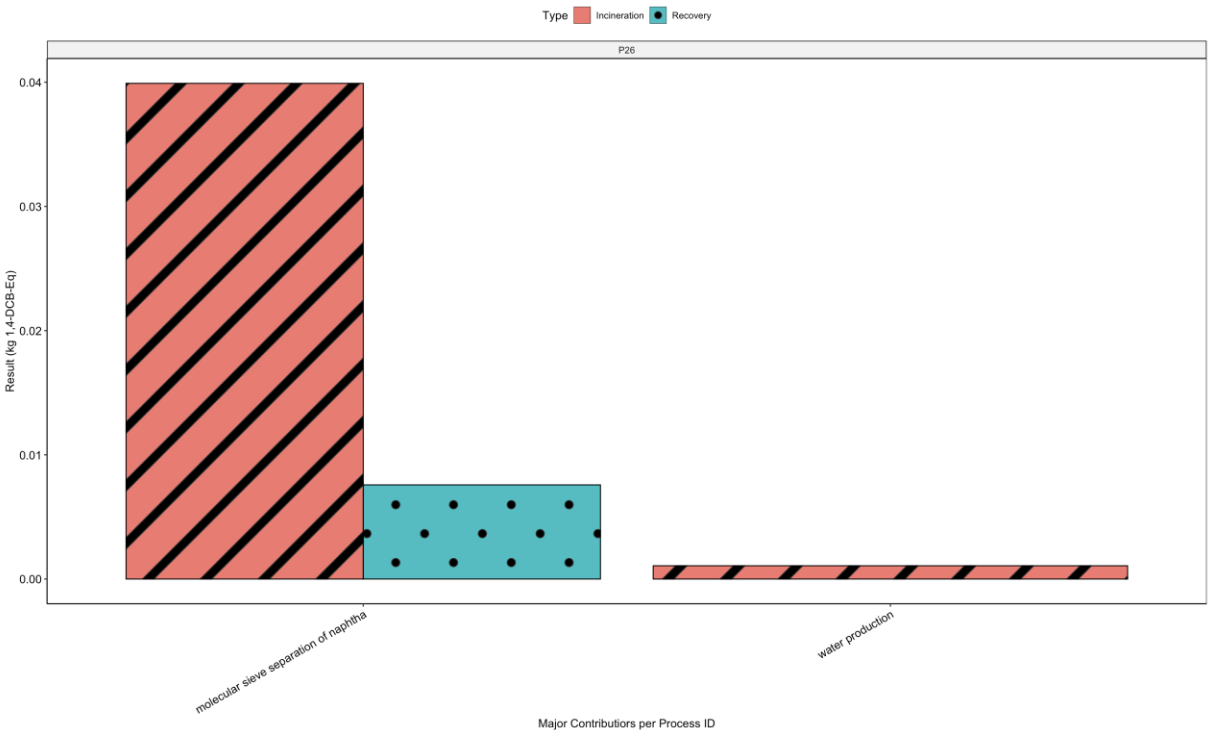

Figure 5-46. Major contributors for Process 26 for freshwater ecotoxicity potential (FETP).

5.6.1.3 Marine Ecotoxicity Potential (METP) Contributors for Antisolvent Processes

Marine ecotoxicity potential (METP) major contributors for antisolvent processes can be found in Figure 5-47 and Figure 5-48 (for P26). Solvent production impacts had elevated results for the incineration option while treatment of spent solvent mixture and electricity production impacts were smaller and similar. Solvent production impacts were significantly reduced in the recovery option while electricity production impacts were increased due to the addition of the solvent recovery system. Treatment of spent solvent mixture impacts were eliminated for the recovery option.

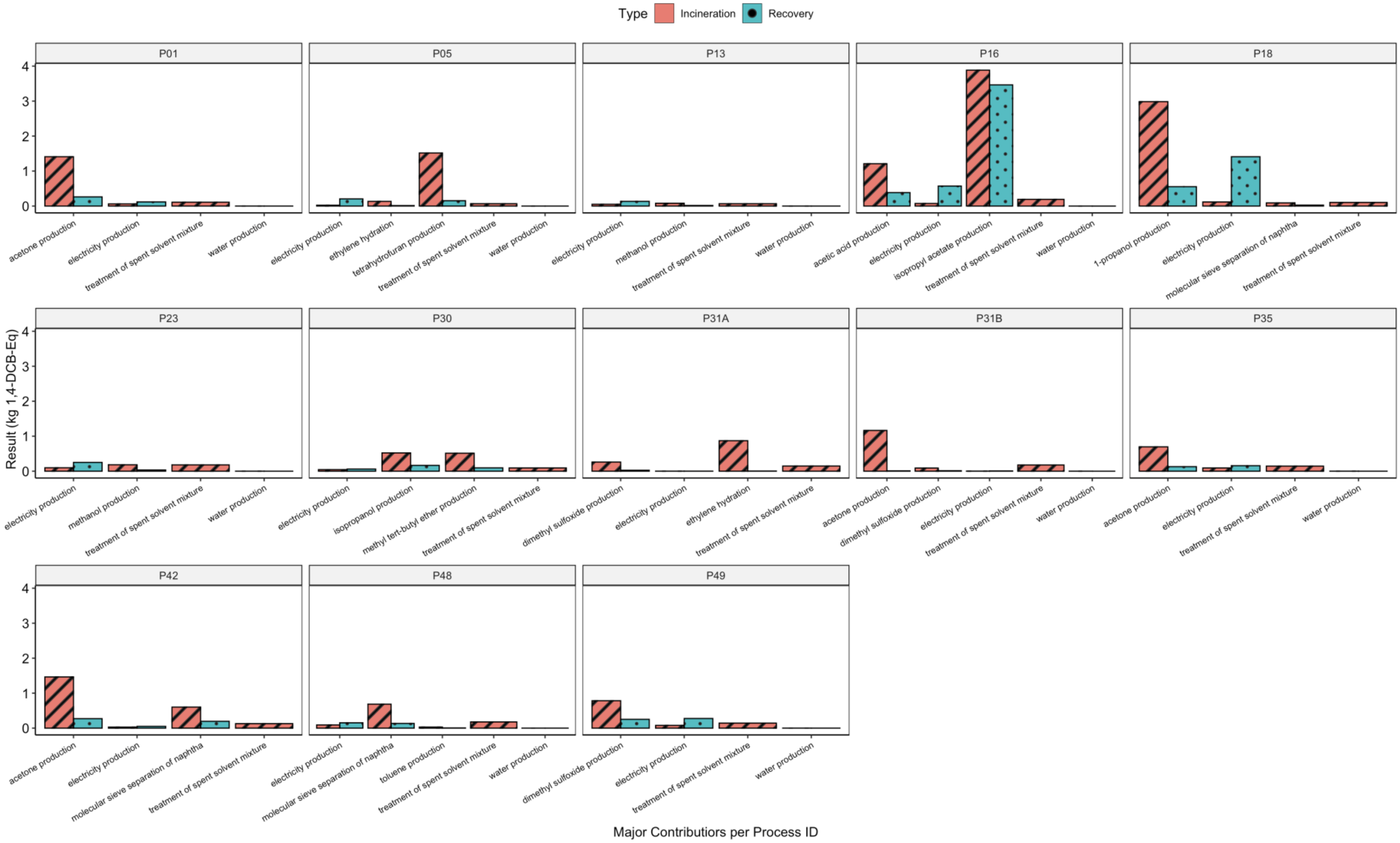

Figure 5-47. Major contributors for each antisolvent crystallization process for marine ecotoxicity potential (METP).

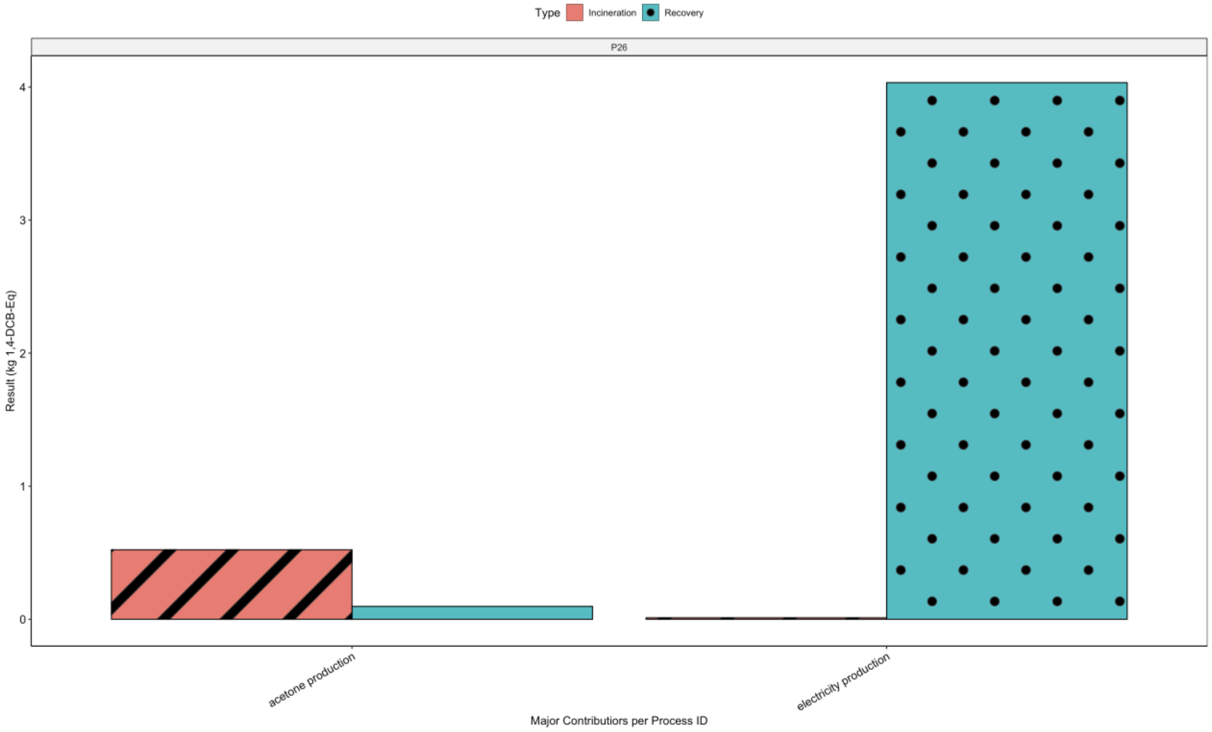

Figure 5-48. Major contributors for Process 26 for marine ecotoxicity potential (METP).

5.6.1.4 Terrestrial Ecotoxicity Potential (TETP) Contributors for Antisolvent Processes

Terrestrial ecotoxicity potential (TETP) major contributors for antisolvent processes can be found in Figure 5-49 and Figure 5-50 (for P26). For the incineration option, solvent production impacts were largest. Electricity production and treatment of spent solvent mixture impacts were lower and similar. For the recovery option, treatment of spent solvent mixture was eliminated while electricity production increased to the additional energy requirement of the added solvent recovery system. Solvent production impacts were reduced in the recovery option.

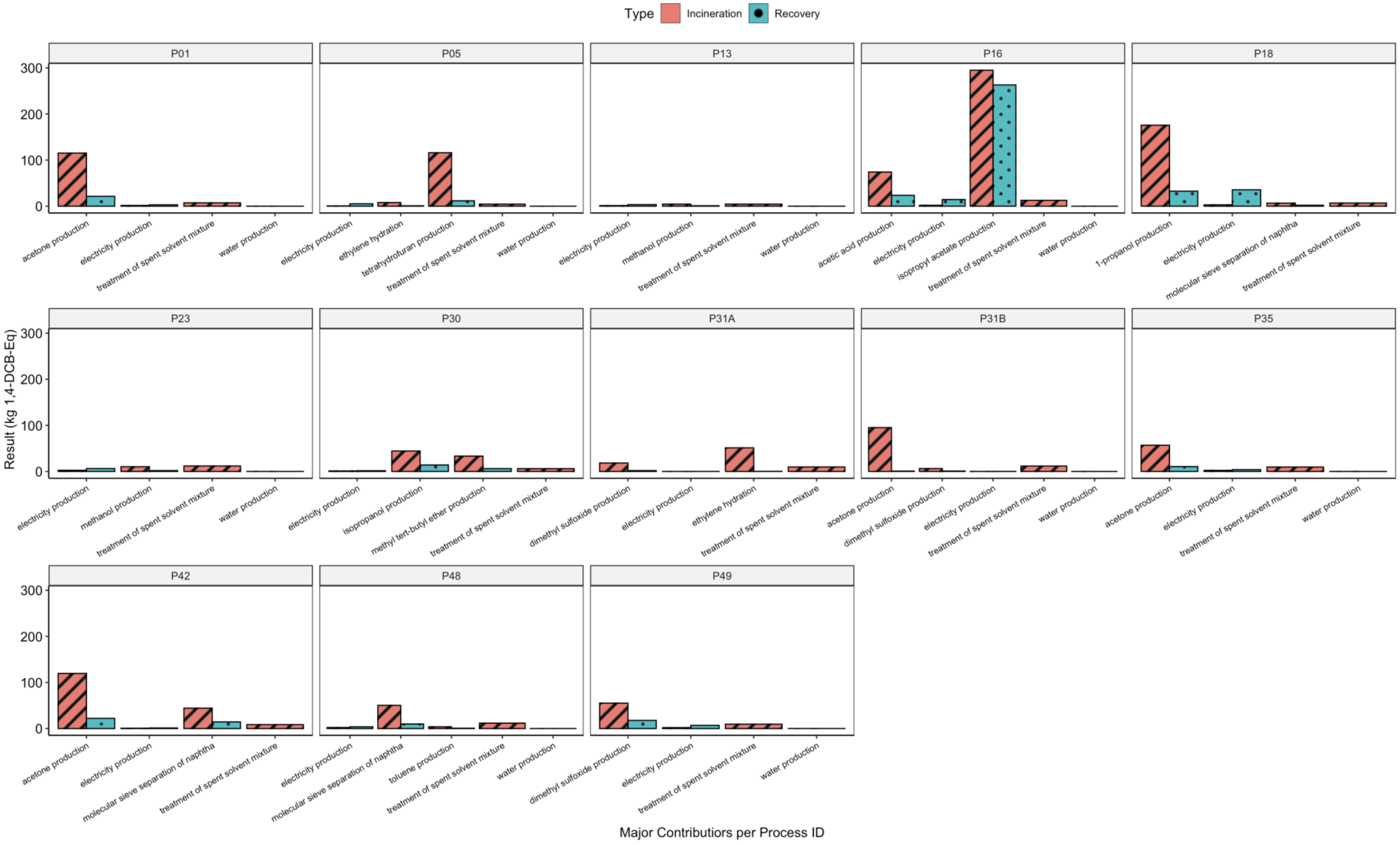

Figure 5-49. Major contributors for each antisolvent crystallization process for terrestrial ecotoxicity potential (TETP).

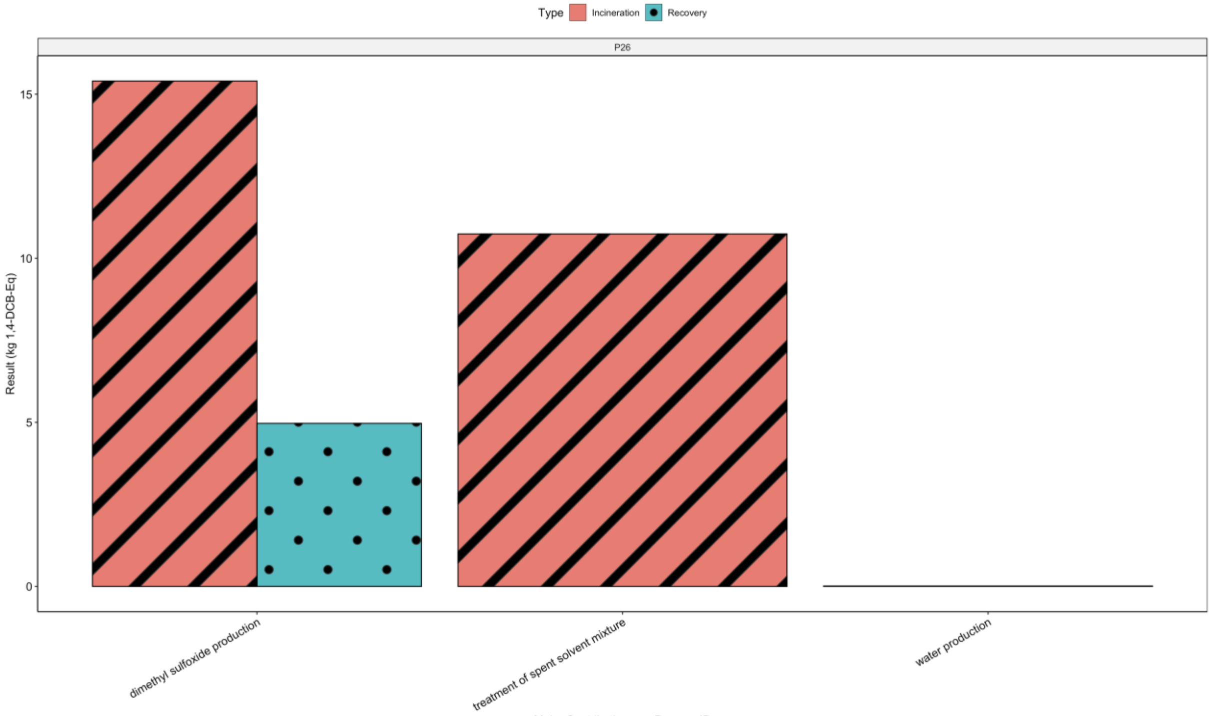

Figure 5-50. Major contributors for Process 26 for terrestrial ecotoxicity potential (TETP).

5.6.1.5 Fossil Fuel Potential (FFP) Contributors for Antisolvent Processes

Fossil fuel potential (FFP) major contributors for antisolvent processes can be found in Figure 5-51 and Figure 5-52 (for P26). For the incineration option, solvent production had the largest impacts. Electricity production and treatment of spent solvent mixture had similar and smaller impacts. For the recovery option, solvent production impacts were greatly reduced and the treatment of spent solvent mixture was eliminated. Electricity production impacts were increased due to the additional energy requirement of implement the solvent recovery system.

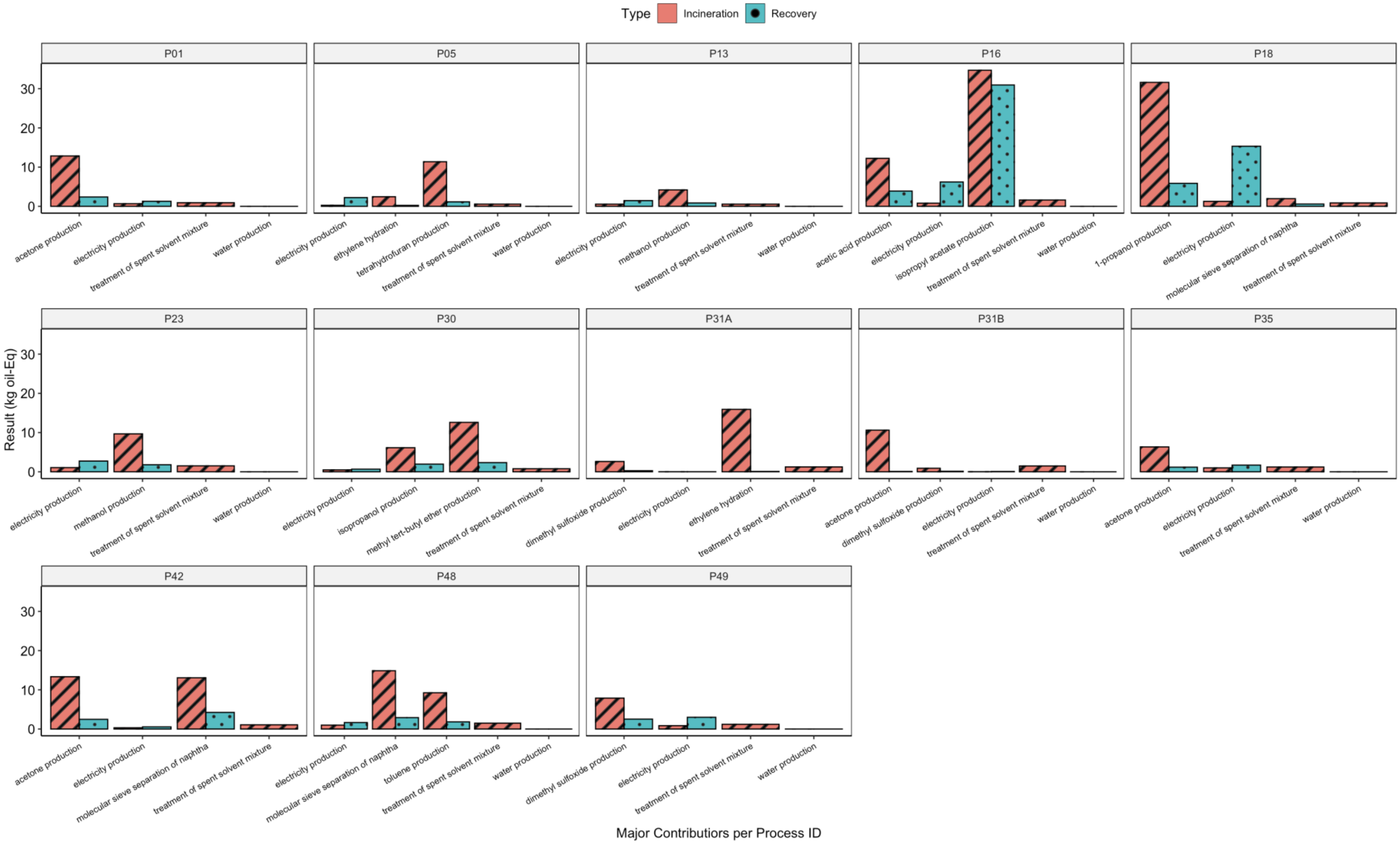

Figure 5-51. Major contributors for each antisolvent crystallization process for fossil fuel potential (FFP).

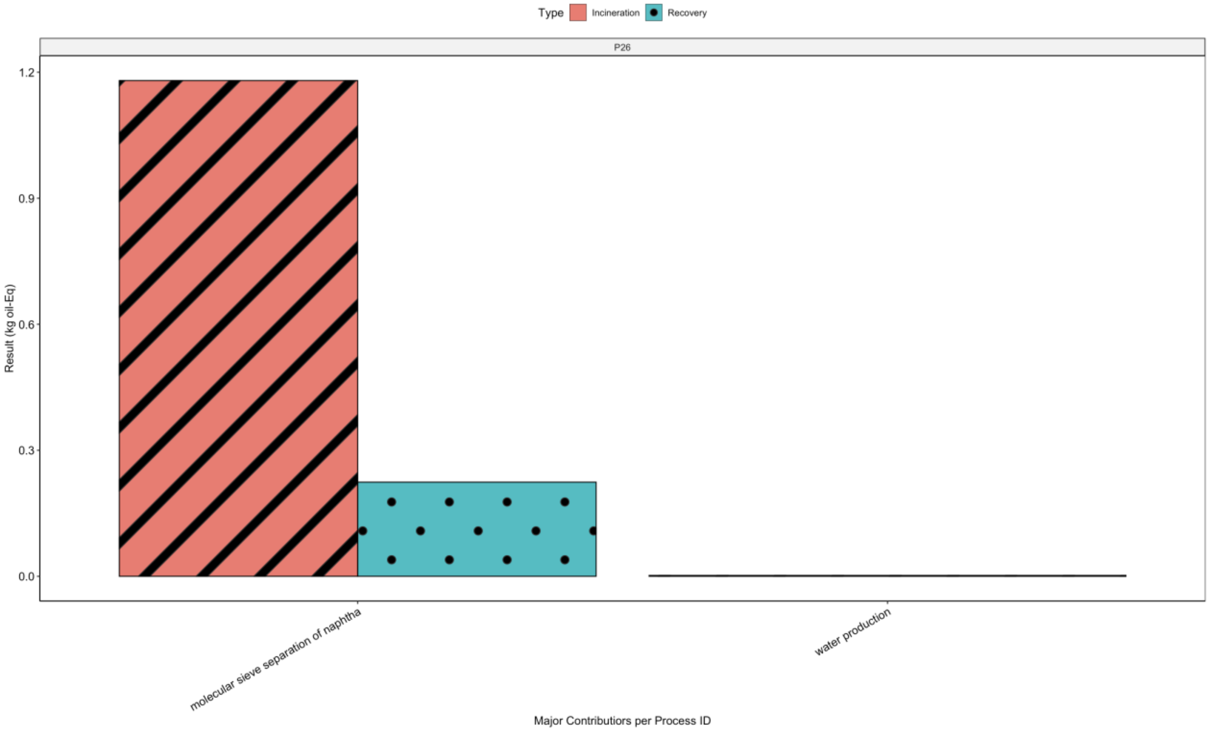

Figure 5-52. Major contributors for Process 26 for fossil fuel potential (FFP).

5.6.1.6 Freshwater Eutrophication Potential (FEP) Contributors for Antisolvent Processes

Freshwater eutrophication potential (FEP) major contributors for antisolvent processes can be found in Figure 5-53 and Figure 5-54 (for P26). For the incineration option, solvent production had the largest impacts, then followed by treatment of spent solvent mixture impacts. Electricity production impacts were relatively low. However, in the recovery option, electricity production was increased due to the additional energy requirement of implementing the solvent recovery systems. Additionally, treatment of spent solvent mixture impacts were eliminated and the production of solvent impacts were lowered from the reuse of solvent from the recovery system.

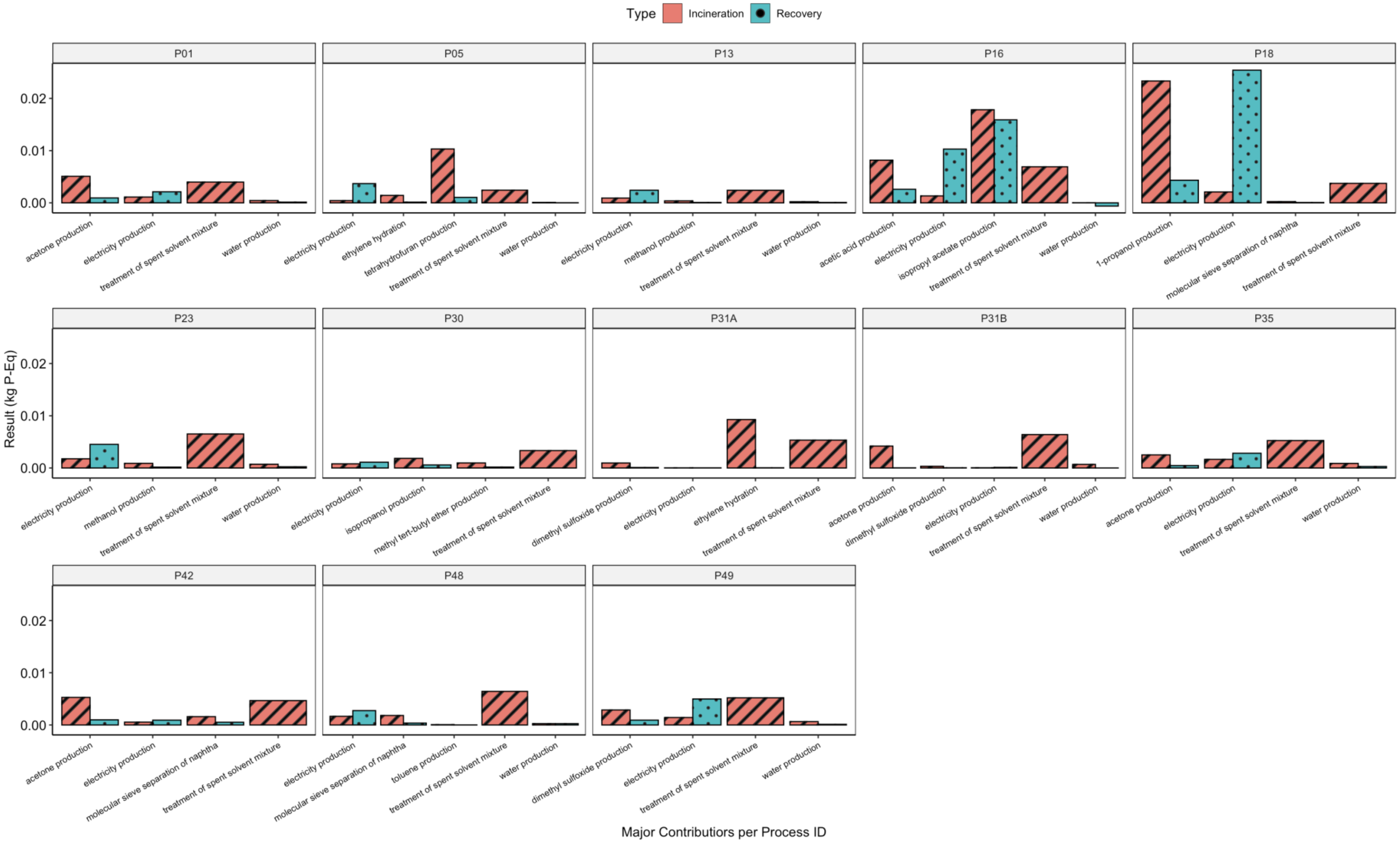

Figure 5-53. Major contributors for each antisolvent crystallization process for freshwater eutrophication potential (FEP).

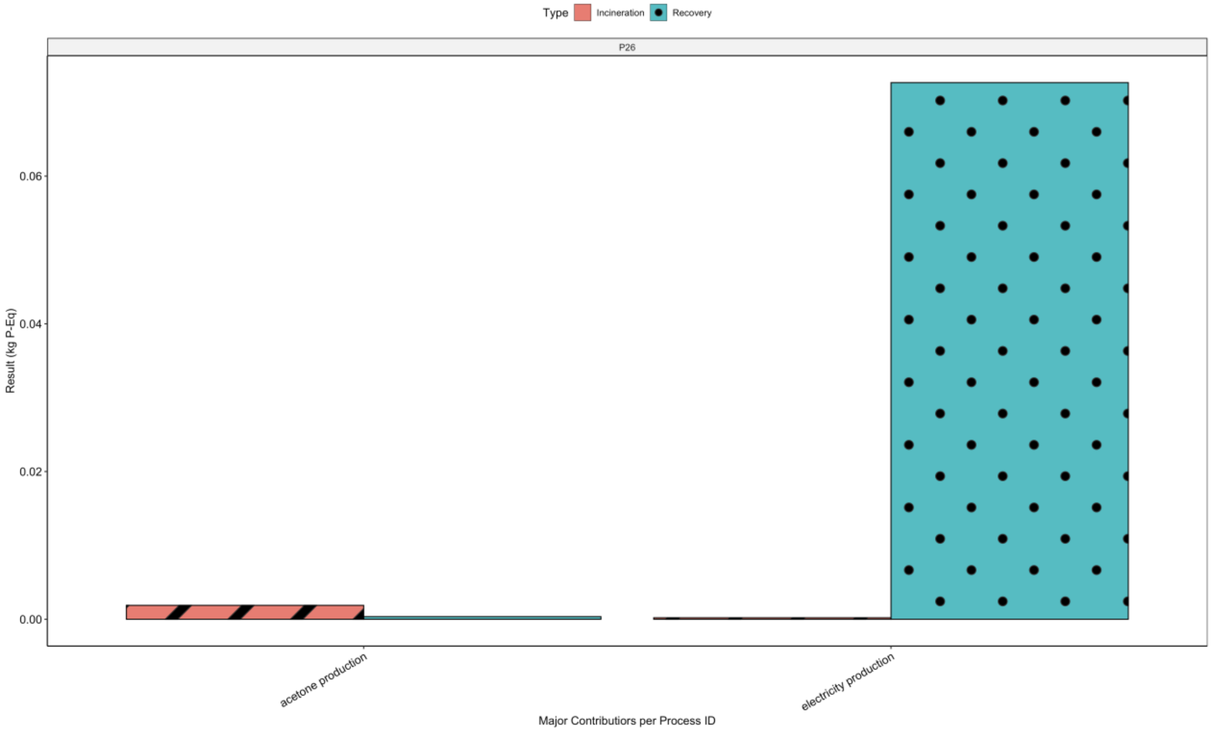

Figure 5-54. Major contributors for Process 26 for freshwater eutrophication potential (FEP).

5.6.1.7 Marine Eutrophication Potential (MEP) Contributors for Antisolvent Processes

Marine eutrophication potential (MEP) major contributors for antisolvent processes can be found in Figure 5-55 and Figure 5-56 (for P26). Treatment of spent solvent mixture impacts and solvent production impacts were largest in the incineration option. Electricity production impacts increased for the recovery option with the implementation of the solvent recovery system. Treatment of spent solvent mixture impacts were eliminated in the recovery option and the solvent production impacts were reduced.

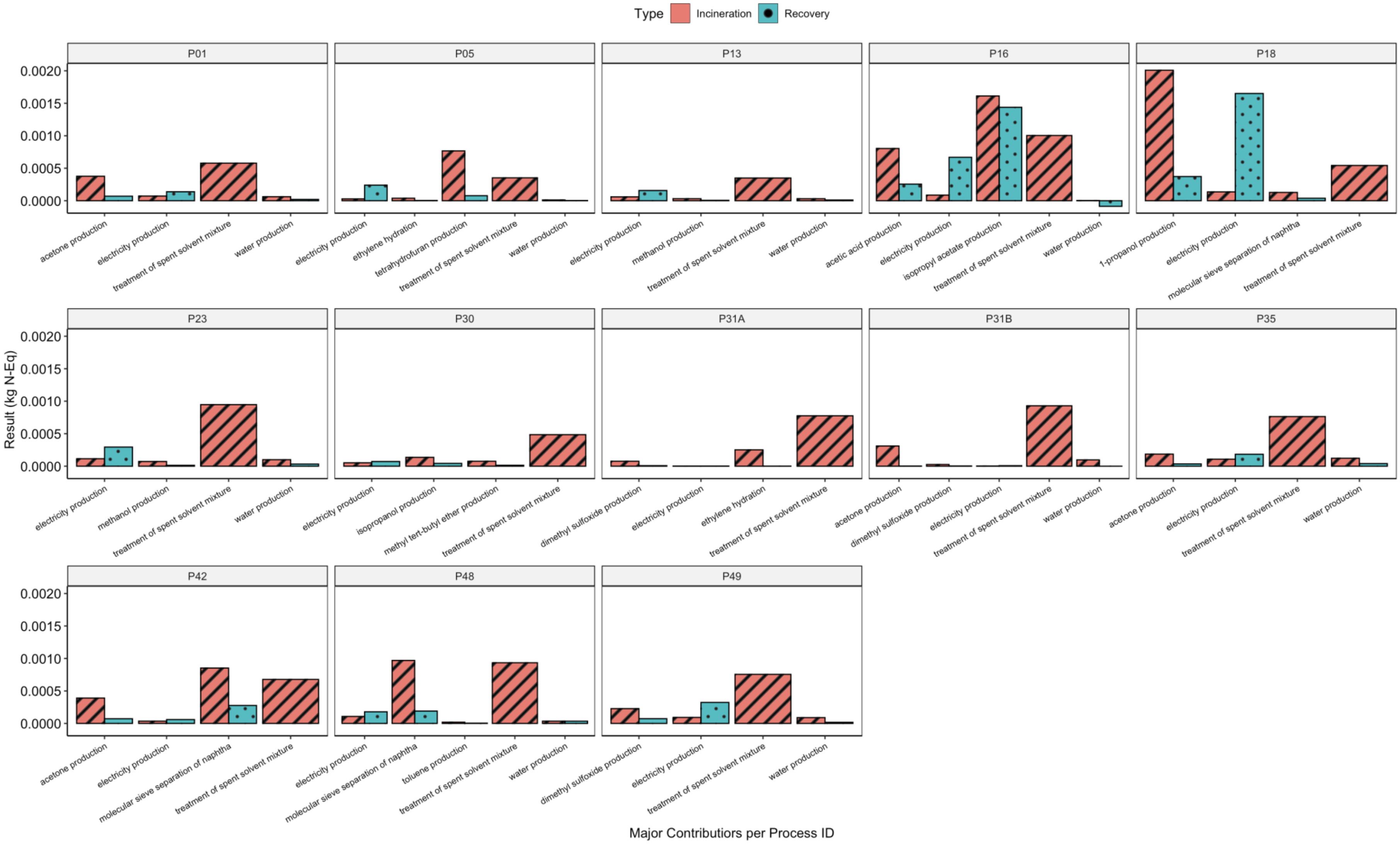

Figure 5-55. Major contributors for each antisolvent crystallization process for marine eutrophication potential (MEP).

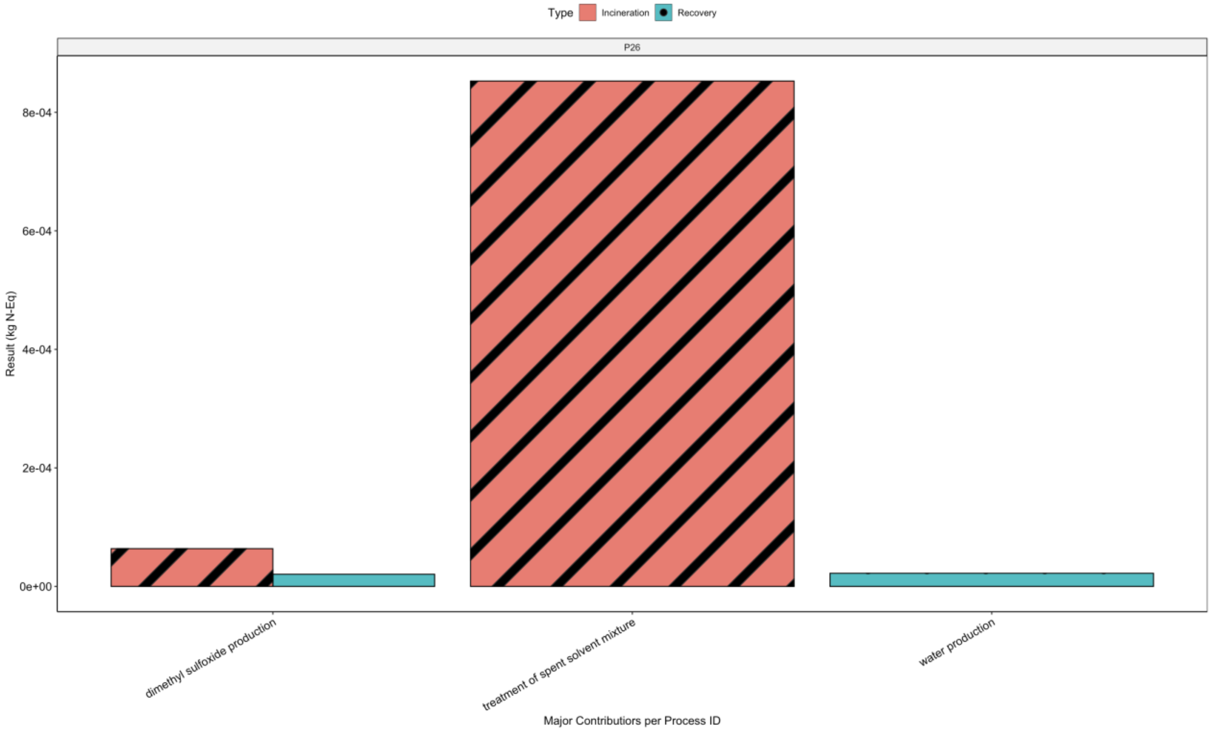

Figure 5-56. Major contributors for Process 26 for marine eutrophication potential (MEP).

5.6.1.8 Human Toxicity Potential – Carcinogenic (HTPc) Contributors for Antisolvent Processes

Human toxicity potential – carcinogenic (HTPc) major contributors for antisolvent processes can be found in Figure 5-57 and Figure 5-58 (for P26). Solvent production impacts were largest in the incineration option. Treatment of spent solvent mixture impacts and electricity production impacts were similar and smaller. For the recovery option, the treatment of spent solvent mixture impacts were eliminated and the solvent production impacts were reduced. Additionally, the electricity production impacts were increased with the implementation of the solvent recovery systems.

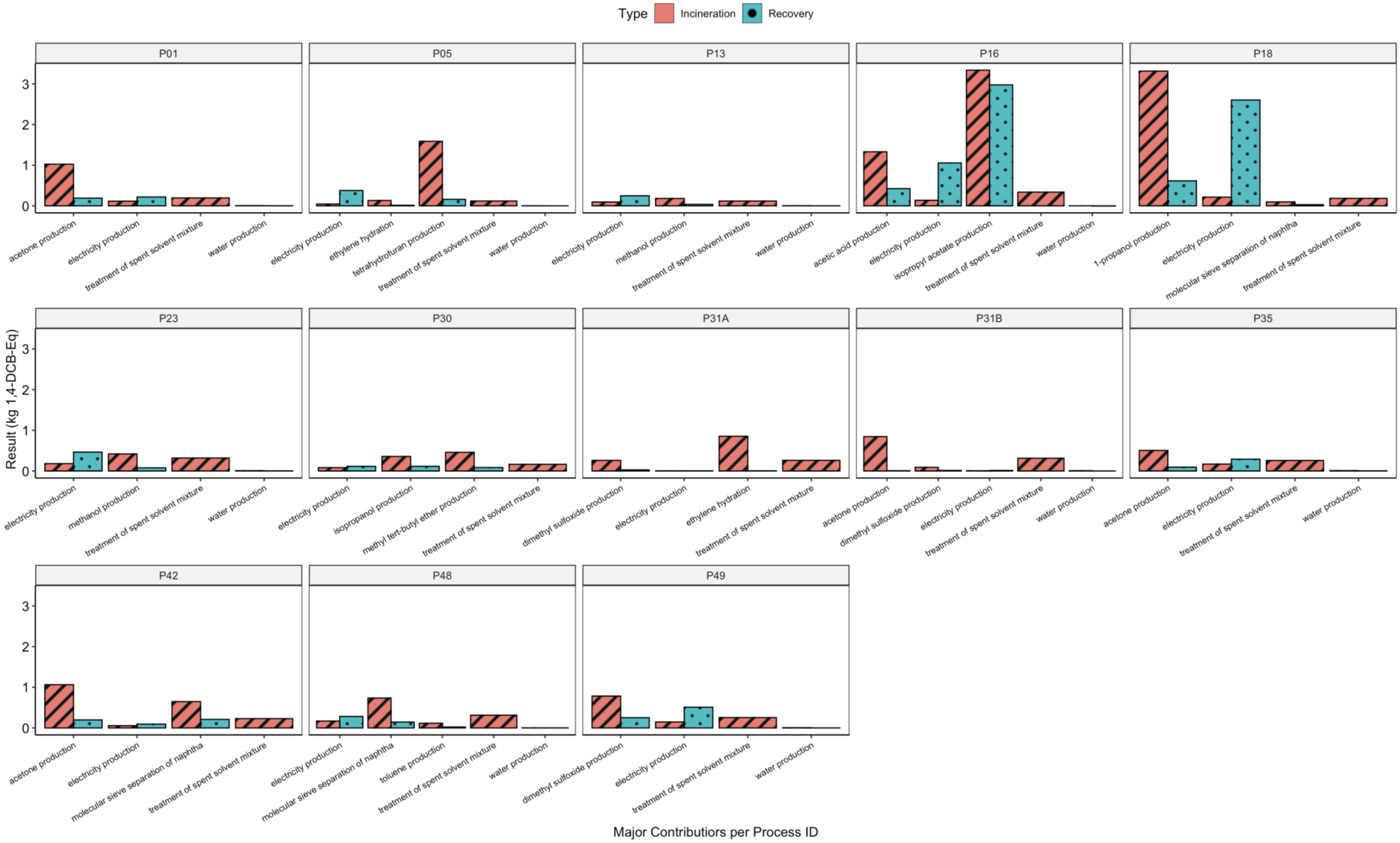

Figure 5-57. Major contributors for each antisolvent crystallization process for human toxicity potential – carcinogenic (HTPc).

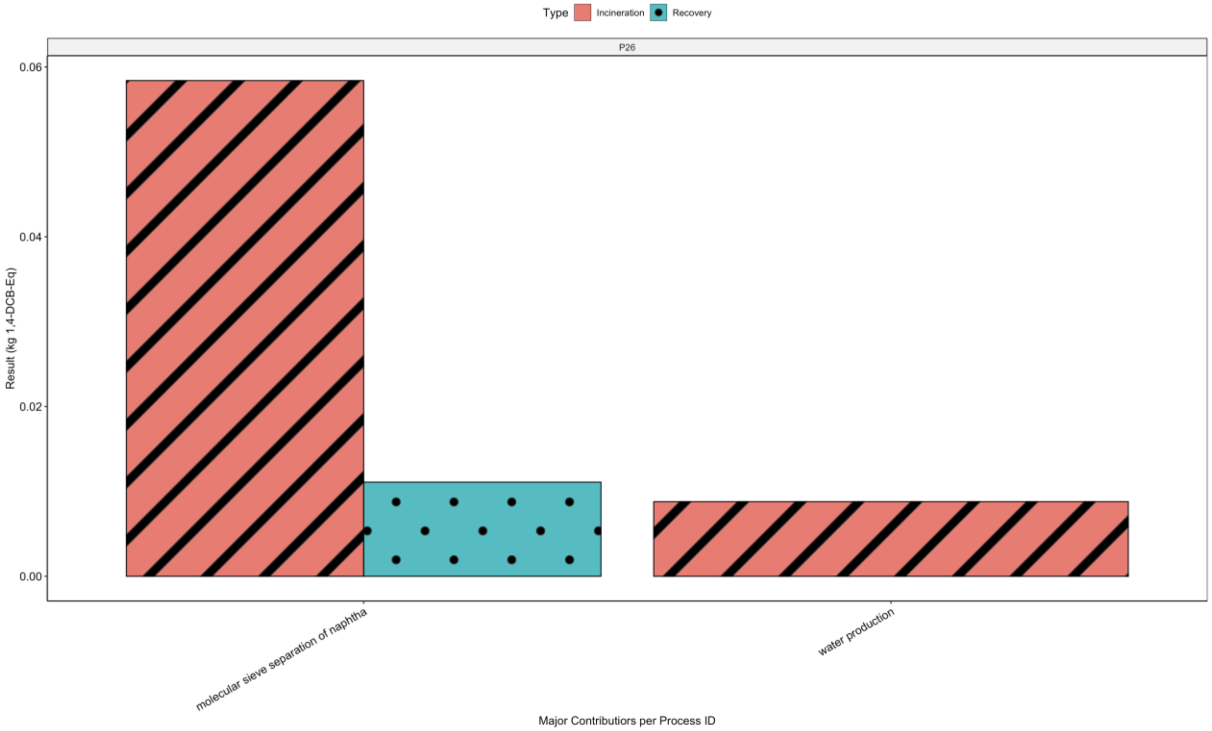

Figure 5-58. Major contributors for Process 26 for human toxicity potential – carcinogenic (HTPc).

5.6.1.9 Human Toxicity Potential – Non-Carcinogenic (HTPnc) Contributors for Antisolvent Processes

Human toxicity potential – non-carcinogenic (HTPnc) major contributors for antisolvent processes can be found in Figure 5-59 and Figure 5-60 (for P26). For the incineration option, the solvent production impacts were largest. The treatment of spent solvent mixture impacts and electricity production impacts were smaller and similar. For the recovery option, electricity production impacts were increased due to the additional energy requirements of the solvent recovery systems. Treatment of spent solvent mixture impacts were eliminated and the solvent production impacts were reduced due to the reuse of solvent from the recovery systems.

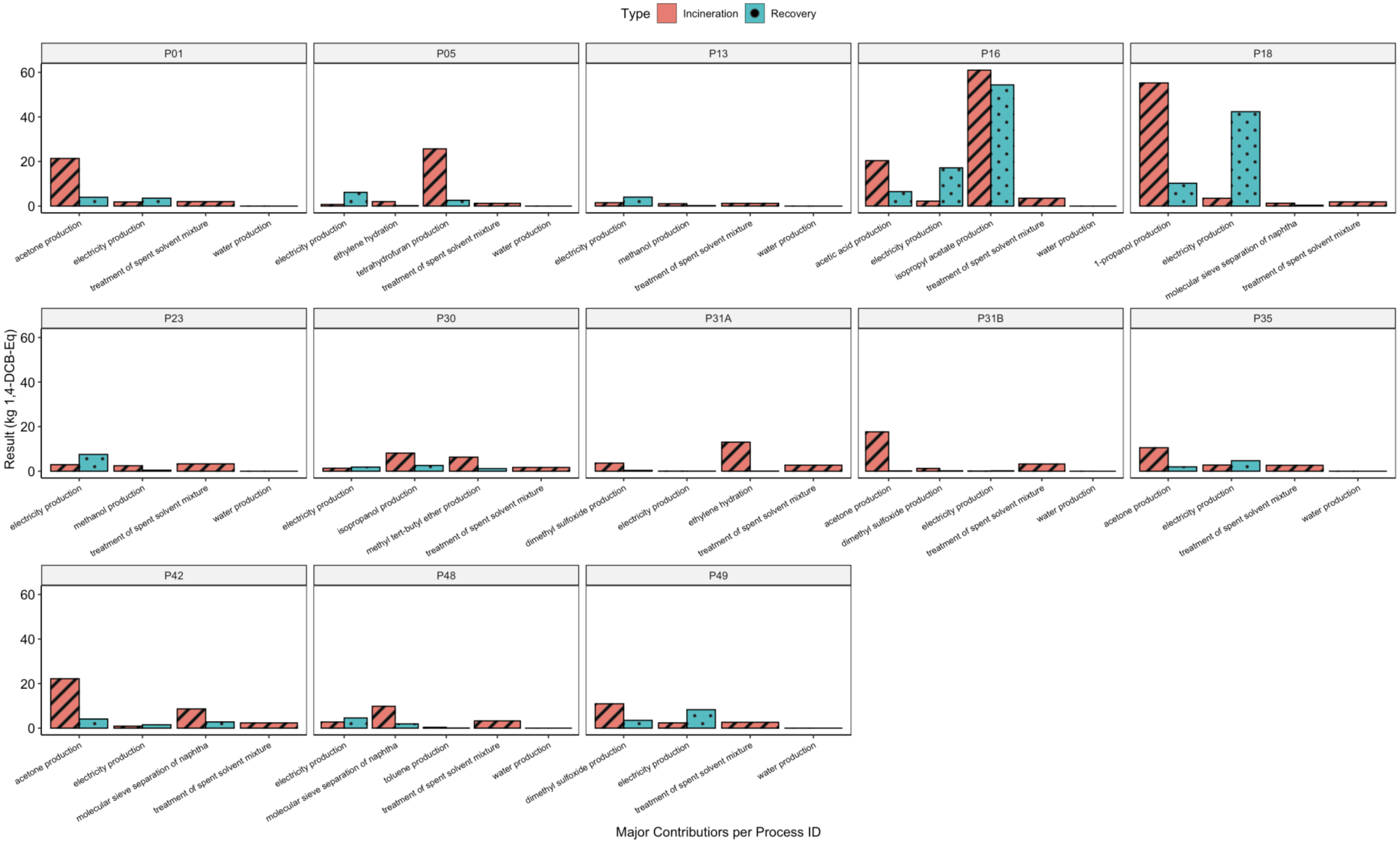

Figure 5-59. Major contributors for each antisolvent crystallization process for human toxicity potential – non-carcinogenic (HTPnc).

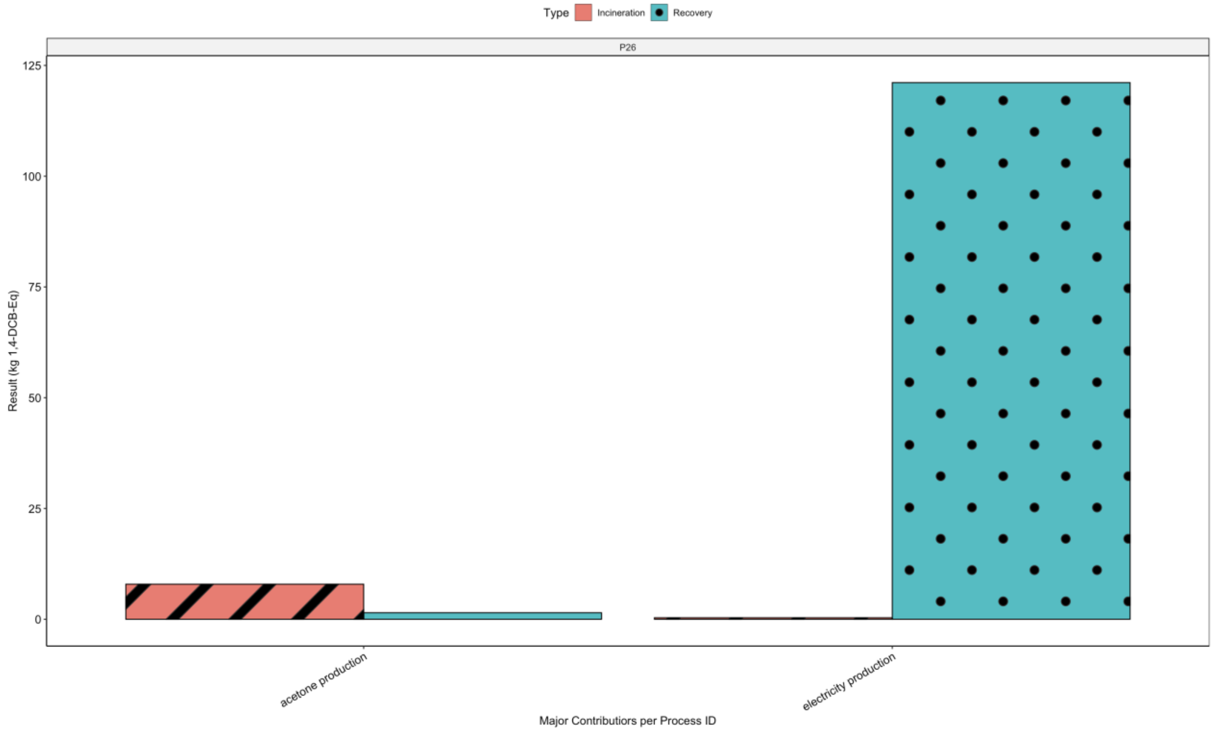

Figure 5-60. Major contributors for Process 26 for human toxicity potential – non-carcinogenic (HTPnc).

5.6.1.10 Ionising Radiation Potential (IRP) Contributors for Antisolvent Processes

Ionising radiation potential (IRP) major contributors for antisolvent processes can be found in Figure 5-61 and Figure 5-62 (for P26). Impacts were largest for solvent production (specifically for tetrahydrofuran, isopropyl acetate, 1-propanol, acetic acid, and acetone) for the incineration option. Electricity production impacts and treatment of spent solvent mixture impacts were much smaller. Solvent production impacts were reduced for the recovery option and treatment of spent solvent mixture impacts were eliminated. Electricity production impacts were increased due to the implementation of the solvent recovery systems.

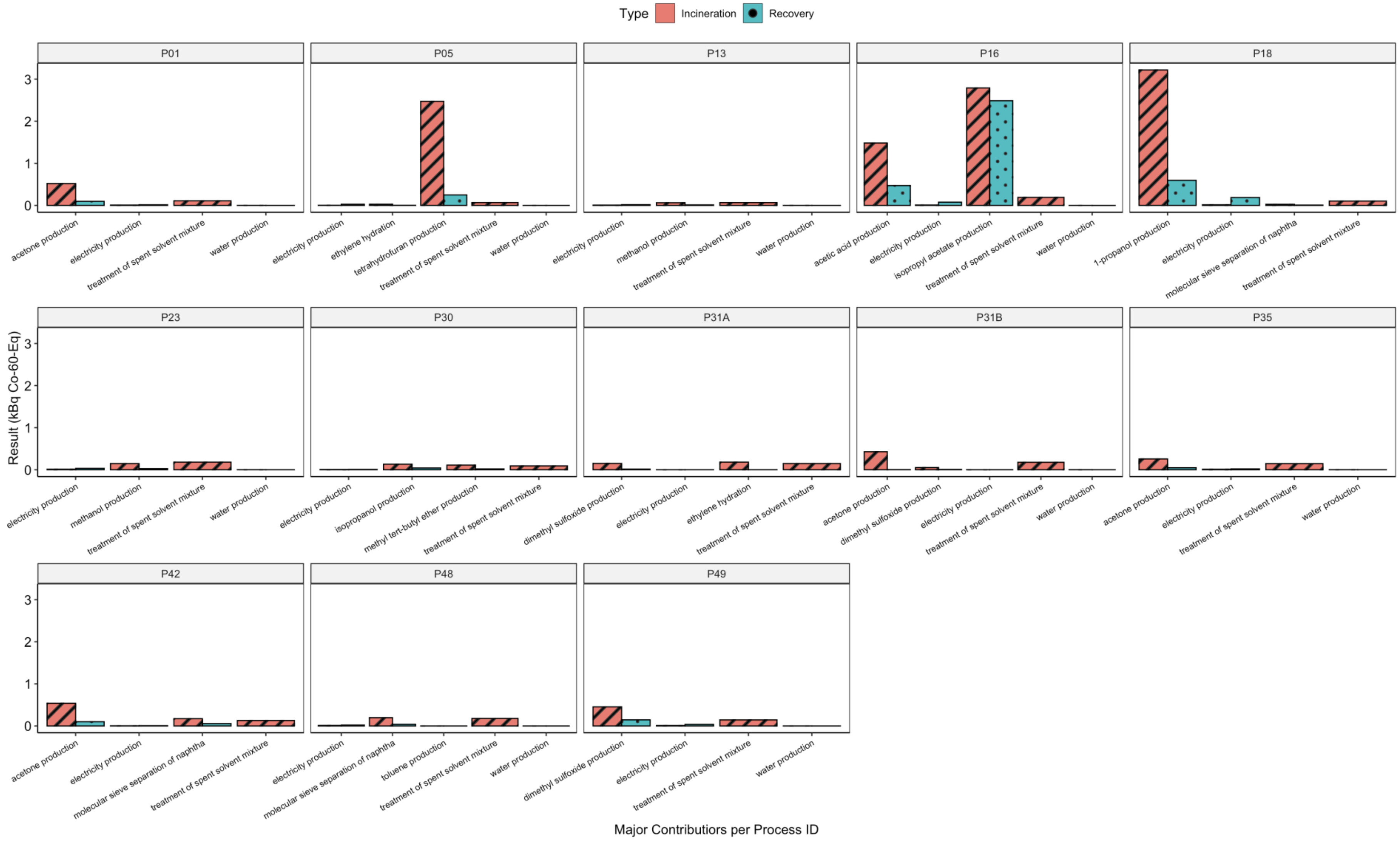

Figure 5-61. Major contributors for each antisolvent crystallization process for ionising radiation potential (IRP).

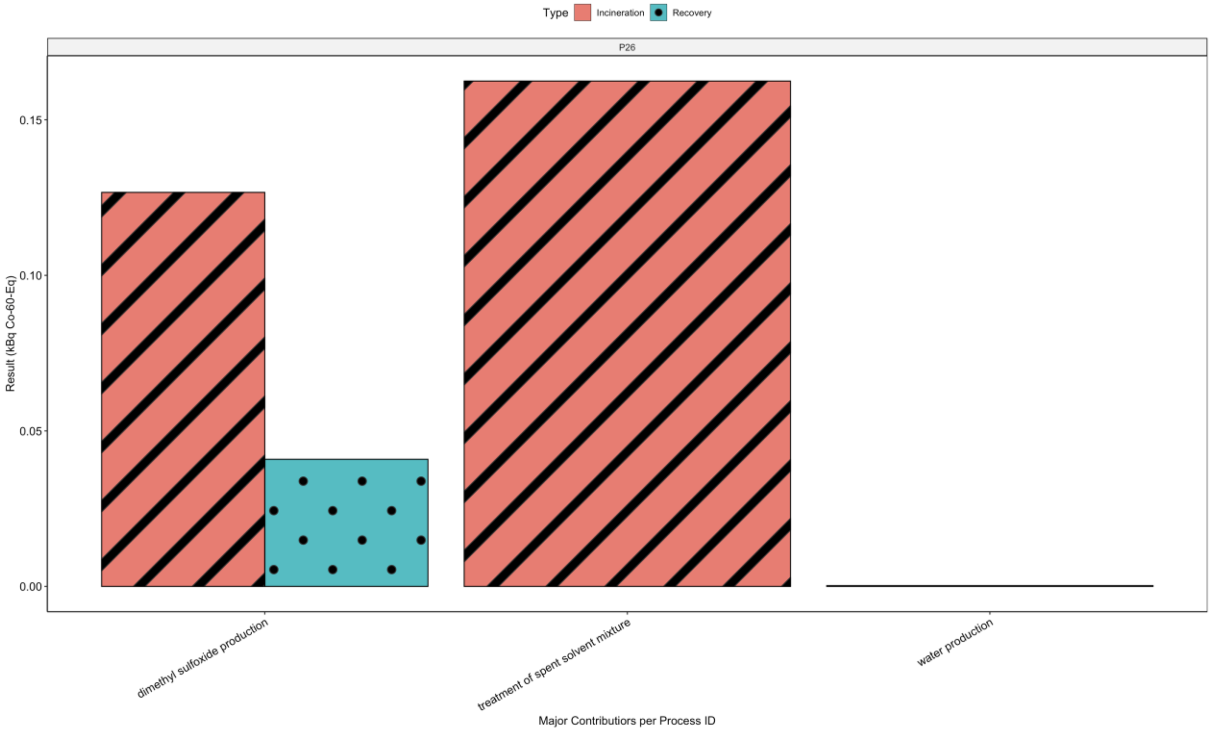

Figure 5-62. Major contributors for Process 26 for ionising radiation potential (IRP).

5.6.1.11 Agricultural Land Occupation (LOP) Contributors for Antisolvent Processes

Agricultural land occupation (LOP) major contributors for antisolvent processes can be found in Figure 5-63 and Figure 5-64 (for P26). For the incineration option, particular solvents production impacts were largest (e.g., tetrahydrofuran, acetic acid, 1-propanol, and isopropyl acetate). For the recovery option, electricity production impacts were higher than for the incineration option due to the additional energy requirement of the solvent recovery system. Treatment of spent solvent mixture impacts was also eliminated in the recovery option.

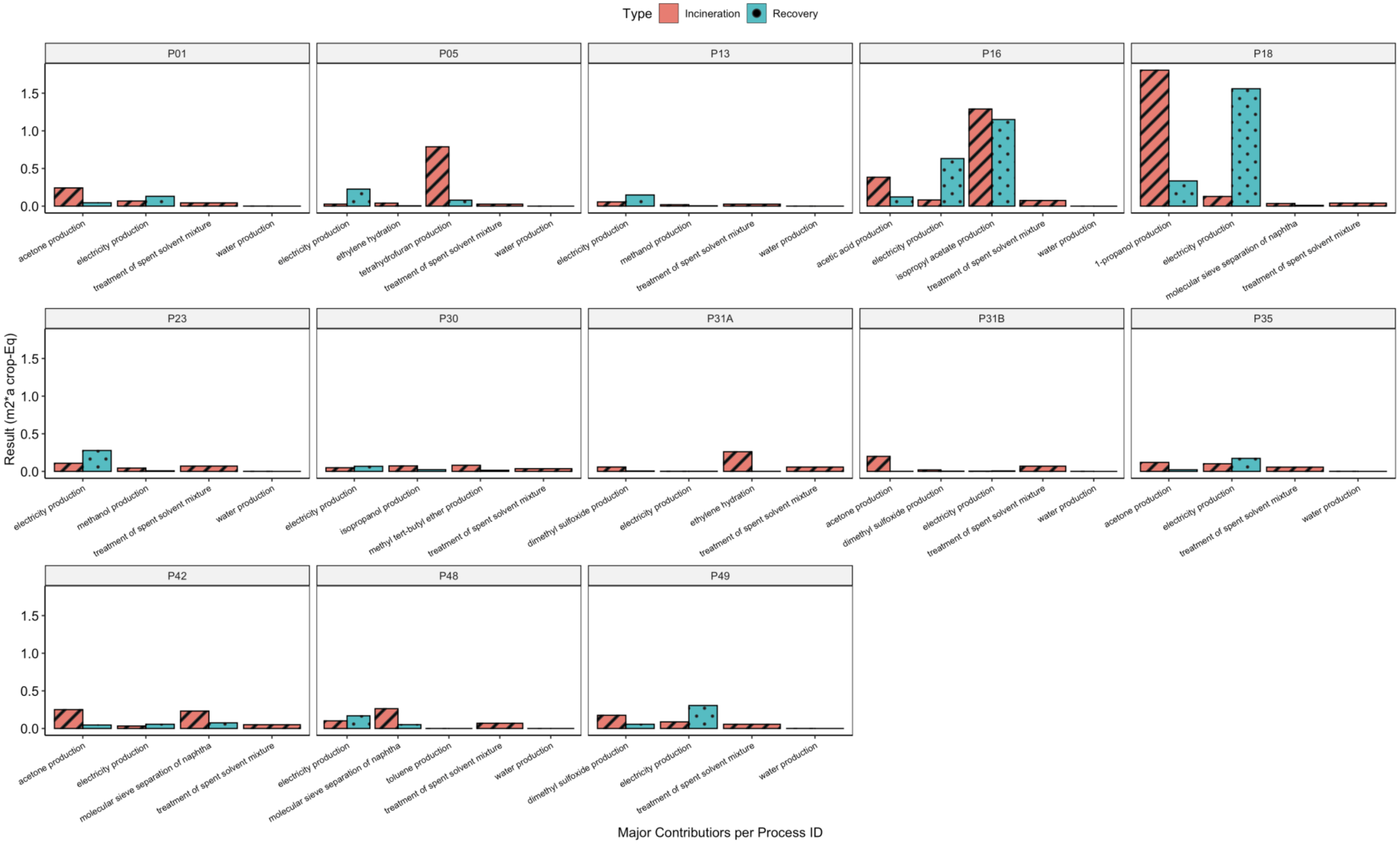

Figure 5-63. Major contributors for each antisolvent crystallization process for agricultural land occupation (LOP).

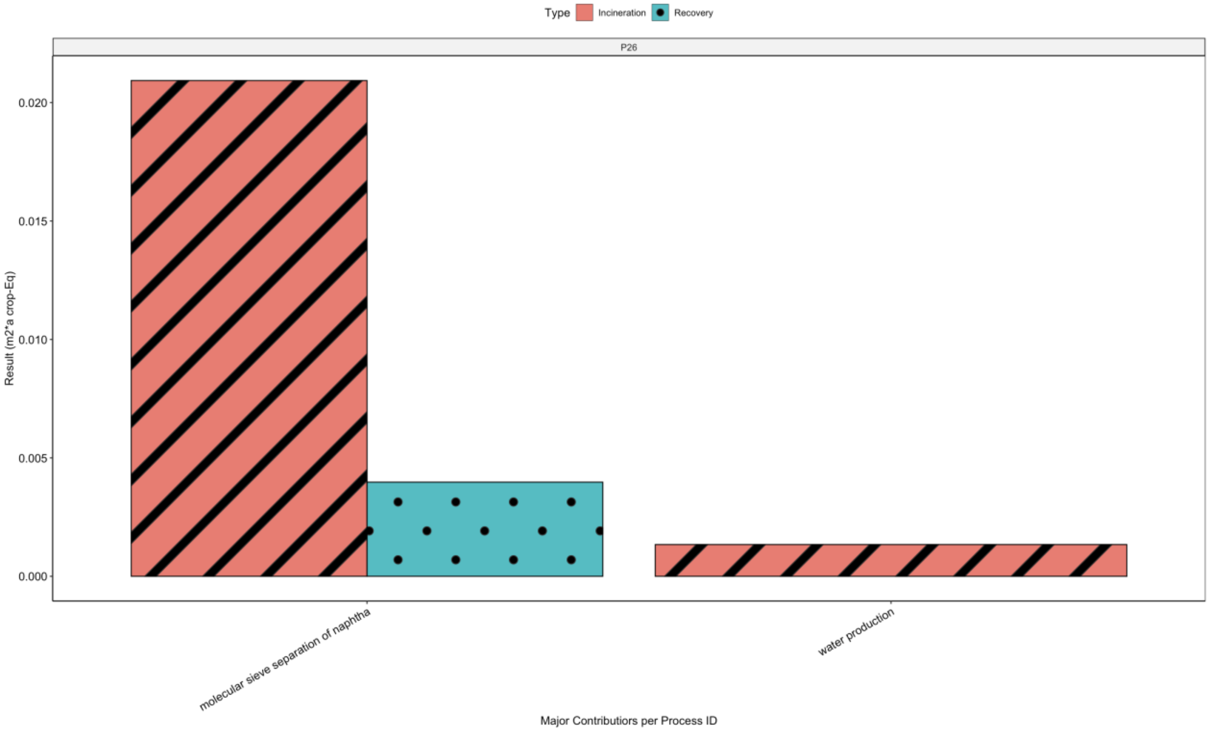

Figure 5-64. Major contributors for Process 26 for agricultural land occupation (LOP).

5.6.1.12 Surplus Ore Potential (SOP) Contributors for Antisolvent Processes

Surplus ore potential (SOP) major contributors for antisolvent processes can be found in Figure 5-65 and Figure 5-66 (for P26). Treatment of spent solvent mixture impacts and solvent production impacts were largest in the incineration option. Solvent production impacts were reduced with the recovery option and treatment of spent solvent mixture impacts were eliminated. Electricity production impacts were increased in the recovery option with the implementation of the solvent recovery system.

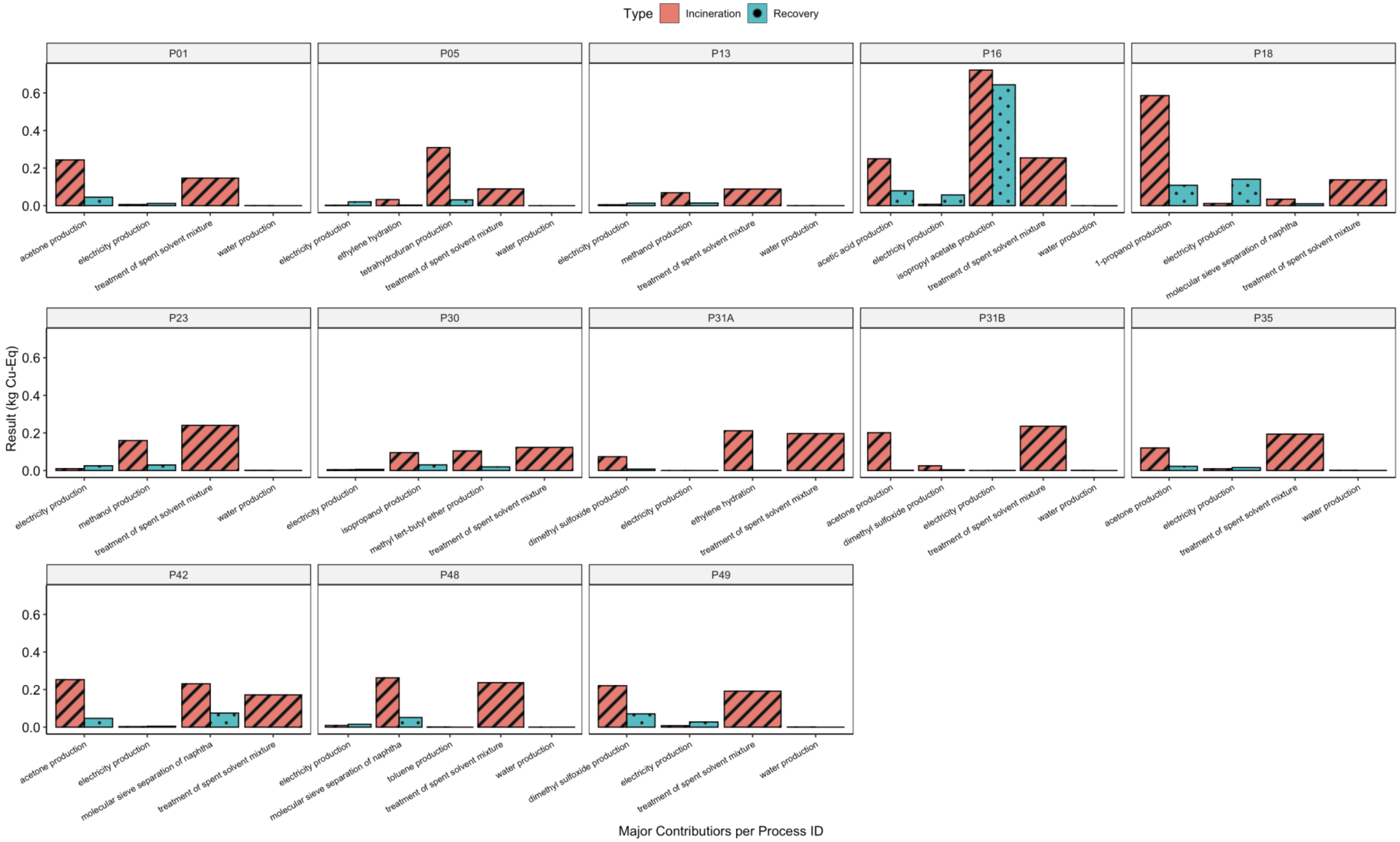

Figure 5-65. Major contributors for each antisolvent crystallization process for surplus ore potential (SOP).

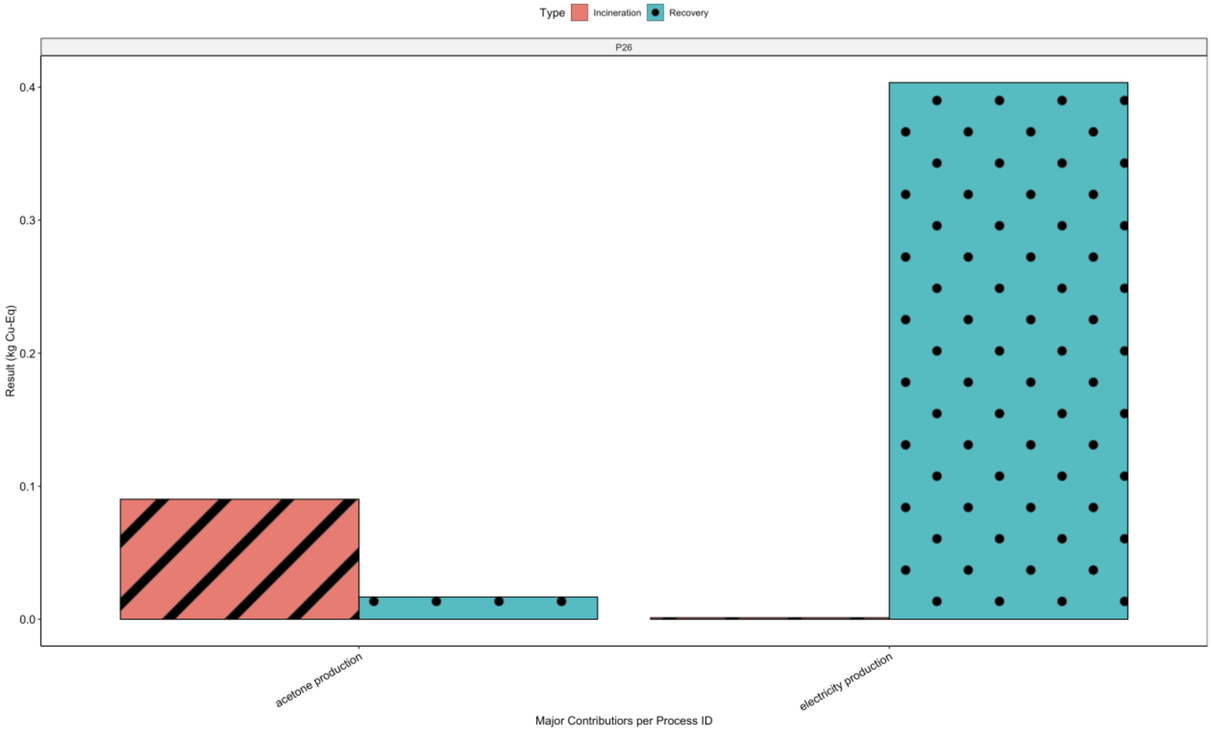

Figure 5-66. Major contributors for Process 26 for surplus ore potential (SOP).

5.6.1.13 Ozone Depletion Potential ($ODP_{infinite}$) Contributors for Antisolvent Processes

Ozone depletion potential ($ODP_{infinite}$) major contributors for antisolvent processes can be found in Figure 5-67 and Figure 5-68 (for P26). Solvent production impacts and treatment of spent solvent mixture impacts were largest for the incineration option. For the recovery option, the treatment of spent solvent mixture impacts was eliminated and the solvent production impacts were greatly reduced. However, electricity production impacts were increased due to the implementation of the solvent recovery systems.

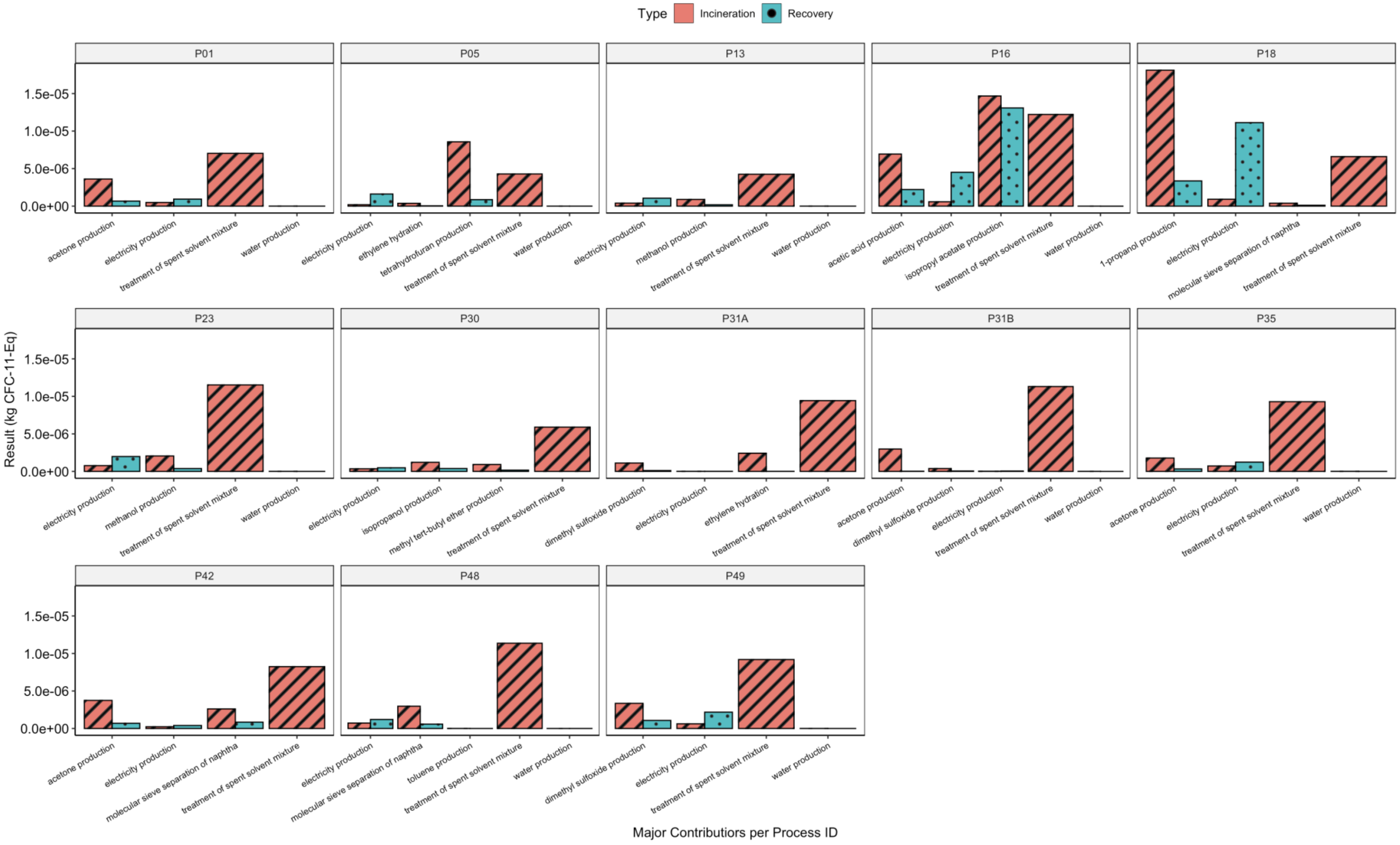

Figure 5-67. Major contributors for each antisolvent crystallization process for ozone depletion potential (ODP$_{\text{infinite}}$).

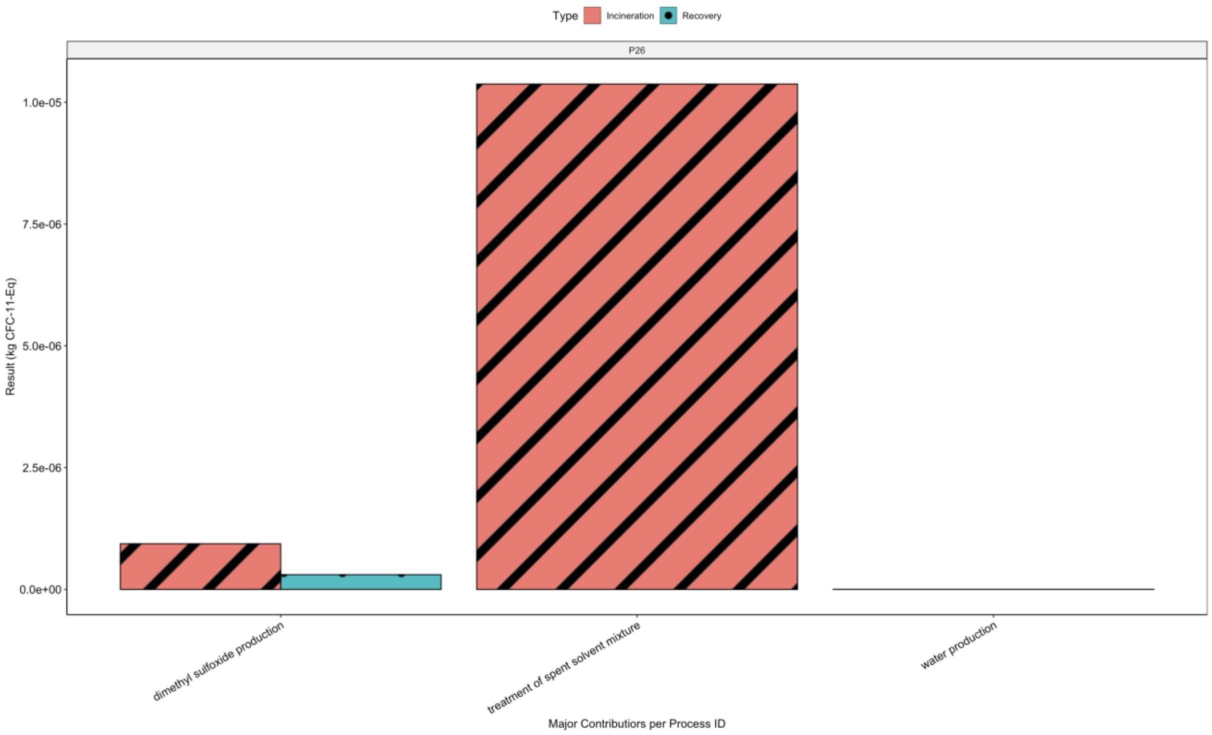

Figure 5-68. Major contributors for Process 26 for ozone depletion potential ($\mathrm{ODP}_{\mathrm{infinite}}$).

5.6.1.14 Particulate Matter Formation Potential (PMFP) Contributors for Antisolvent Processes

Particulate matter formation potential (PMFP) major contributors for antisolvent processes can be found in Figure 5-69 and Figure 5-70 (for P26). For the incineration option, solvent production had the largest impacts. Treatment of spent solvent mixture impacts and electricity production impacts were smaller and similar for the incineration option. For the recovery option, electricity production impacts increased due to the energy requirements of the solvent recovery systems, but the treatment of spent solvent mixture impacts were eliminated. Additionally, solvent production impacts were lowered with reuse of solvents.

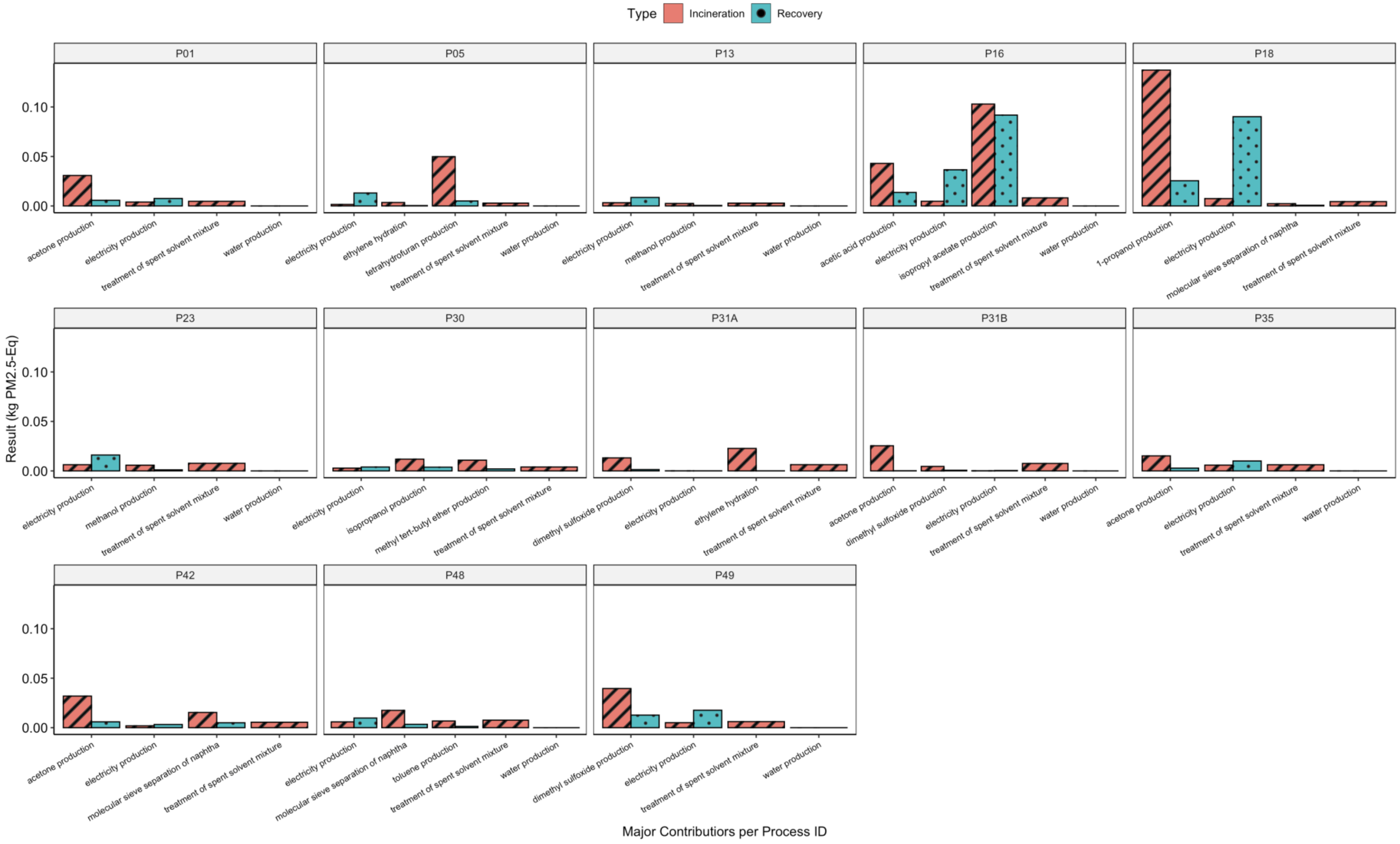

Figure 5-69. Major contributors for each antisolvent crystallization process for particulate matter formation potential (PMFP).

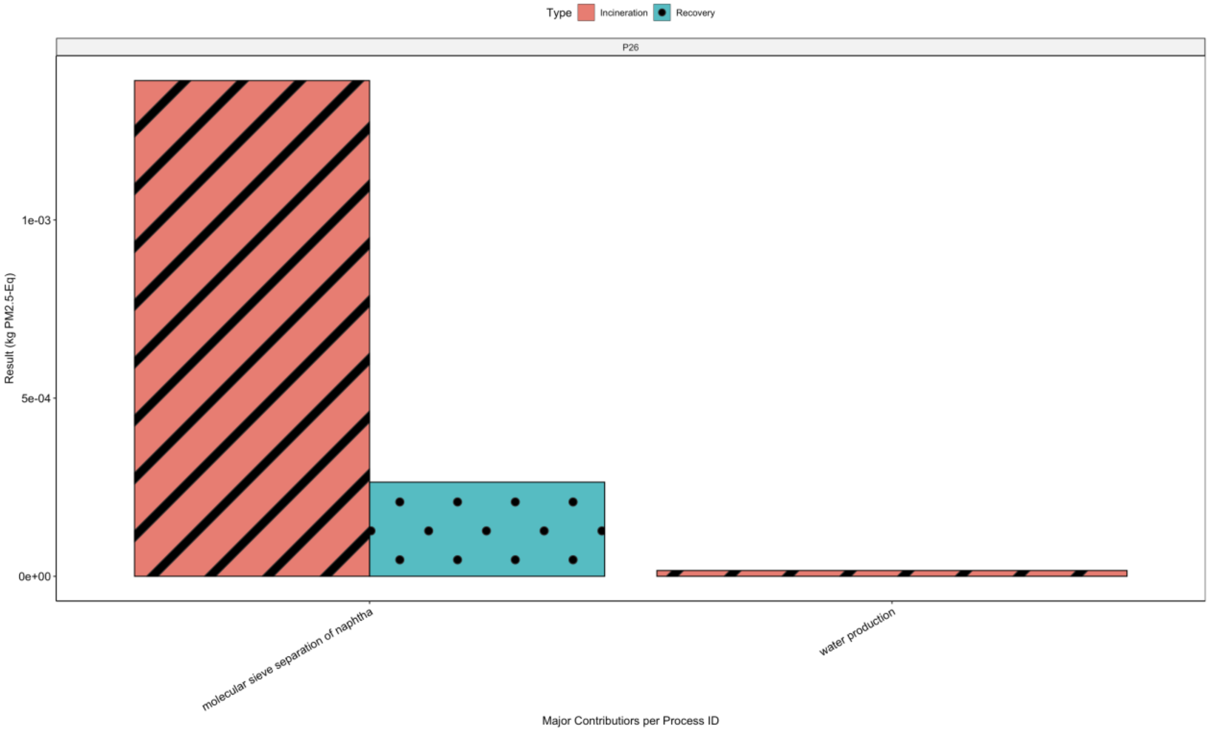

Figure 5-70. Major contributors for Process 26 for particulate matter formation potential (PMFP).

5.6.1.15 Photochemical Oxidant Formation Potential – Humans (HOFP) Contributors for Antisolvent Processes

Photochemical oxidant formation potential – humans (HOFP) major contributors for antisolvent processes can be found in Figure 5-71 and Figure 5-72. Solvent production impacts were largest in the incineration option, then followed by treatment of spent solvent mixture impacts. For the recovery option, electricity production impacts rose due to the implementation of the solvent recovery systems, while treatment of spent solvent mixture impacts were eliminated. Further, solvent production impacts were reduced with the reuse of solvent.

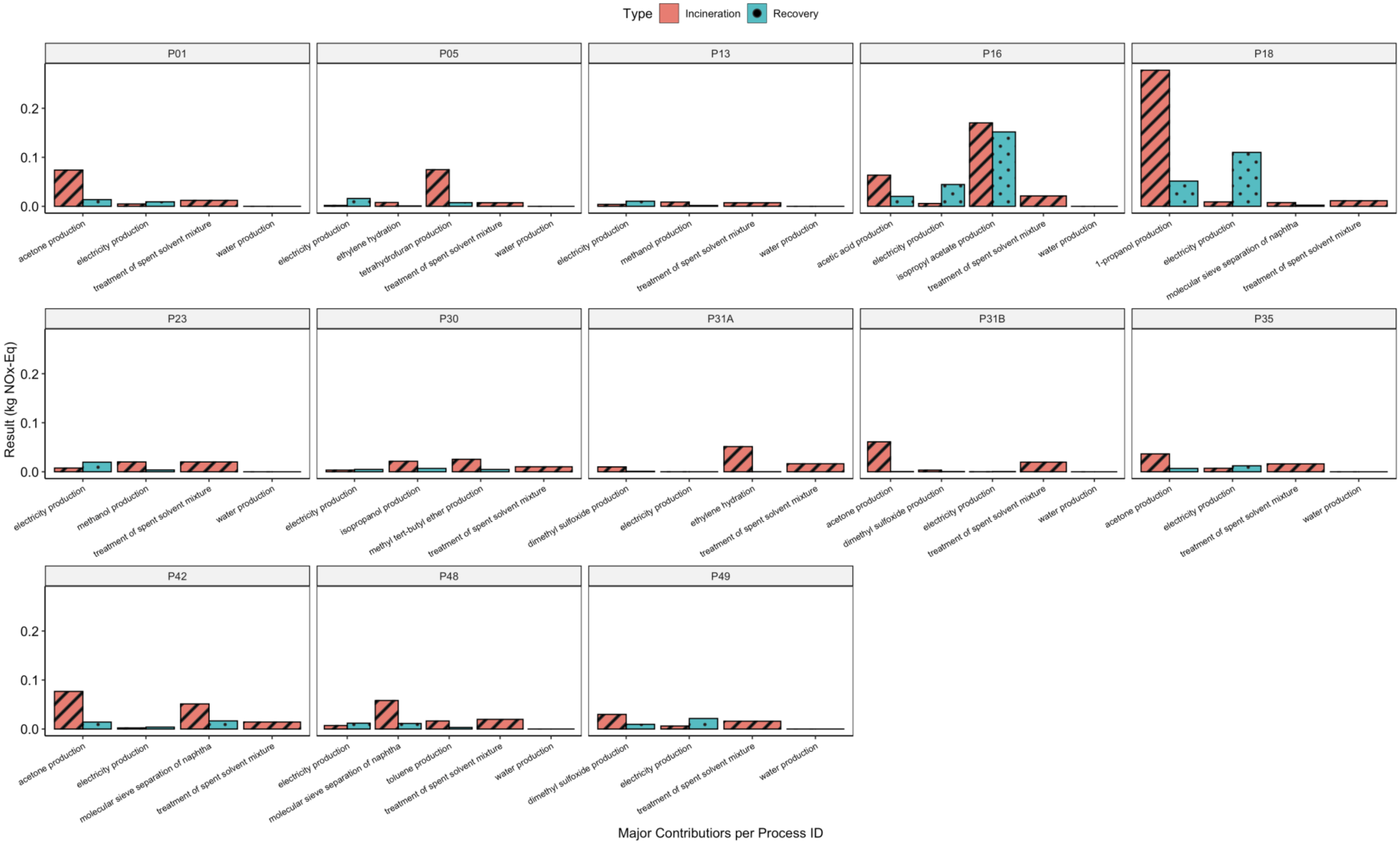

Figure 5-71. Major contributors for each antisolvent crystallization process for photochemical oxidant formation potential – humans (HOFP).

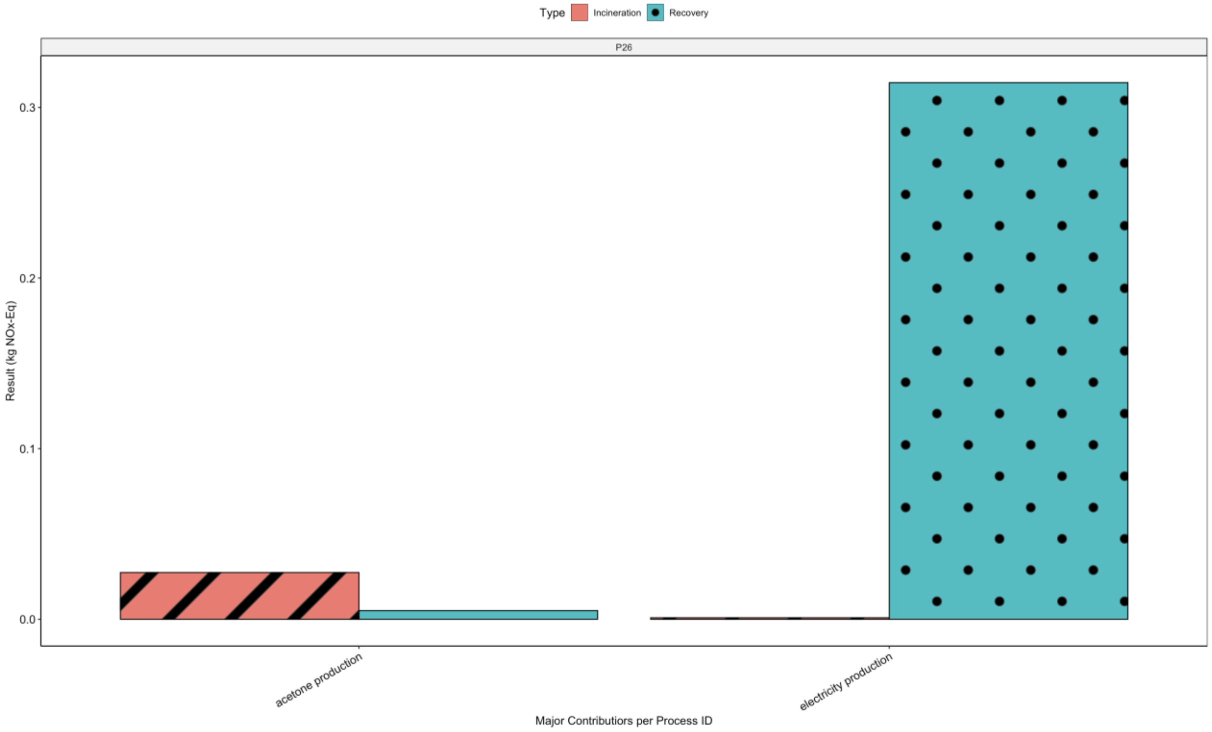

Figure 5-72. Major contributors for Process 26 for photochemical oxidant formation potential – humans (HOFP).

5.6.1.16 Photochemical Oxidant Formation Potential – Ecosystems (EOFP) Contributors for Antisolvent Processes

Photochemical oxidant formation potential – ecosystems (EOFP) major contributors for antisolvent processes can be found in Figure 5-73 and Figure 5-74 (for P26). Similar to HOFP, EOFP impacts for the incineration option were largest for solvent production and then treatment of spent solvent mixtures. Further, electricity production impacts increased with the implementation of solvent recovery systems while solvent production impacts decreased. Treatment of spent solvent mixture impacts were eliminated in the recovery option.

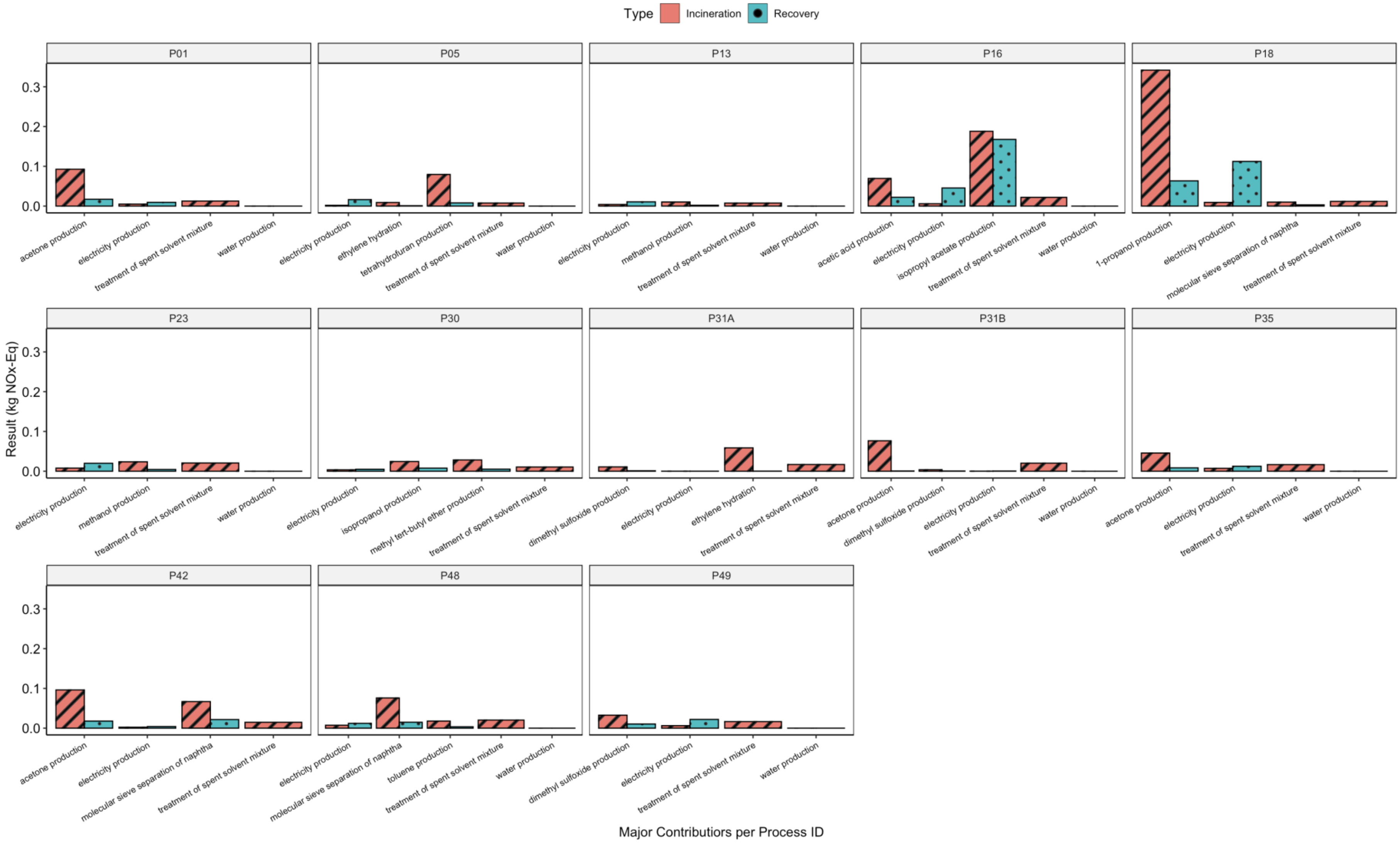

Figure 5-73. Major contributors for each antisolvent crystallization process for photochemical oxidant formation potential – ecosystems (EOFP).

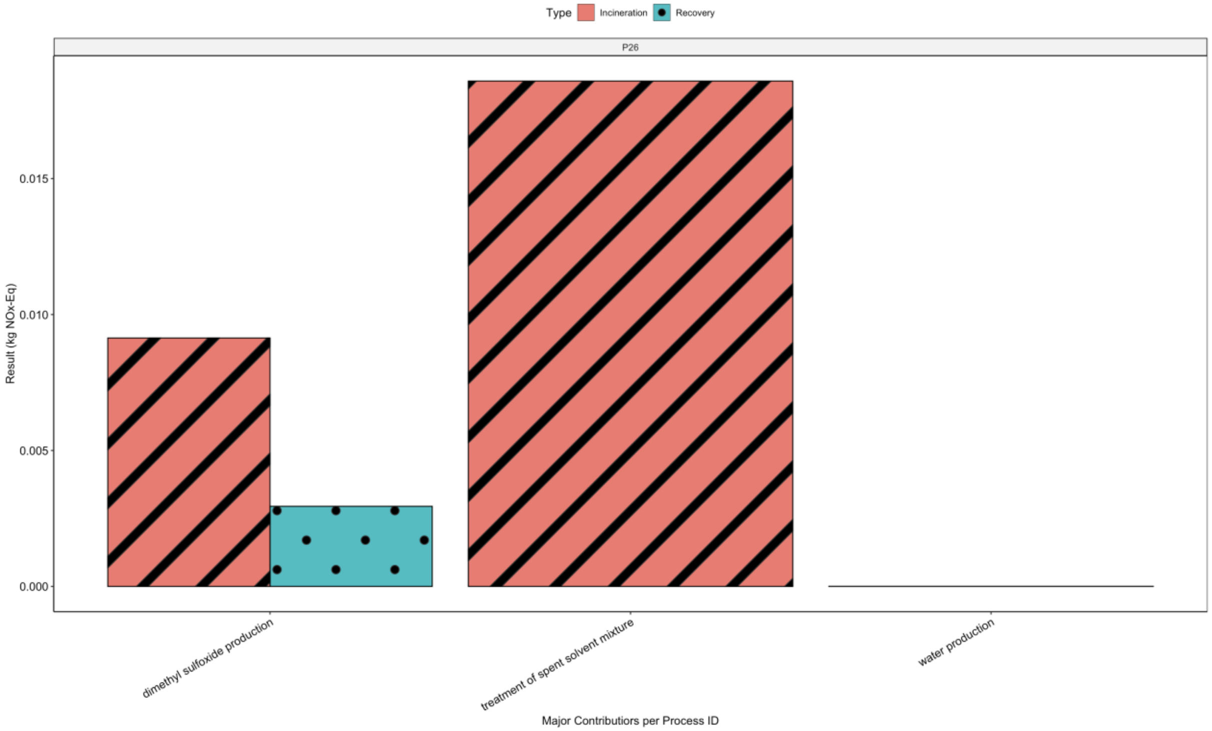

Figure 5-74. Major contributors for Process 26 for photochemical oxidant formation potential – ecosystems (EOFP).

5.6.1.17 Water Consumption Potential (WCP) Contributors for Antisolvent Processes

Water consumption potential (WCP) major contributors for antisolvent processes can be found in Figure 5-75 and Figure 5-76 (for P26). For the incineration option, solvent production impacts were largest, especially for tetrahydrofuran, acetic acid, isopropyl acetate, and 1-propanol. Electricity production impacts increased in the recovery option due to the additional energy requirements of the solvent recovery systems while treatment of spent solvent mixture impacts was eliminated. Solvent production impacts were also reduced in the recovery option.

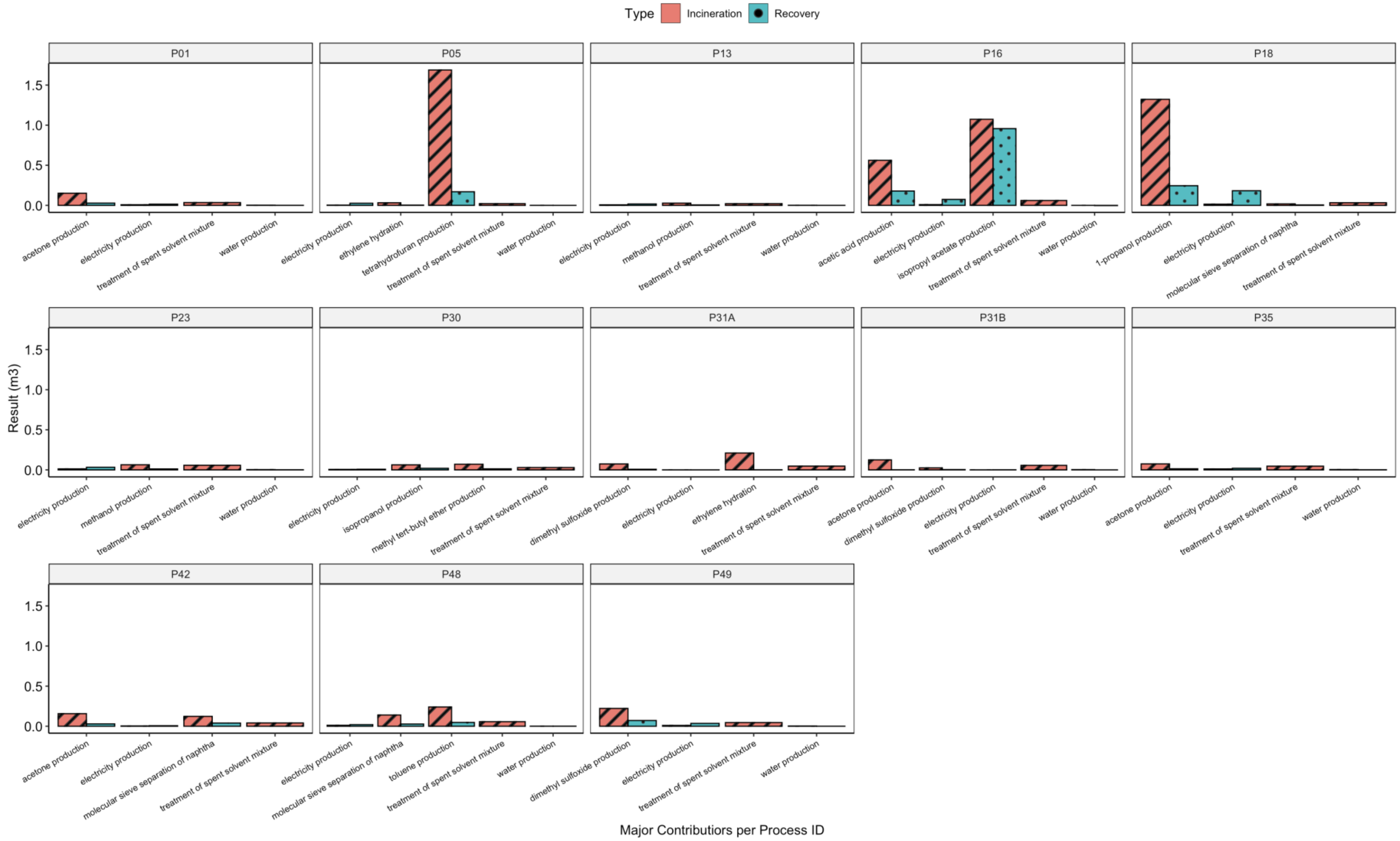

Figure 5-75. Major contributors for each antisolvent crystallization process for water consumption potential (WCP).

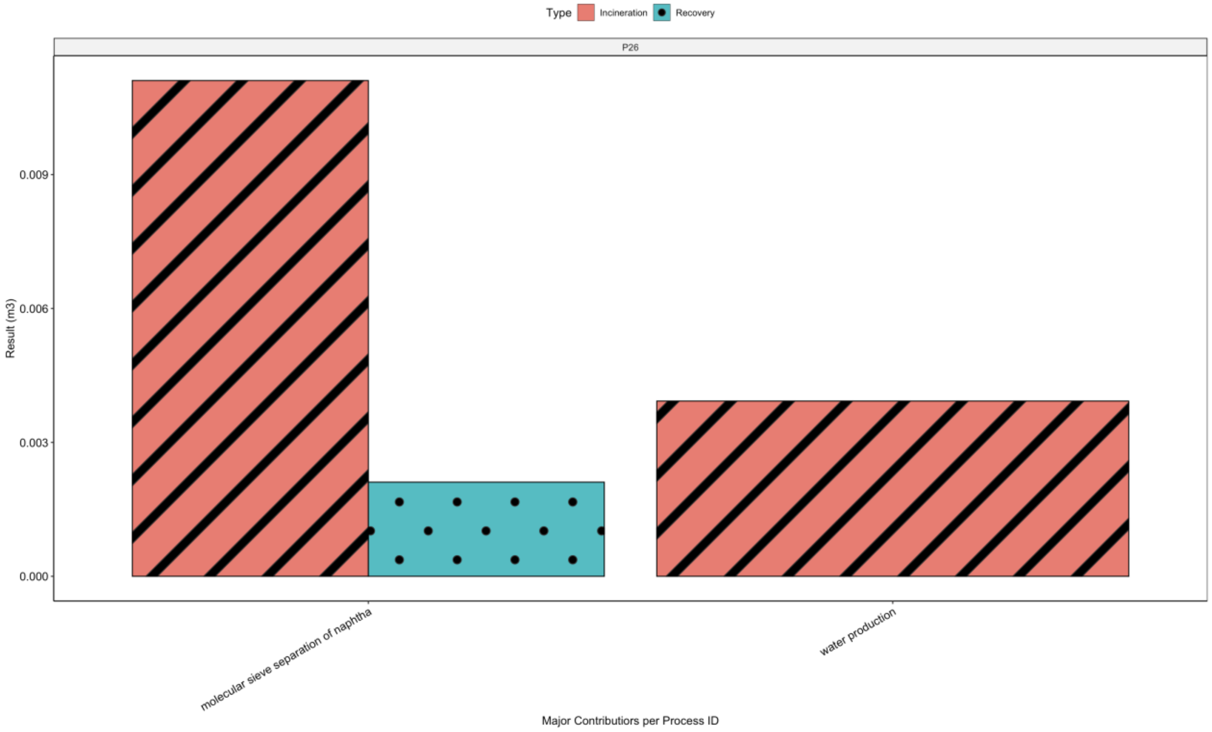

Figure 5-76. Major contributors for Process 26 for water consumption potential (WCP).

Throughout all impact categories, electricity production was much higher in P16, P18, and P26 for the recovery option when compared the incineration option. P18 and P26 electricity production was increased due to the small (less than 2ºC) temperature difference between boiling solvents (i.e., typically between heptane, 1-propanol, and water) being recovered. This caused an elevated reflux ratio due to the poor separation conditions and in turn higher energy requirements. In these cases, an alternative separation method should be examined (e.g., pervaporation or membrane) so that the energy requirement for the solvent requirement system can be reduced. P16 had high electricity production impacts due to elevated operating temperature for the column (because the two solvents to be separated were water and acetic acid, which have boiling points of 100ºC and 118ºC).

The major contributors for the antisolvent processes were solvent production for all impact categories. For some impact categories, treatment of spent solvent mixtures was also a major contributor. In general, electricity production was not a major contributor for the incineration options; however, it did become a major contributor in the recovery option. This is due to the additional energy requirements for the implementation of the solvent recovery systems. Solvent production impacts were reduced in all impact categories for the recovery option. This was thanks to the reuse of solvent generated from the solvent recovery systems. Additionally, with the implementation of the solvent recovery systems, the treatment of spent solvent mixture impacts could be eliminated.

5.6.2 Major Cooling Crystallization Environmental Impact Contributors

The major contributors for cooling crystallization processes for all impact categories can be found below.

5.6.2.1 Terrestrial Acidification Potential (TAP) Contributors for Cooling Processes

Terrestrial acidification potential (TAP) major contributors for cooling processes can be found in Figure 5-77. For the incineration option, solvent production impacts are largest. Treatment of spent solvent mixture impacts and electricity impacts are similar for this option. However, in the recovery option, the treatment of spent solvent mixture impacts were eliminated and the electricity production impacts increased while the solvent production impacts decreased. Market for dimethylacetamide (related to the transportation of the solvent) in P34 produced a negative impact in the recovery option. This suggests that the reuse of dimethylacetamide can reduce transportation impacts associated with the solvent.

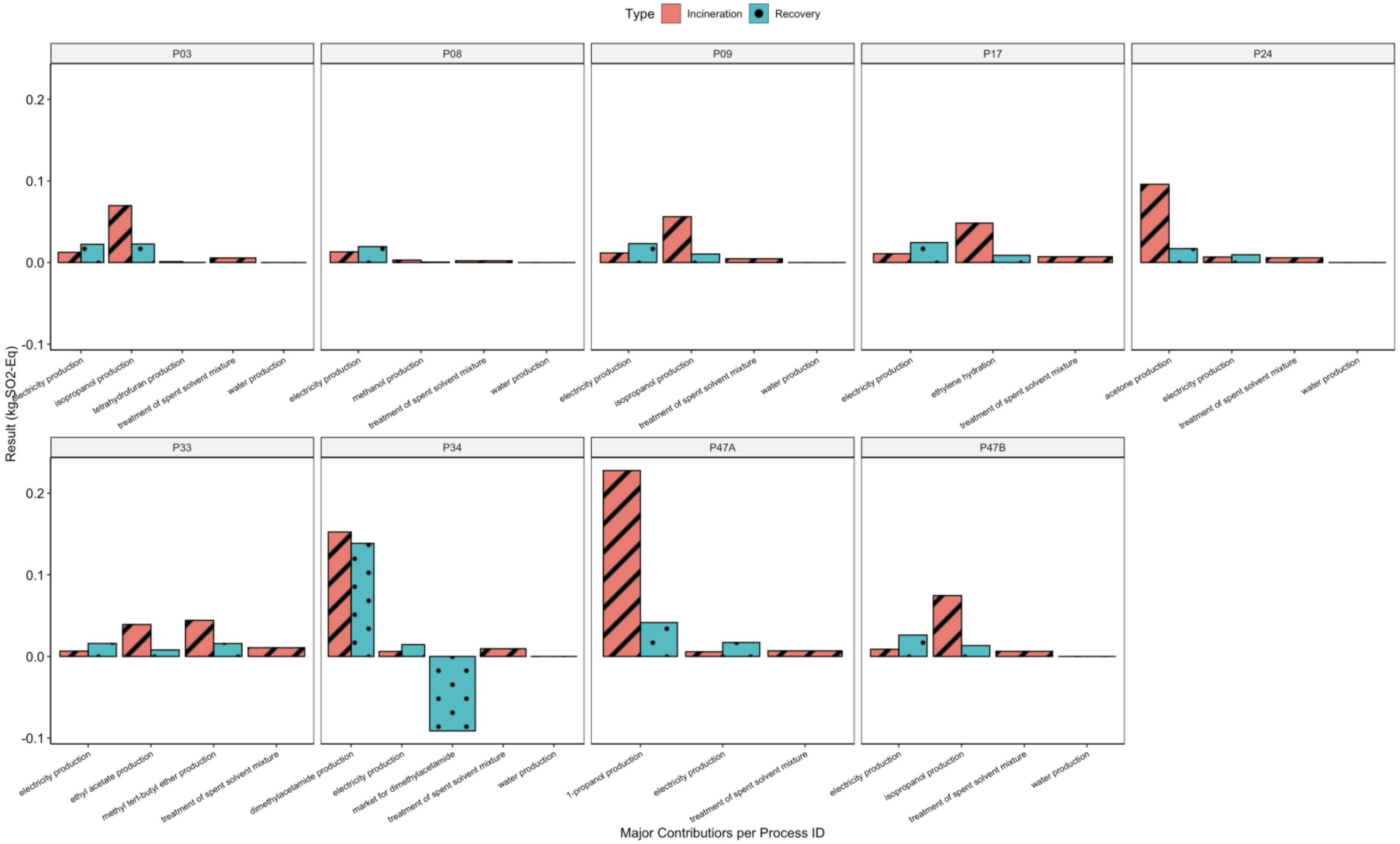

Figure 5-77. Major contributors for each cooling crystallization process for terrestrial acidification potential (TAP).

5.6.2.2 Global Warming Potential (GWP100) Contributors for Cooling Processes

Global warming potential (GWP100) major contributors for cooling processes can be found in Figure 5-78. Treatment of spent solvent mixture and solvent production showed the largest impacts in the incineration option. Electricity production impacts were smaller for incineration but rose with the recovery option due to the additional energy requirement from the implementation of the solvent recovery systems. Treatment of spent solvent mixture impacts were eliminated in the recovery option and there was a reduction in the solvent production impacts. Like TAP, GWP100 showed a negative market for dimethylacetamide impact in P34 suggesting that the reuse of solvent has a positive effect on transportation of dimethylacetamide.

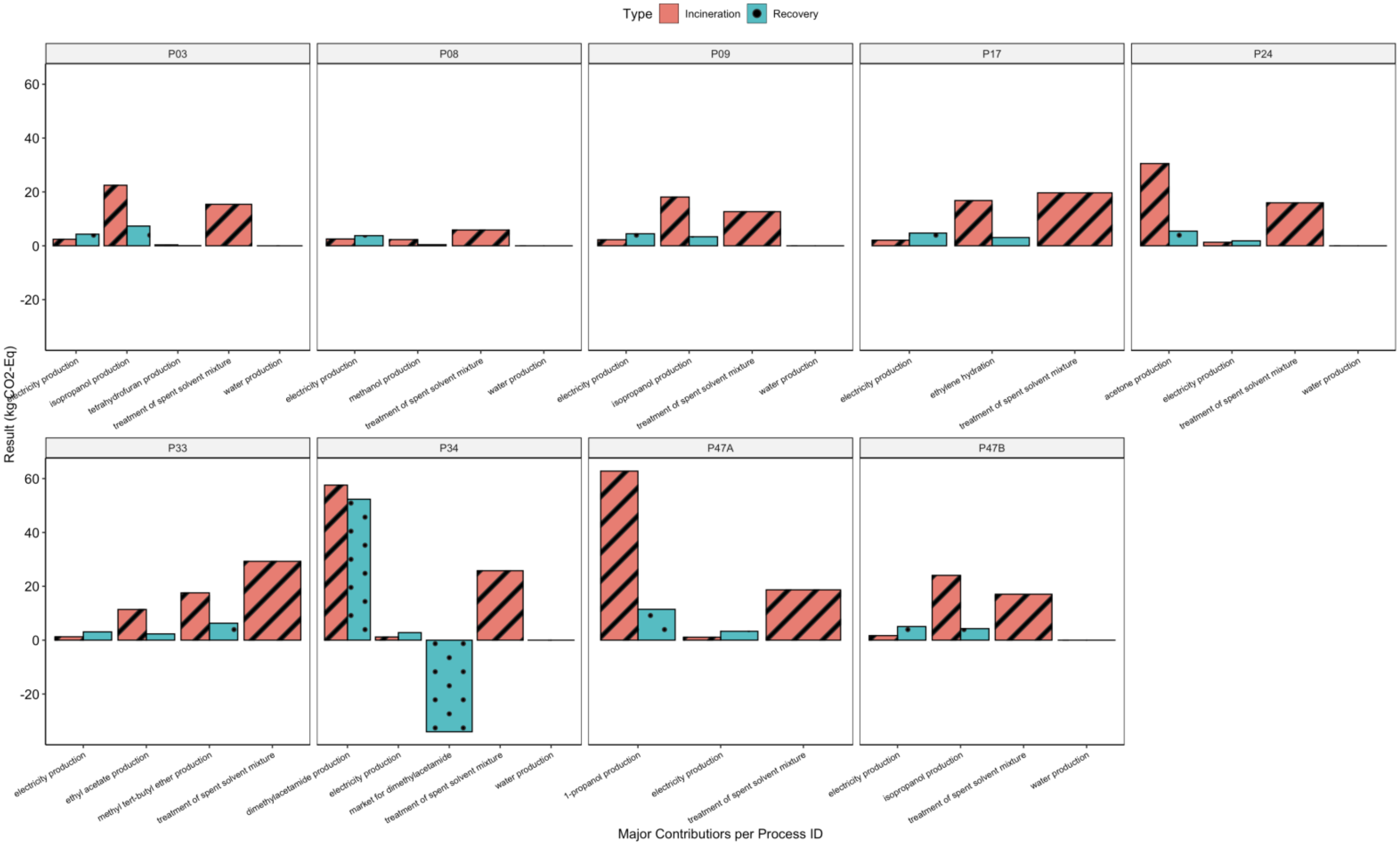

Figure 5-78. Major contributors for each cooling crystallization process for global warming potential (GWP100).

5.6.2.3 Freshwater Ecotoxicity Potential (FETP) Contributors for Cooling Processes

Freshwater ecotoxicity potential (FETP) major contributors for cooling processes can be found in Figure 5-79. Solvent production impacts were largest in the incineration option and decreased in the recovery option. Electricity production impacts and treatment of spent solvent mixture impacts were similar for incineration but electricity production impacts rose in the recovery option while treatment of spent solvent mixture impacts were eliminated. The recovery option had a positive effect on the market for dimethylacetamide impacts in P34.

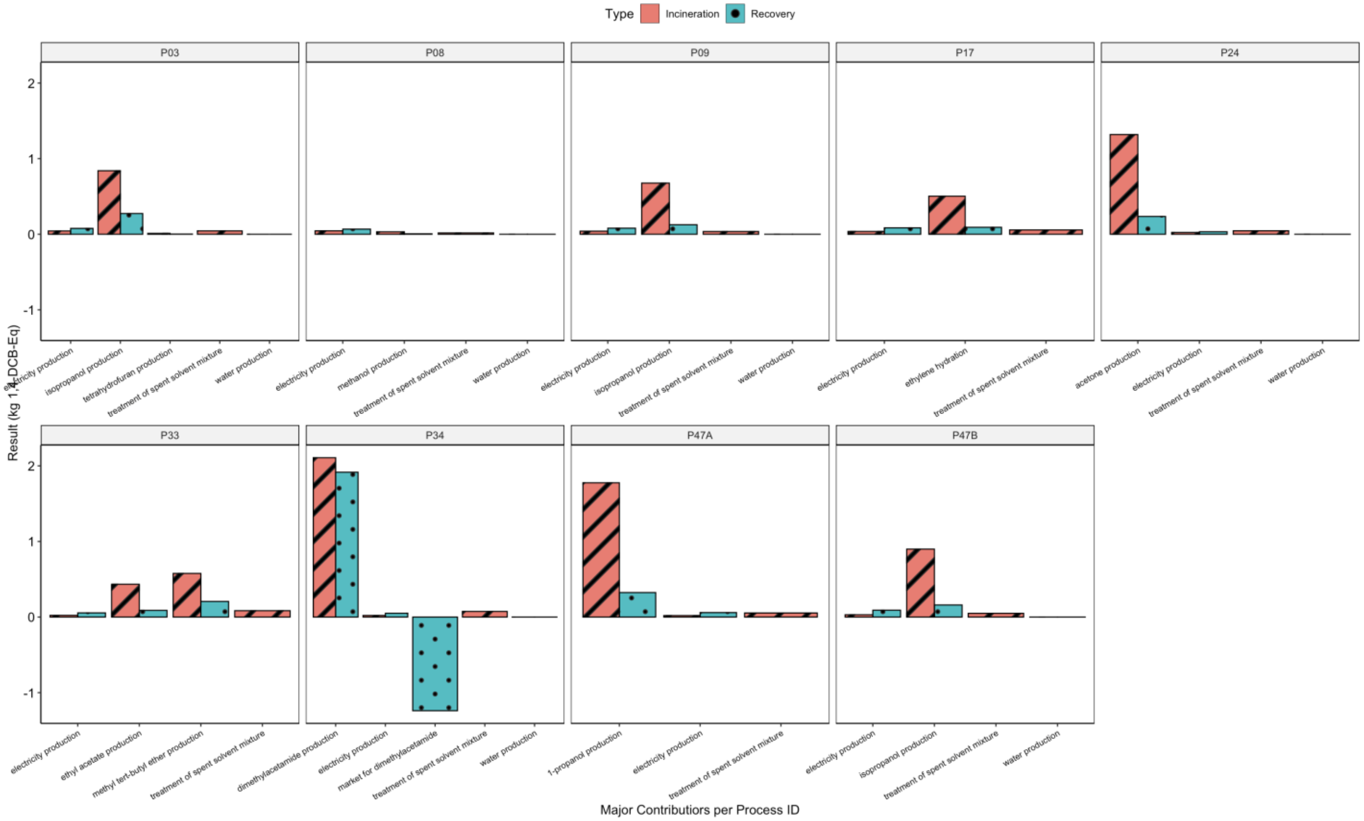

Figure 5-79. Major contributors for each cooling crystallization process for freshwater ecotoxicity potential (FETP).

5.6.2.4 Marine Ecotoxicity Potential (METP) Contributors for Cooling Processes

Marine ecotoxicity potential (METP) major contributors for cooling processes can be found in Figure 5-80. Solvent production showed the largest impacts in the incineration option. Electricity production and treatment of spent solvent mixture impacts were similar and lower than solvent production impacts. For the recovery option, electricity production impacts increased, solvent production impacts decreased, and treatment of spent solvent mixture impacts were eliminated. The recovery option also showed a positive effect on the market for dimethylacetamide impacts for P34.

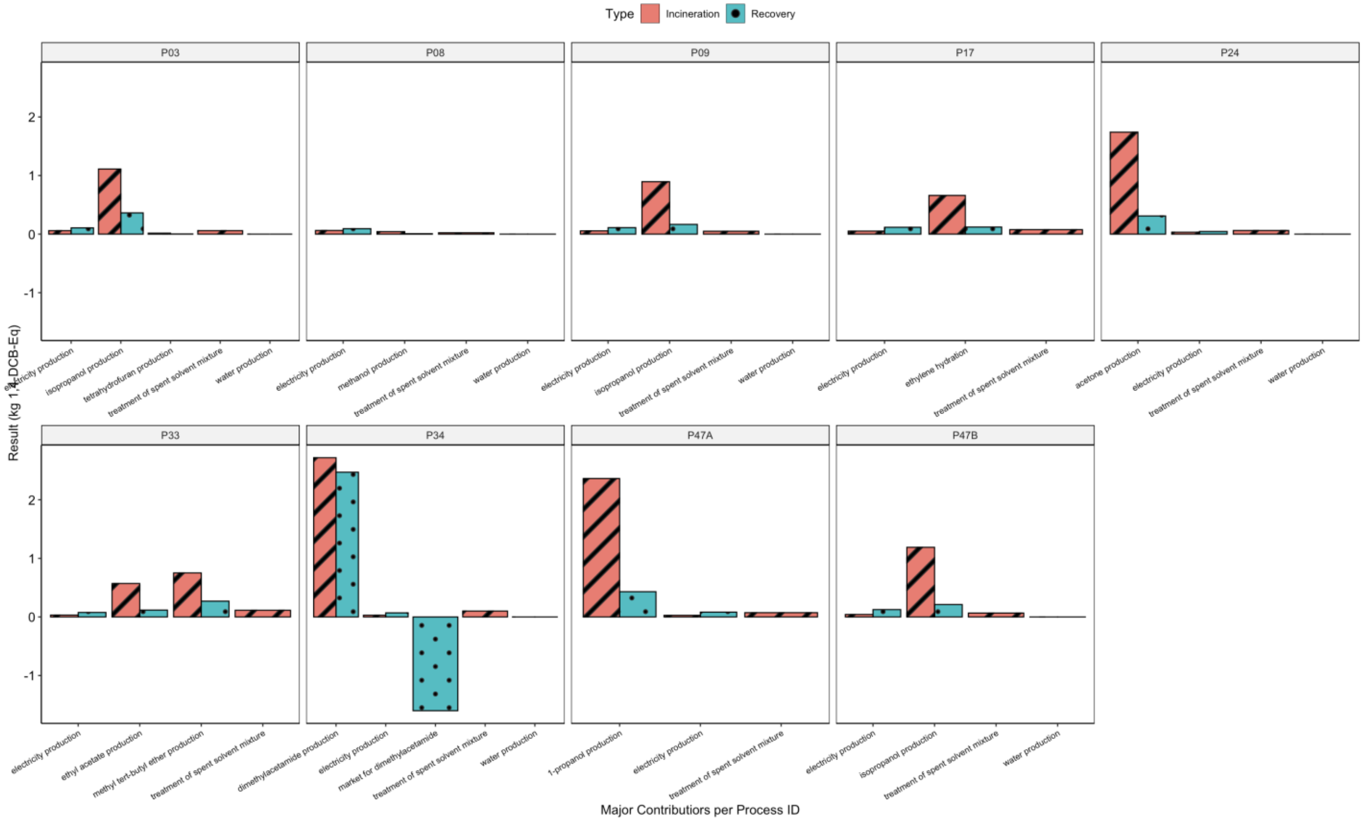

Figure 5-80. Major contributors for each cooling crystallization process for marine ecotoxicity potential (METP).

5.6.2.5 Terrestrial Ecotoxicity Potential (TETP) Contributors for Cooling Processes

Terrestrial ecotoxicity potential (TETP) major contributors for cooling processes can be found in Figure 5-80. Results show that solvent production had the largest impacts for the incineration option. Electricity production was increased in the recovery option due to the additional energy requirement from the solvent recovery systems. Treatment of spent solvent mixture impact was eliminated in the recovery option. Additionally, the market for dimethylacetamide showed a positive effect on the TETP impacts in the recovery option.

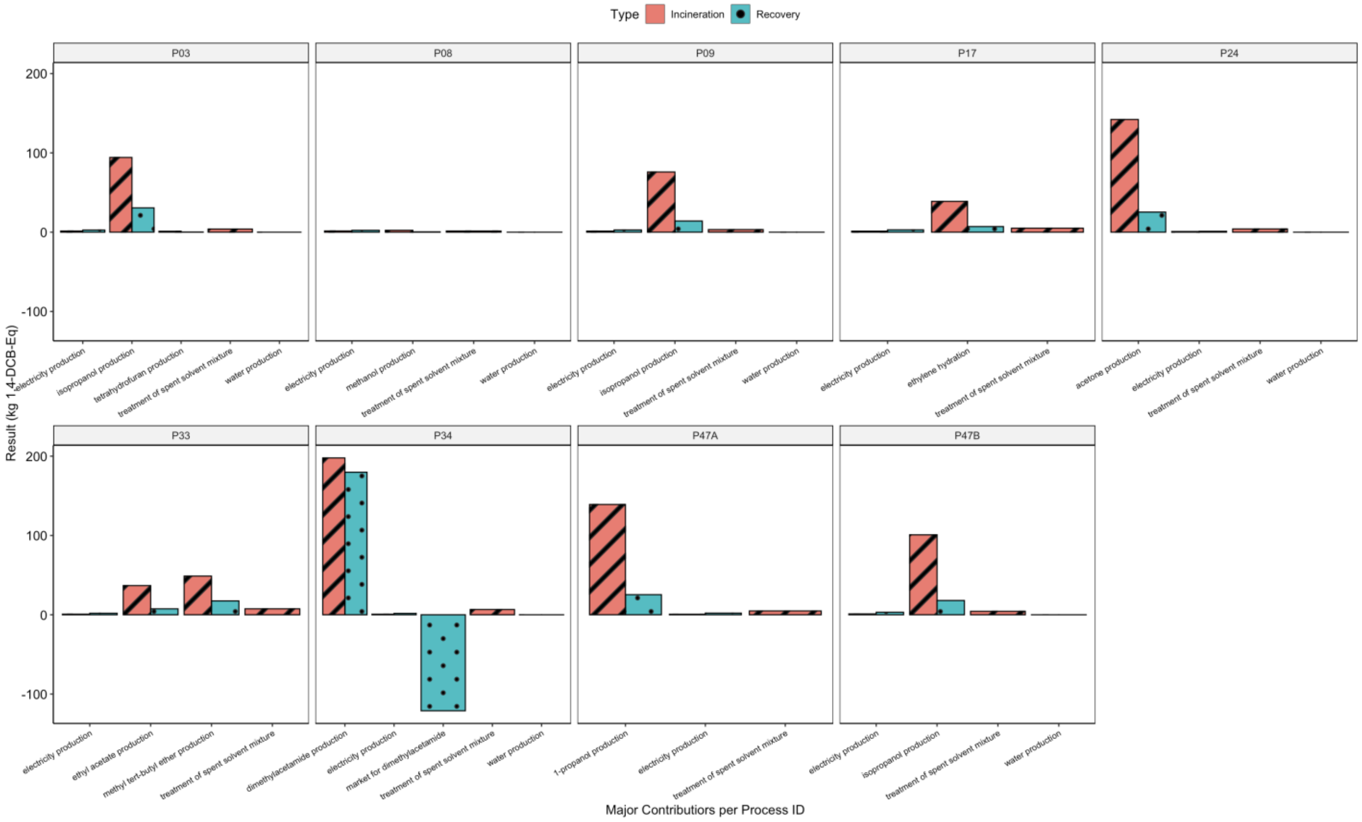

Figure 5-81. Major contributors for each cooling crystallization process for terrestrial ecotoxicity potential (TETP).

5.6.2.6 Fossil Fuel Potential (FFP) Contributors for Cooling Processes

Fossil fuel potential (FFP) major contributor for cooling processes can be found in Figure 5-82. Solvent production showed the largest impacts in the incineration option and then decreased in the recovery option due to the reuse of solvent. Electricity production and treatment of spent solvent mixture impacts were similar for the incineration option. Electricity production impacts increased with the additional energy requirement of the solvent recovery systems and treatment of spent solvent mixture impacts were eliminated. Market for dimethylacetamide in the recovery option showed a positive effect on the FFP impacts.

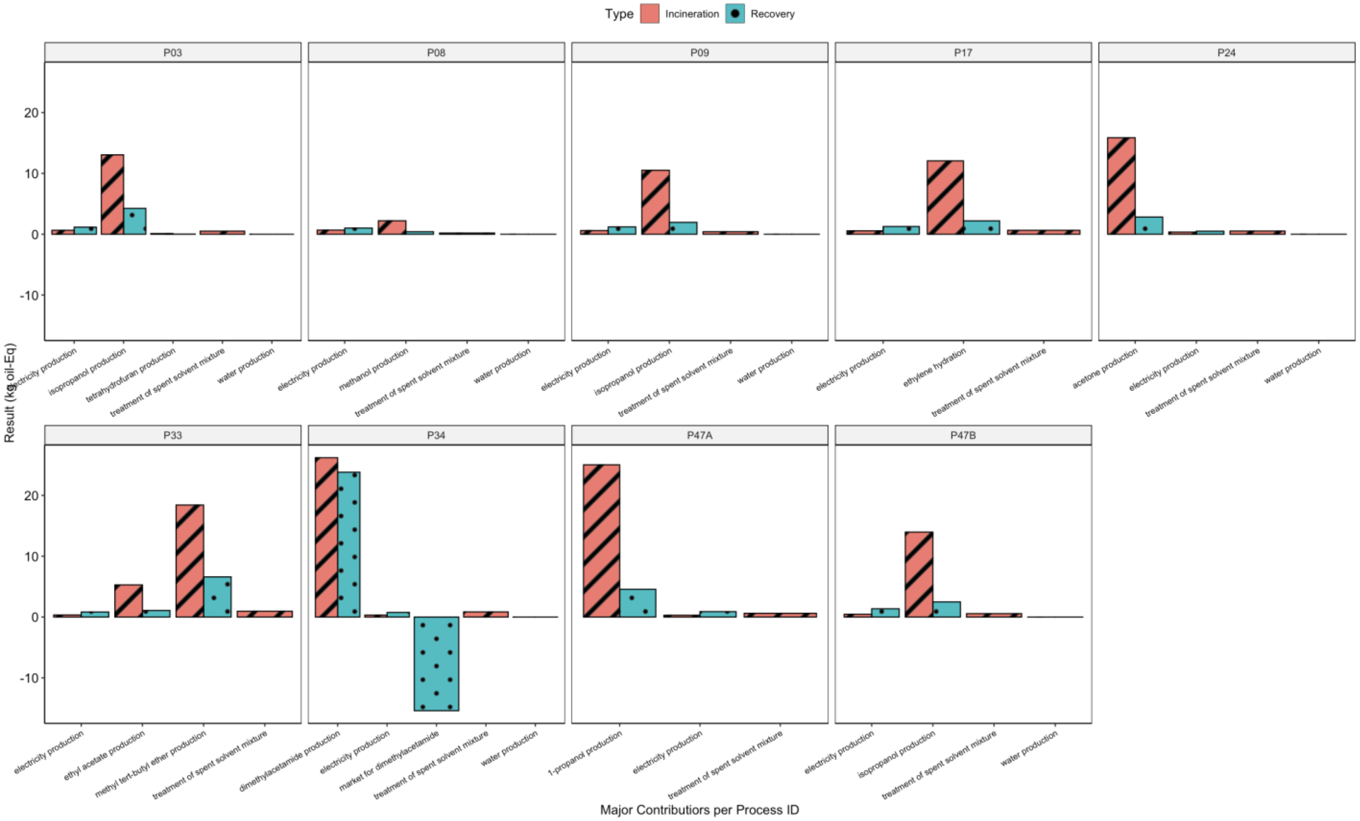

Figure 5-82. Major contributors for each cooling crystallization process for fossil fuel potential (FFP).

5.6.2.7 *Freshwater Eutrophication Potential (FEP) Contributors for Cooling Processes*

Freshwater eutrophication potential (FEP) major contributors for cooling processes can be found in Figure 5-83. Solvent production and treatment of spent solvent mixture showed the largest impacts in the incineration option. Solvent production impacts decreased and treatment of spent solvent mixture impacts were eliminated for the recovery option. Electricity production impacts increased in the recovery option with the implementation of the solvent recovery systems. Market for dimethylacetamide showed a positive effect on the FEP impacts for the recovery option.

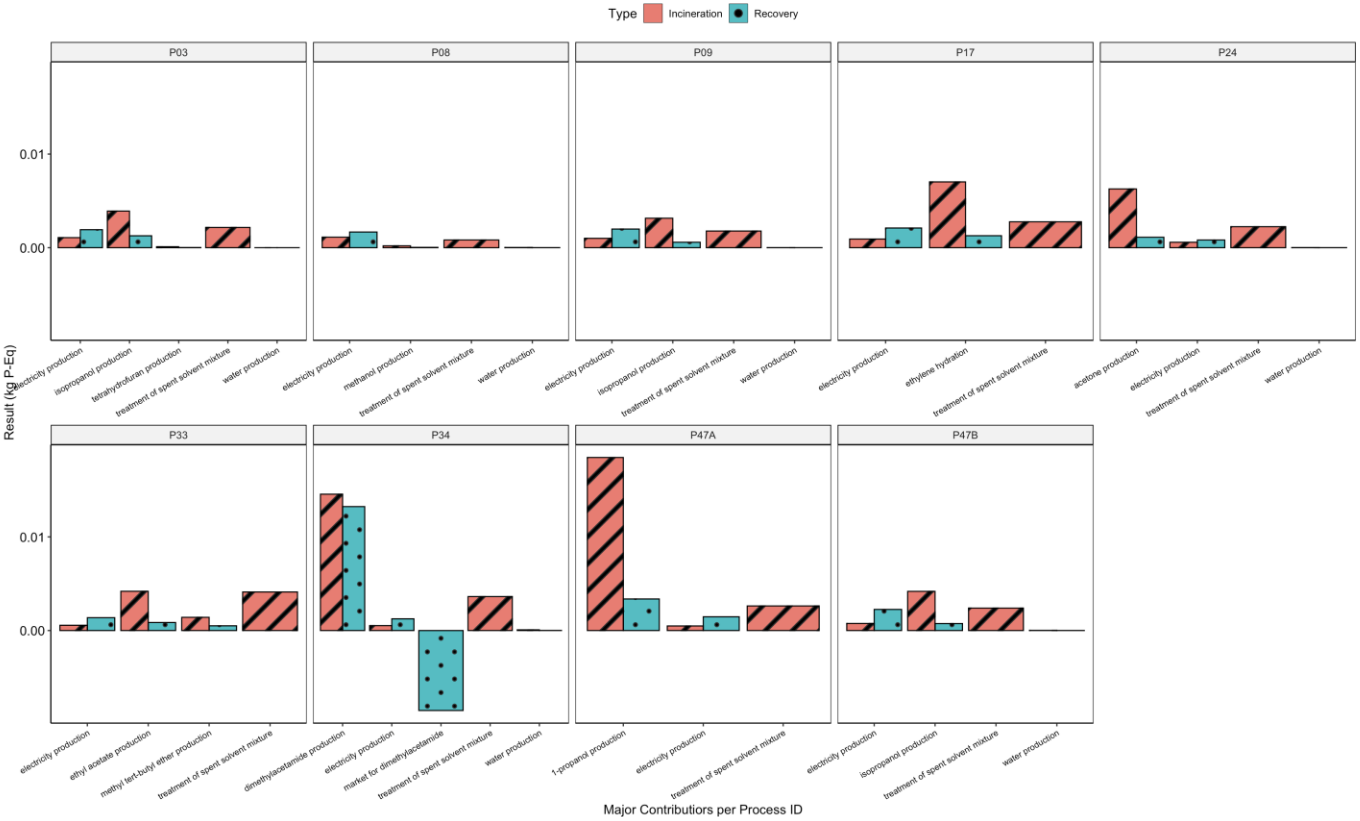

Figure 5-83. Major contributors for each cooling crystallization process for freshwater eutrophication potential (FEP).

5.6.2.8 Marine Eutrophication Potential (MEP) Contributors for Cooling Processes

Marine eutrophication potential (MEP) major contributors for cooling processes can be found in Figure 5-84.All contributor impacts were near-zero for both incineration and recovery options, except for large impacts for dimethylacetamide production in P34 and a positive effect of the recovery option on the market for dimethylacetamide.

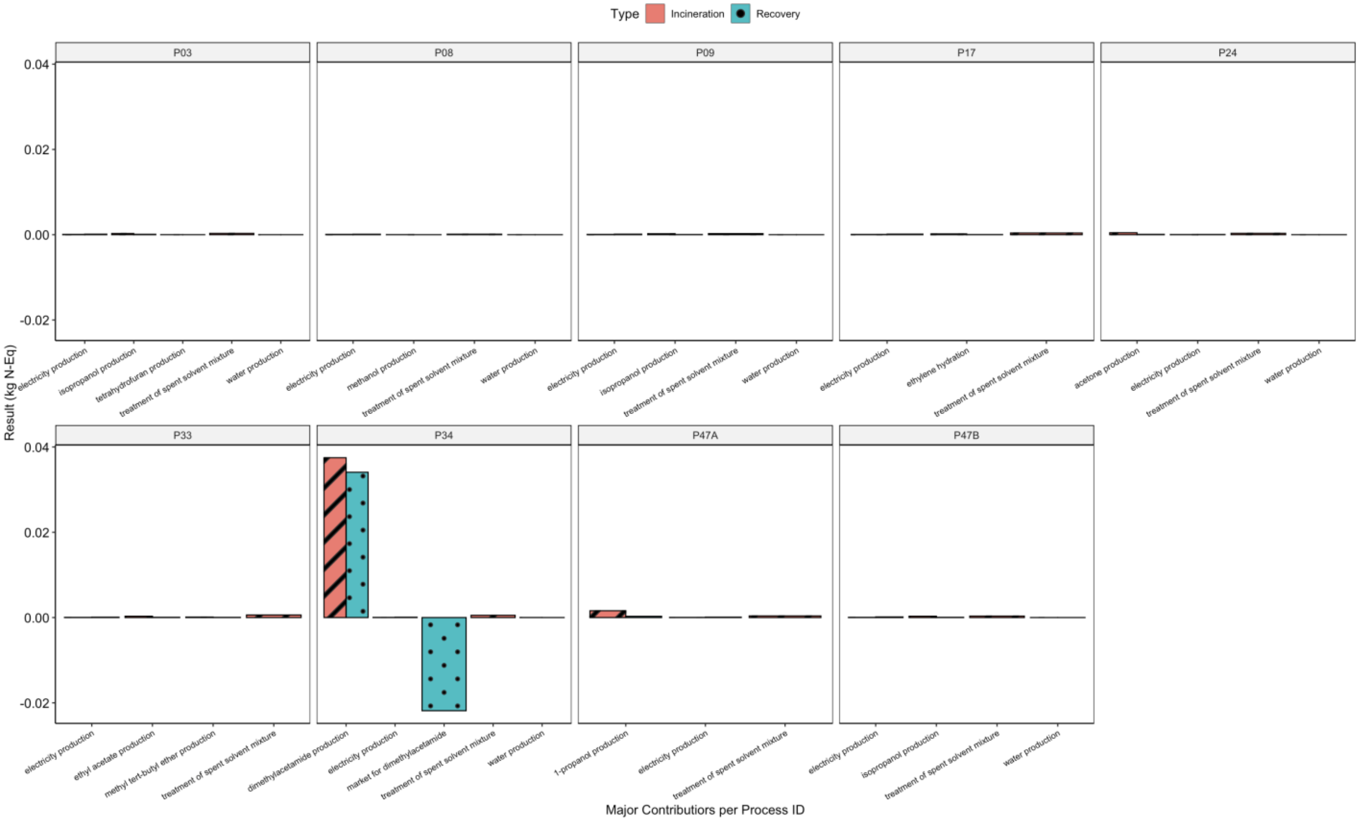

Figure 5-84. Major contributors for each cooling crystallization process for marine eutrophication potential (MEP).

5.6.2.9 Human Toxicity Potential – Carcinogenic (HTPc) Contributors for Cooling Processes

Human toxicity potential – carcinogenic (HTPc) major contributors for cooling processes can be found in Figure 5-85. Solvent production showed the largest impacts in the incineration option. Treatment of spent solvent mixture and electricity production impacts were similar for this option. Treatment of spent solvent mixture impacts were eliminated in the recovery option and the electricity production impacts were increased. Solvent production impacts decreased in the recovery option with the reuse of solvent. There was a positive effect on the HTPc impacts during the recovery option for the market for dimethylacetamide.

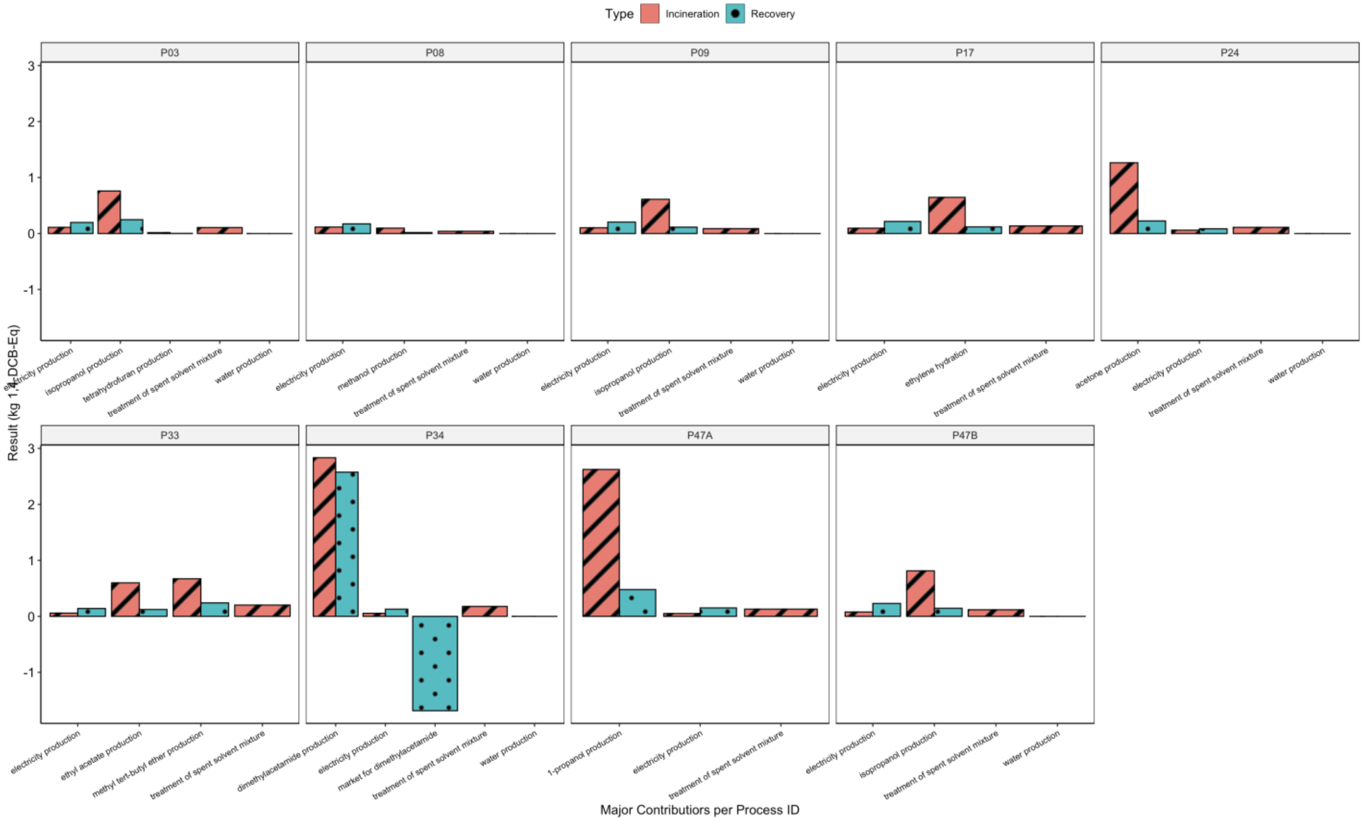

Figure 5-85. Major contributors for each cooling crystallization process for human toxicity potential – carcinogenic (HTPc).

5.6.2.10 Human Toxicity Potential – Non-Carcinogenic (HTPnc) Contributors for Cooling Processes

Human toxicity potential – non-carcinogenic (HTPnc) major contributors for cooling processes can be found in Figure 5-86. Solvent production impacts were largest in the incineration option and then decreased in the recovery option. Electricity production rose in the recovery option when compared to the incineration option. Treatment of spent solvent mixture impacts were eliminated in the recovery option and were similar to electricity production impacts in the incineration option. Market for dimethylacetamide showed a positive effect on the HTPnc impacts in the recovery option due to the reuse of solvent.

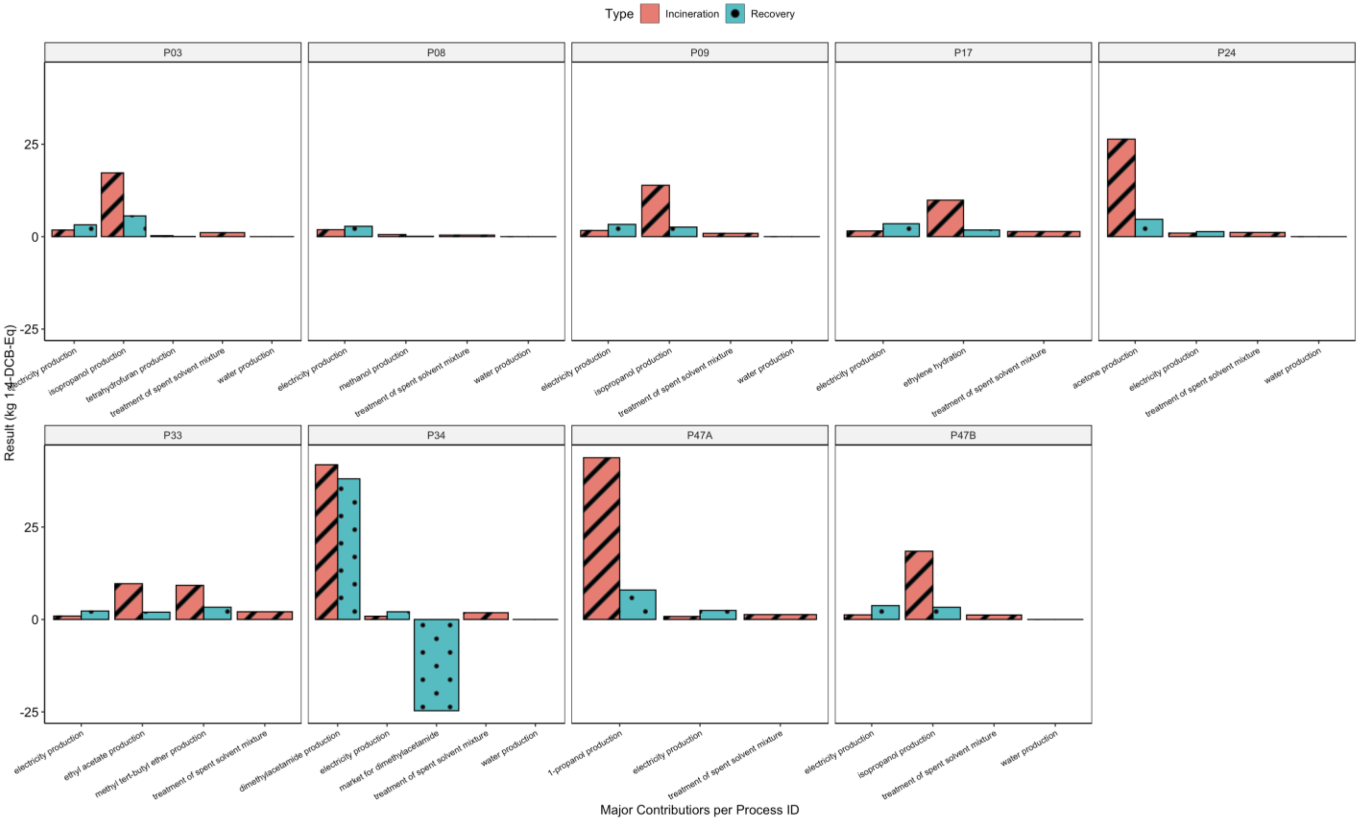

Figure 5-86. Major contributors for each cooling crystallization process for human toxicity potential – non-carcinogenic (HTPnc).

5.6.2.11 Ionising Radiation Potential (IRP) Contributors for Cooling Processes

Ionising radiation potential (IRP) major contributors for cooling processes can be found in Figure 5-87. Solvent production showed the largest impacts in the incineration option and were significantly decreased in the recovery option. Treatment of spent solvent mixture and electricity production showed similar results for the incineration option but electricity production impacts rose and treatment of spent solvent mixture impacts were eliminated for the recovery option. Market for dimethylacetamide production showed a positive effect on IRP impacts for the recovery option.

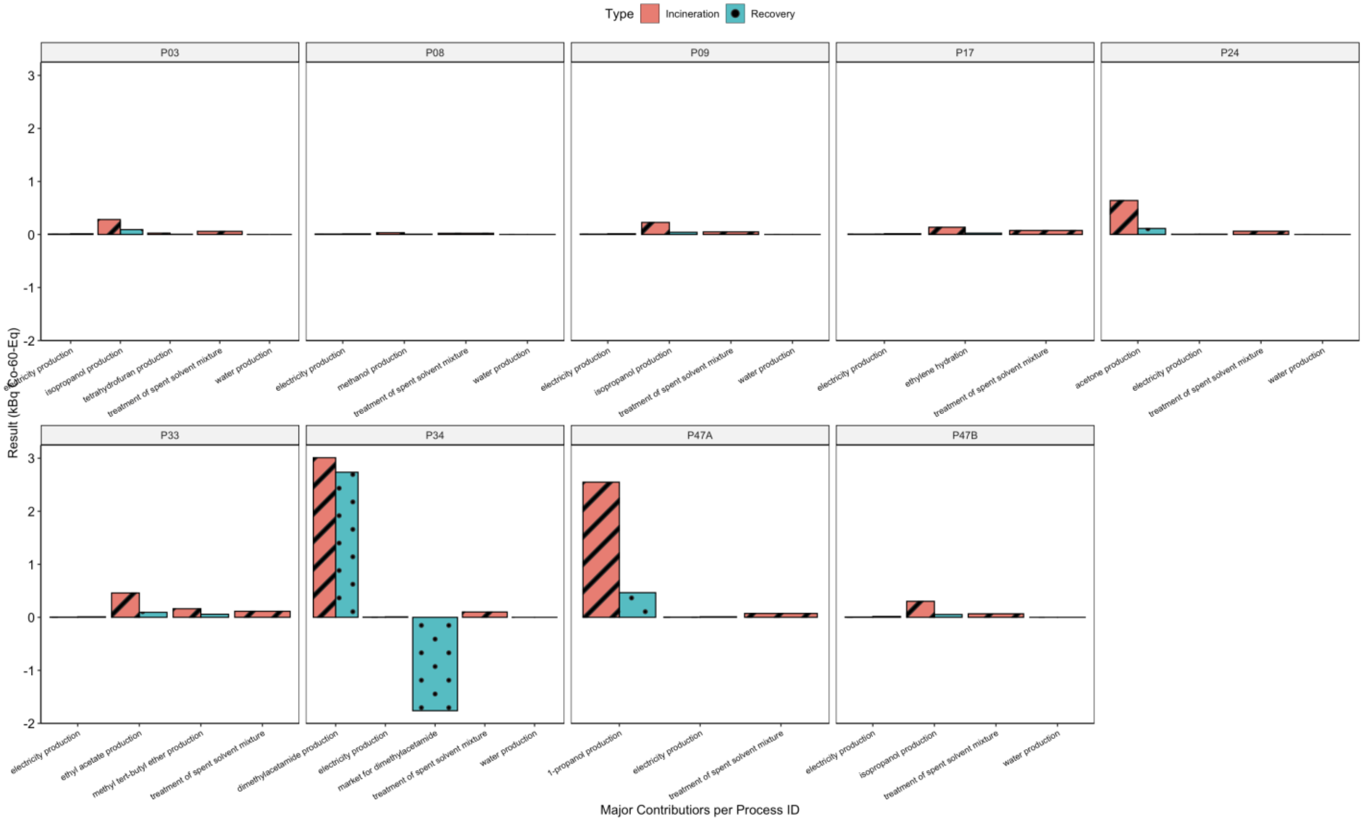

Figure 5-87. Major contributors for each cooling crystallization process for ionising radiation potential (IRP).

5.6.2.12 Agricultural Land Occupation (LOP) Contributors for Cooling Processes

Agricultural land occupation (LOP) major contributors for cooling processes can be found in Figure 5-88. Solvent production impacts were largest in the incineration option and significantly decreased, with the reuse of solvent, in the recovery option. Electricity production and treatment of spent solvent mixture impacts were similar for the incineration option but electricity production impacts increased in the recovery option with the implementation of solvent recovery systems while treatment of spent solvent mixture impacts were eliminated. There was a positive effect of the LOP impacts in the recovery option with the market of dimethylacetamide in P34.

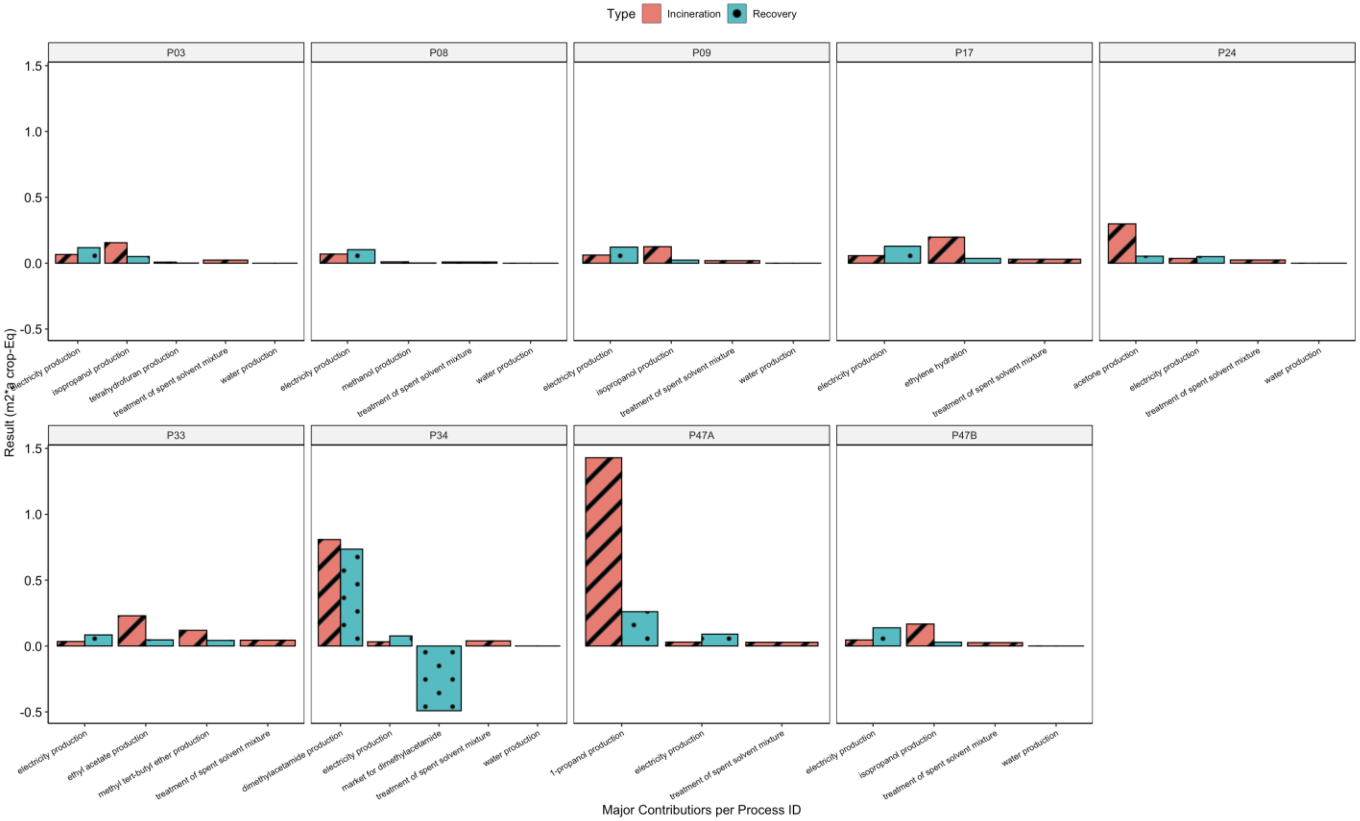

Figure 5-88. Major contributors for each cooling crystallization process for agricultural land occupation (LOP).

5.6.2.13 Surplus Ore Potential (SOP) Contributors for Cooling Processes

Surplus ore potential (SOP) major contributors for cooling processes can be found in Figure 5-89. Solvent production and treatment of spent solvent mixtures had the largest impacts for the incineration option. Electricity production impacts rose from the incineration option to the recovery option due to the additional energy requirement from the implementation of the solvent recovery systems. Treatment of spent solvent mixture impacts were eliminated in the recovery option and solvent production impacts were reduced. Market for dimethylacetamide in P34 had a positive effect on the SOP impacts in the recovery option.

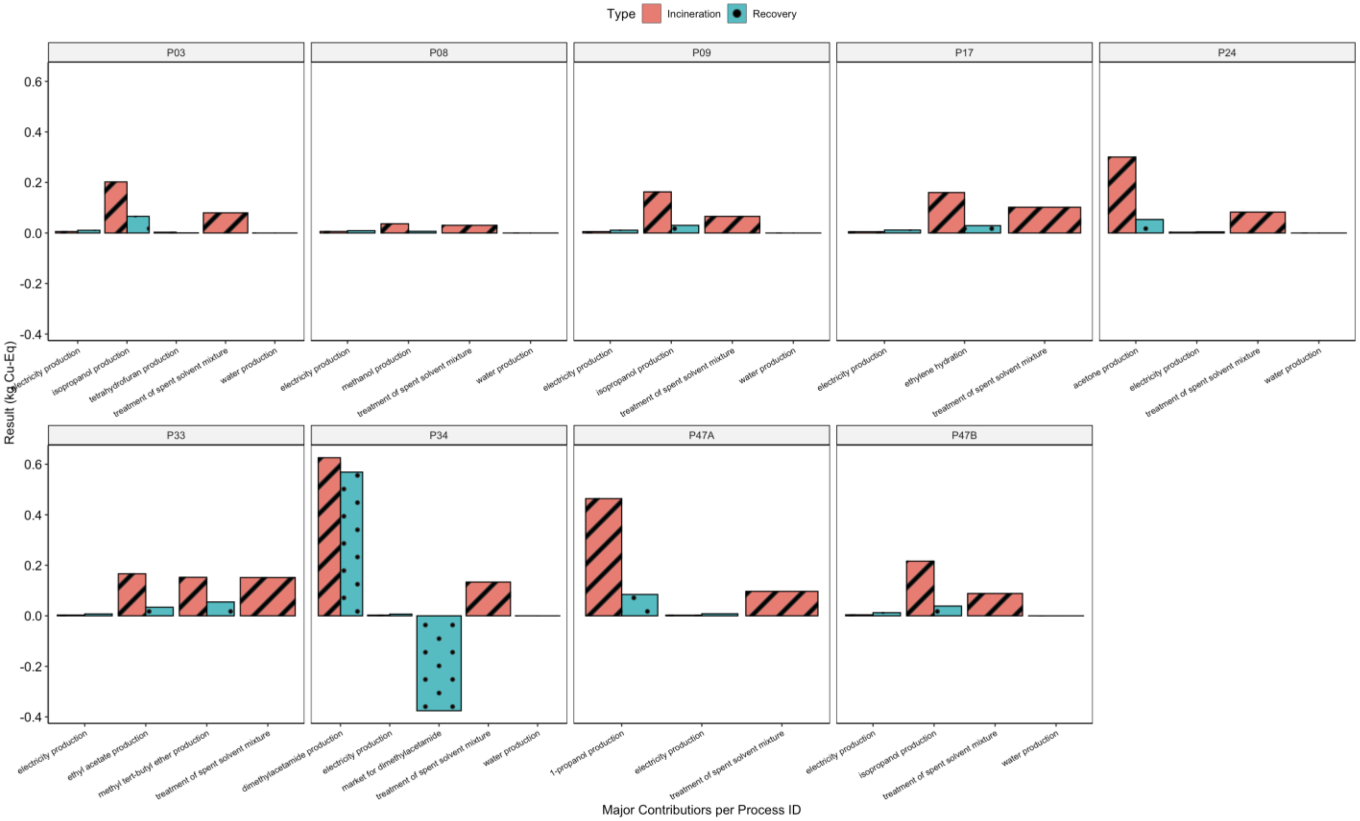

Figure 5-89. Major contributors for each cooling crystallization process for surplus ore potential (SOP).

5.6.2.14 Ozone Depletion Potential (ODP$_{infinite}$) Contributors for Cooling Processes

Ozone depletion potential (ODP$_{\text{infinite}}$) major contributors for cooling processes can be found in Figure 5-90. Treatment of spent solvent mixture and solvent production impacts were the main contributors in the incineration option. Electricity production rose for the recovery option with the implementation of the solvent recovery systems while treatment of spent solvent mixture impacts were eliminated. Solvent production impacts were significantly lower in the recovery option with the reuse of solvents. Market for dimethylacetamide in P34 showed a positive effect on the ODP$_{\text{infinite}}$ impacts.

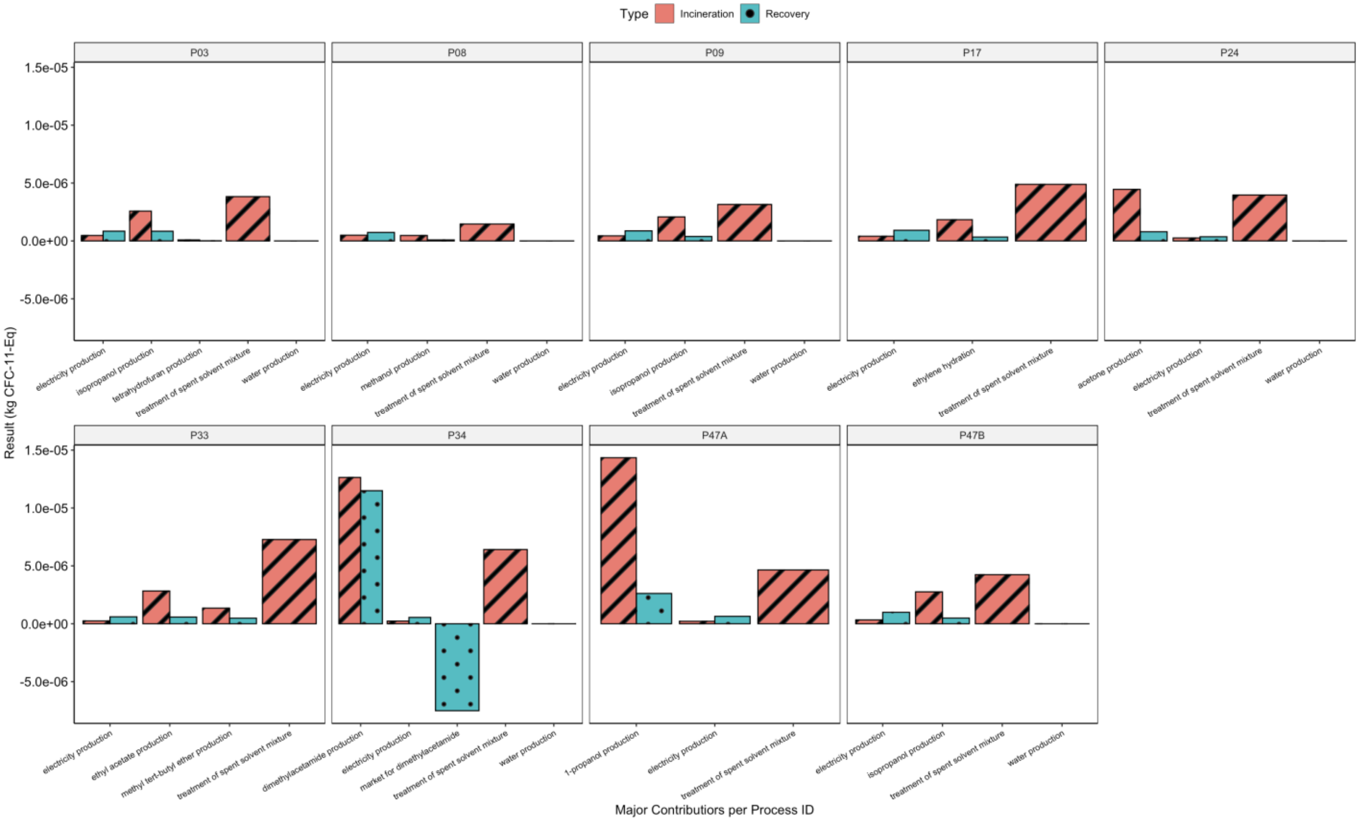

Figure 5-90. Major contributors for each cooling crystallization process for ozone depletion potential (ODP$_{\text{infinite}}$).

5.6.2.15 Particulate Matter Formation Potential (PMFP) Contributors for Cooling Processes

Particulate matter formation potential (PMFP) major contributors for cooling processes can be found in Figure 5-91. For the incineration option, solvent production showed to be the largest impacts. Electricity production and treatment of spent solvent mixture impacts were similar but electricity production impacts increased in the recovery option and treatment of spent solvent mixture impacts were eliminated. Solvent production impacts decreased for the recovery option due to reuse of solvents. Market for dimethylacetamide had a positive impact on PMFP impacts in the recovery option.

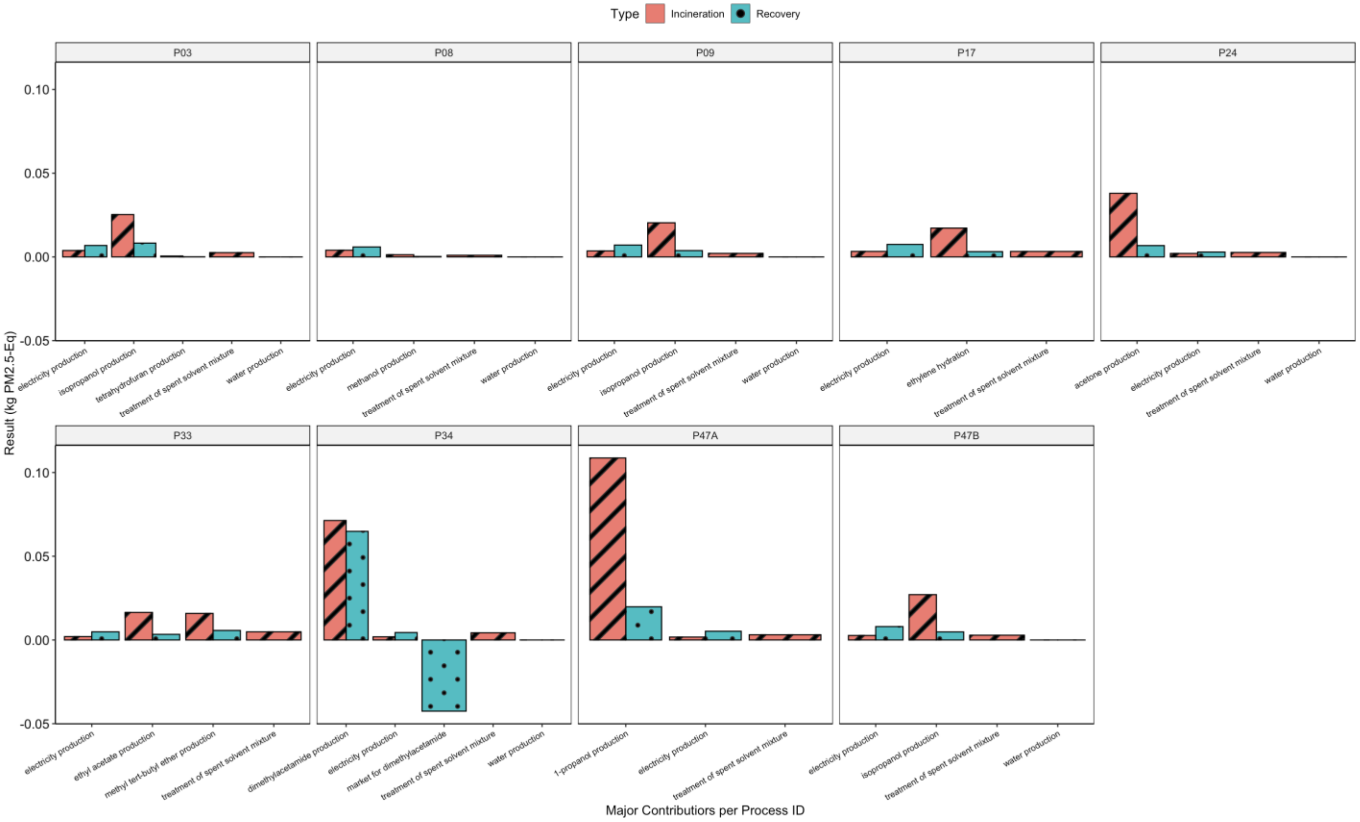

Figure 5-91. Major contributors for each cooling crystallization process for particulate matter formation potential (PMFP).

5.6.2.16 Photochemical Oxidant Formation Potential – Humans (HOFP) Contributors for Cooling Processes

Photochemical oxidant formation potential – humans (HOFP) major contributors for cooling processes can be found in Figure 5-92. For the incineration option, the largest impacts were from the solvent production. Treatment of spent solvent mixture and electricity production impacts were similar. Electricity production rose, solvent production decreased, and treatment of spent solvent mixture impacts were eliminated in the recovery option. A positive effect on the HOFP impacts was noticed for the market of dimethylacetamide in P34.

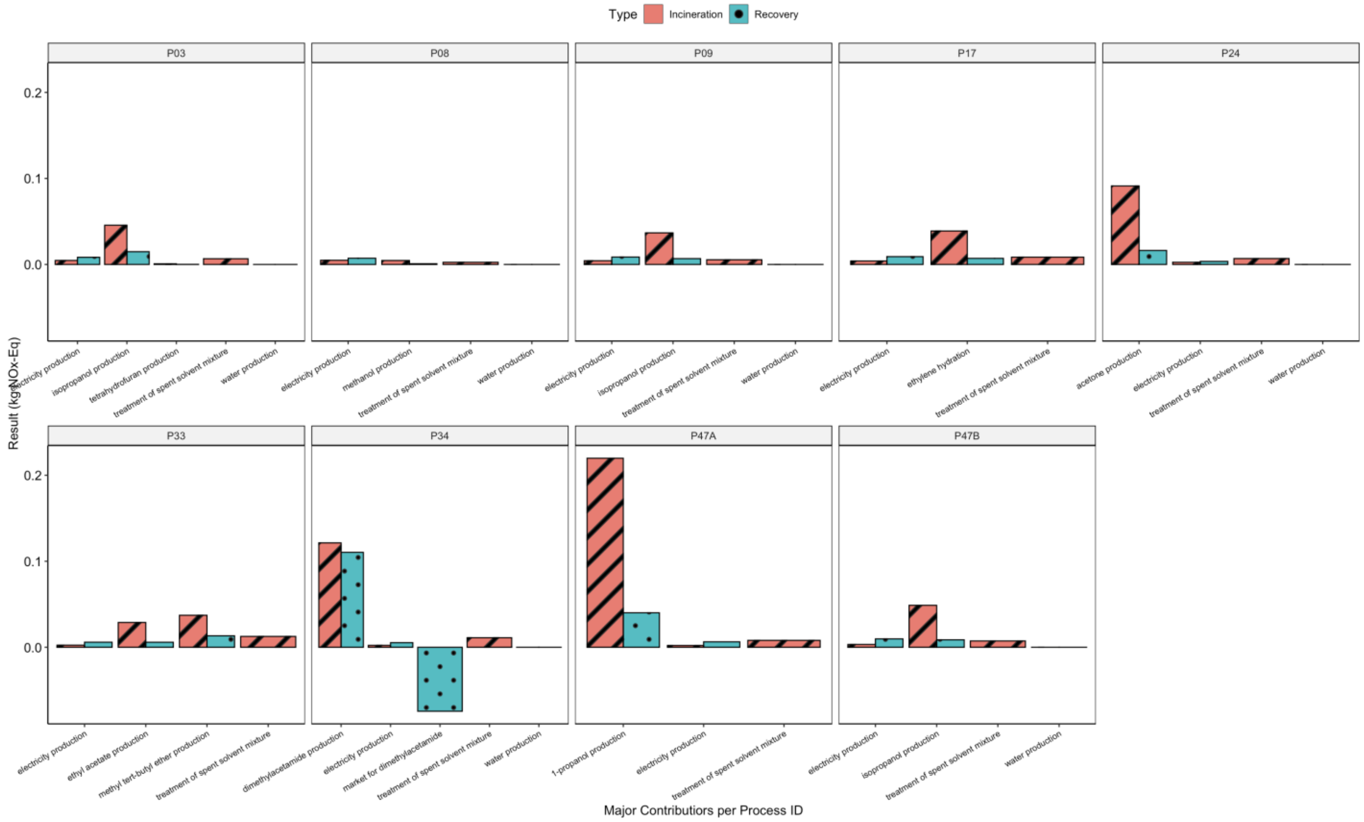

Figure 5-92. Major contributors for each cooling crystallization process for photochemical oxidant formation potential – humans (HOFP).

5.6.2.17 Photochemical Oxidant Formation Potential – Ecosystems (EOFP) Contributors for Cooling Processes

Photochemical oxidant formation potential – ecosystems (EOFP) major contributors for cooling processes can be found in Figure 5-93. Similarly to HOFP, EOFP's major contributor for the incineration option was solvent production. Electricity production and treatment of spent solvent mixture impacts were similar. Solvent production impacts decreased, electricity production impacts increased, and treatment of spent solvent mixture impacts were eliminated in the recovery option.

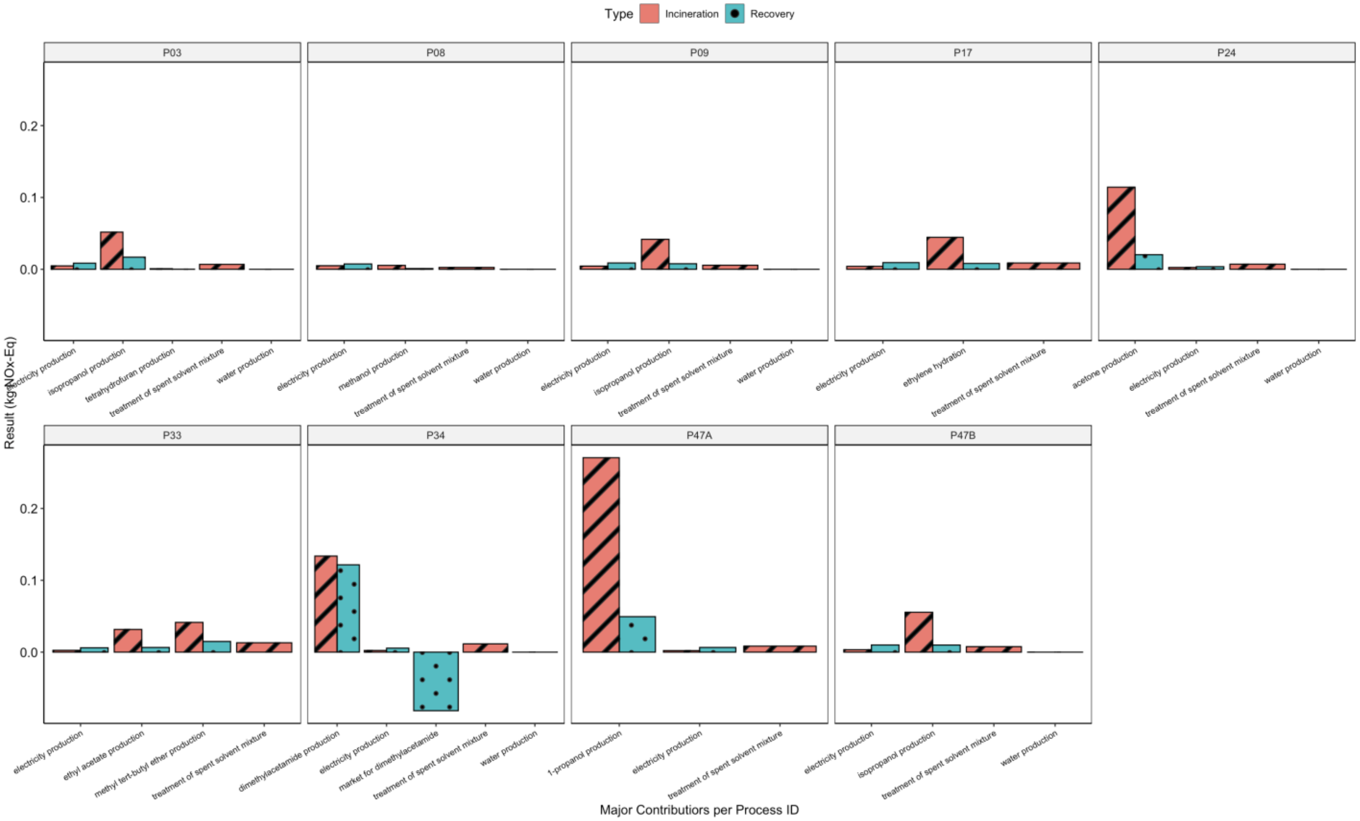

Figure 5-93. Major contributors for each cooling crystallization process for photochemical oxidant formation potential – ecosystems (EOFP).

5.6.2.18 Water Consumption Potential (WCP) Contributors for Cooling Processes

Water consumption potential (WCP) major contributors for cooling processes can be found in Figure 5-94. Largest impacts for the incineration option comes from solvent production. Electricity production impacts increased from the incineration option to the recovery option due to the additional energy requirement required for the solvent recovery systems. Treatment of spent solvent mixture impacts was eliminated in the recovery option and the solvent production impacts reduced. Market for dimethylacetamide showed a positive effect on the WCP impacts for the recovery option.

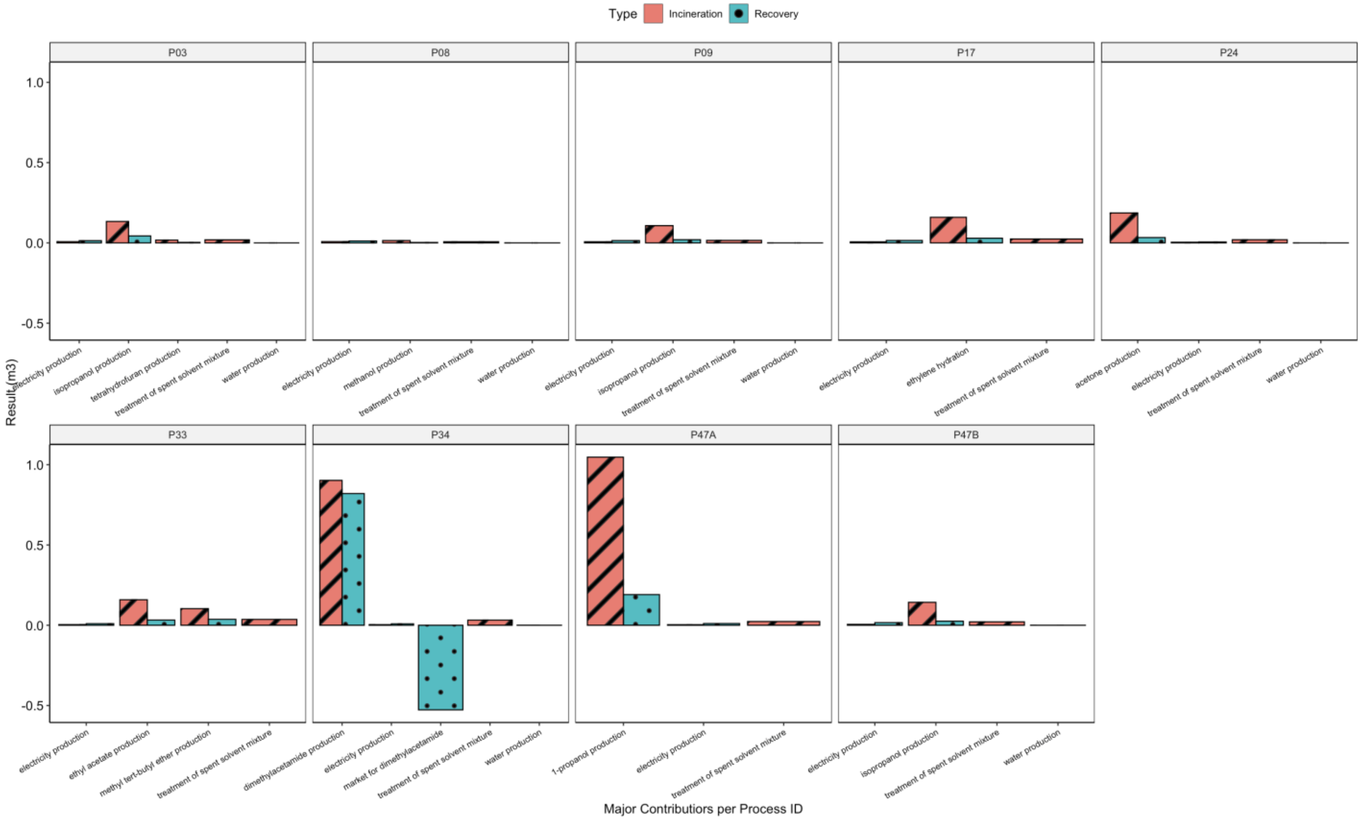

Figure 5-94. Major contributors for each cooling crystallization process for water consumption potential (WCP).

Overall, for cooling processes, the largest contributor for all impact categories was the production of solvent. Treatment of spent solvent mixture and electricity production impacts were similar for most impact categories for the incineration option. Electricity production impacts increased in all impact categories for the recovery option due to the additional energy requirement required from the implementation of the solvent recovery systems. With the reuse of solvent in the recovery option, solvent production impacts significantly decreased across all impact categories. Since solvent was being reused in processes, the treatment of spent solvent mixture impacts could be eliminated in the recovery option. The market for dimethylacetamide had a negative impact result throughout all categories. The market for dimethylacetamide is associated with the transportation of the solvent. This suggests that there is a positive effect on implementing solvent recovery systems for the transportation of dimethylacetamide.

5.6.3 Major Evaporative Crystallization Environmental Impact Contributors

The major contributors for all impact categories for evaporative crystallization processes will be examined below.

5.6.3.1 Terrestrial Acidification Potential (TAP) Contributors for Evaporative Processes

Terrestrial acidification potential (TAP) major contributors can be found in Figure 5-96. For the incineration option, solvent production showed the largest impacts. Electricity production and treatment of spent solvent mixture impacts were similar. For the recovery option, solvent production impacts significantly decreased, electricity production impacts increased, and treatment of spent solvent mixture impacts were eliminated. Tetrahydrofuran production showed a negative impact in P40. This suggest that the implementation of solvent recovery systems and reuse of solvent has a positive effect on tetrahydrofuran production.

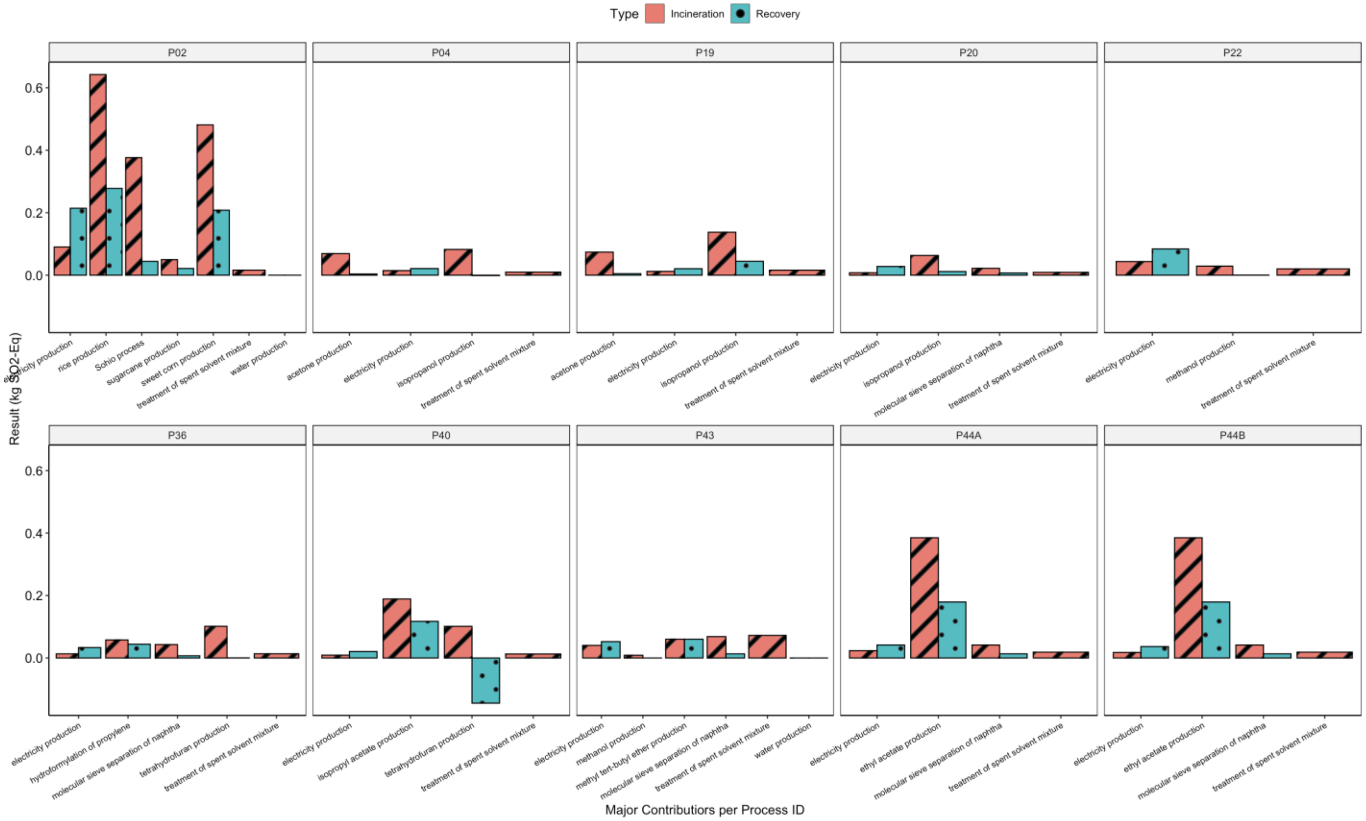

Figure 5-95. Major contributors for each evaporative crystallization process for terrestrial acidification potential (TAP).

5.6.3.2 Global Warming Potential (GWP100) Contributors for Evaporative Processes

Global warming potential (GWP100) major contributors for evaporative processes can be found in Figure 5-96. Solvent production and treatment of spent solvent mixture had the largest impacts for the incineration option. For the recovery option, solvent production impacts were significantly decreased and treatment of spent solvent mixture impacts were eliminated. Electricity production was increased in the recovery option due to the energy requirement of the solvent recovery systems. Tetrahydrofuran production had a positive effect for GWP100 impacts in the recovery option.

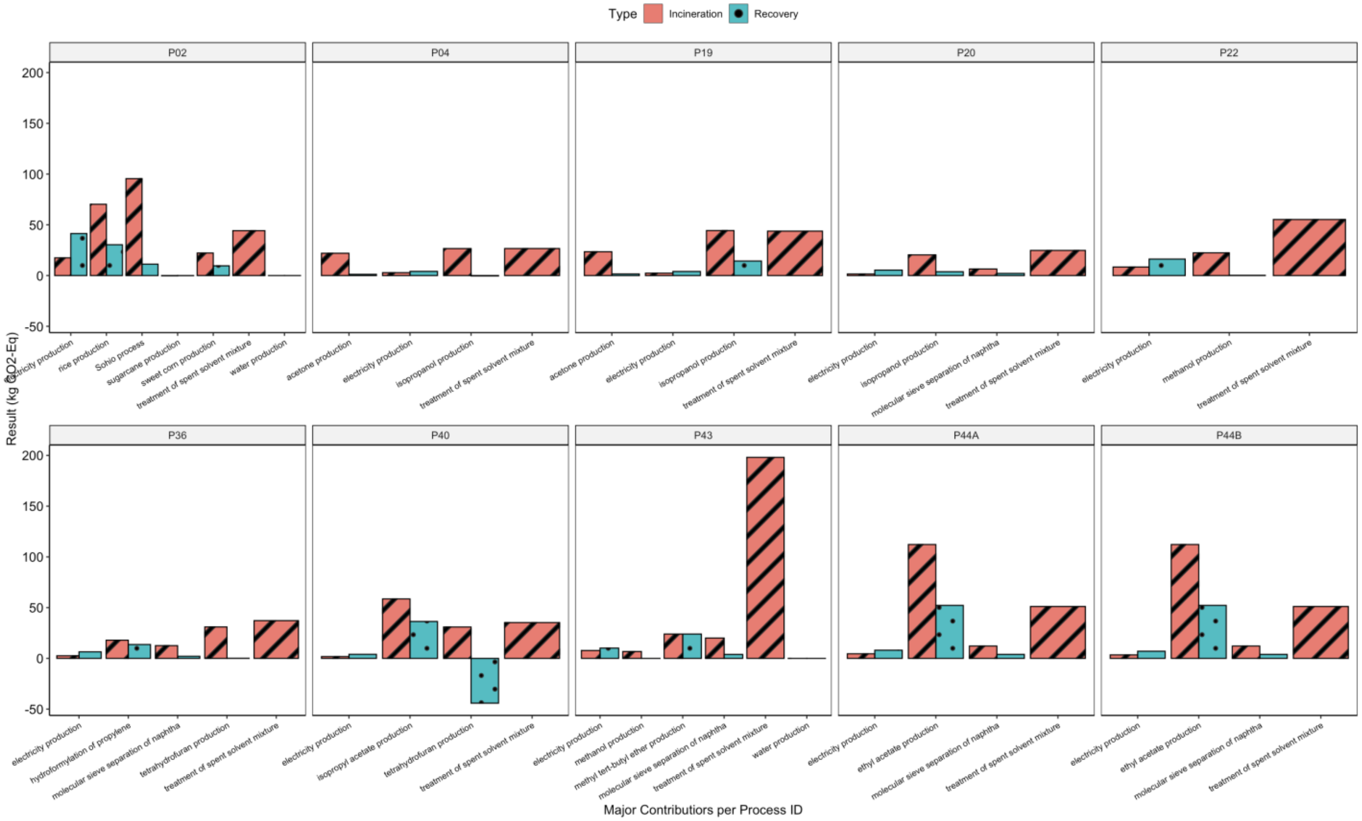

Figure 5-96. Major contributors for each evaporative crystallization process for global warming potential (GWP100).

5.6.3.3 *Freshwater Ecotoxicity Potential (FETP) Contributors for Evaporative Processes*

Freshwater ecotoxicity potential (FETP) major contributors for evaporative processes can be found in Figure 5-97. Solvent production had the largest impact in the incineration option. Electricity production and treatment of spent solvent mixture impacts were similar for the incineration option. Solvent production impacts decreased, electricity production impacts increased, and treatment of spent solvent mixture impacts were eliminated for the recovery option. Tetrahydrofuran production impacts had a positive effect on FETP impacts for P40 in the recovery option.

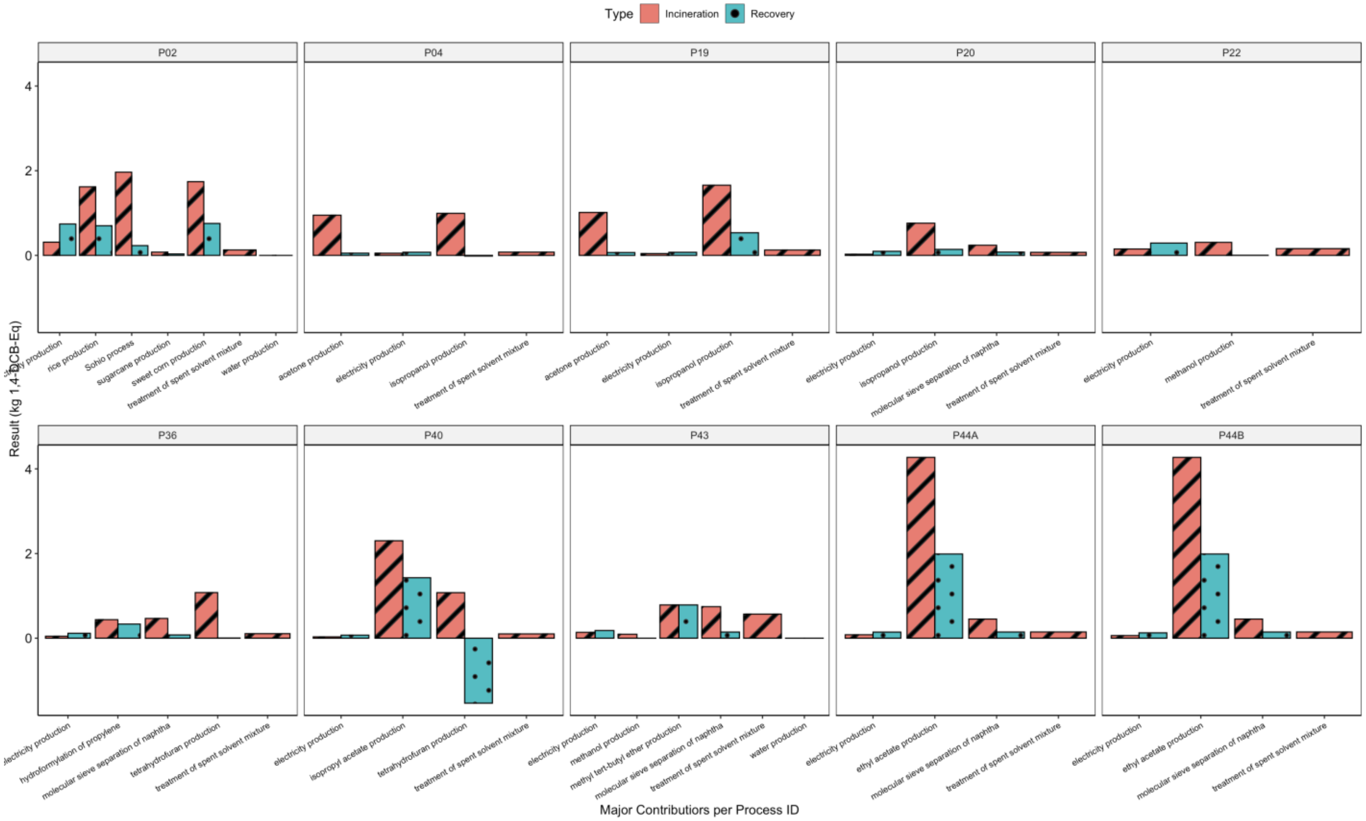

Figure 5-97. Major contributors for each evaporative crystallization process for freshwater ecotoxicity potential (FETP).

5.6.3.4 Marine Ecotoxicity Potential (METP) Contributors for Evaporative Processes

Marine ecotoxicity potential (METP) major contributors for evaporative processes can be found in Figure 5-98. Solvent production impacts were largest in the incineration option and then decreased for the recovery option. Electricity production and treatment of spent solvent mixture impacts were similar for the incineration option, but electricity production impacts increased with the implementation of the solvent recovery systems in the recovery option while the treatment of spent solvent mixture impacts were eliminated. There was a positive effect on METP impacts for P40 with the tetrahydrofuran production in the recovery option.

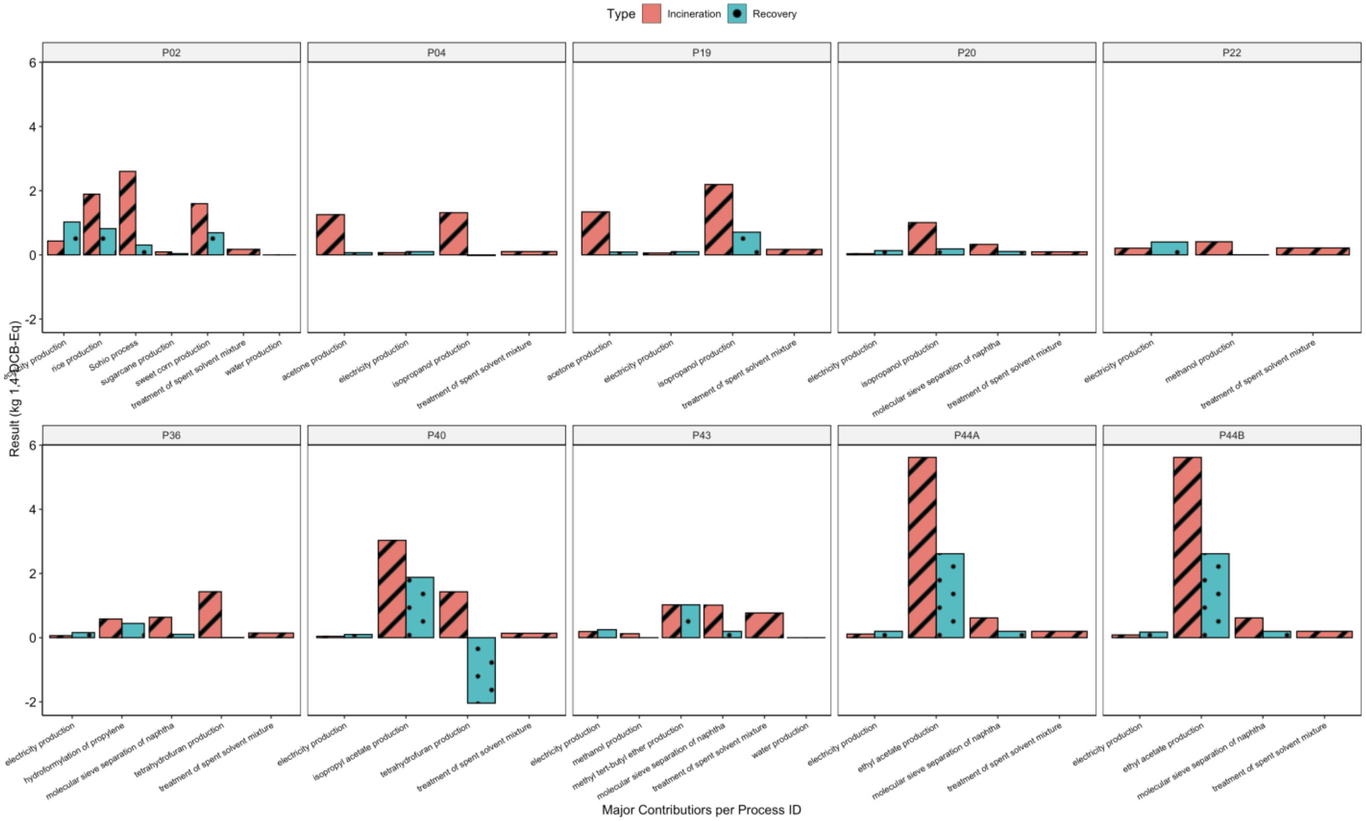

Figure 5-98. Major contributors for each evaporative crystallization process for marine ecotoxicity potential (METP).

5.6.3.5 Terrestrial Ecotoxicity Potential (TETP) Contributors for Evaporative Processes

Terrestrial ecotoxicity potential (TETP) major contributors for evaporative processes can be found in Figure 5-99. For the incineration option, solvent production had the largest impacts. Treatment of spent solvent mixture and electricity production impacts were similar for the incineration option. Electricity production impacts were increased for the recovery option and the treatment of spent solvent mixture impacts were eliminated. Tetrahydrofuran showed a positive effect in P40 for the TETP impacts in the recovery option.

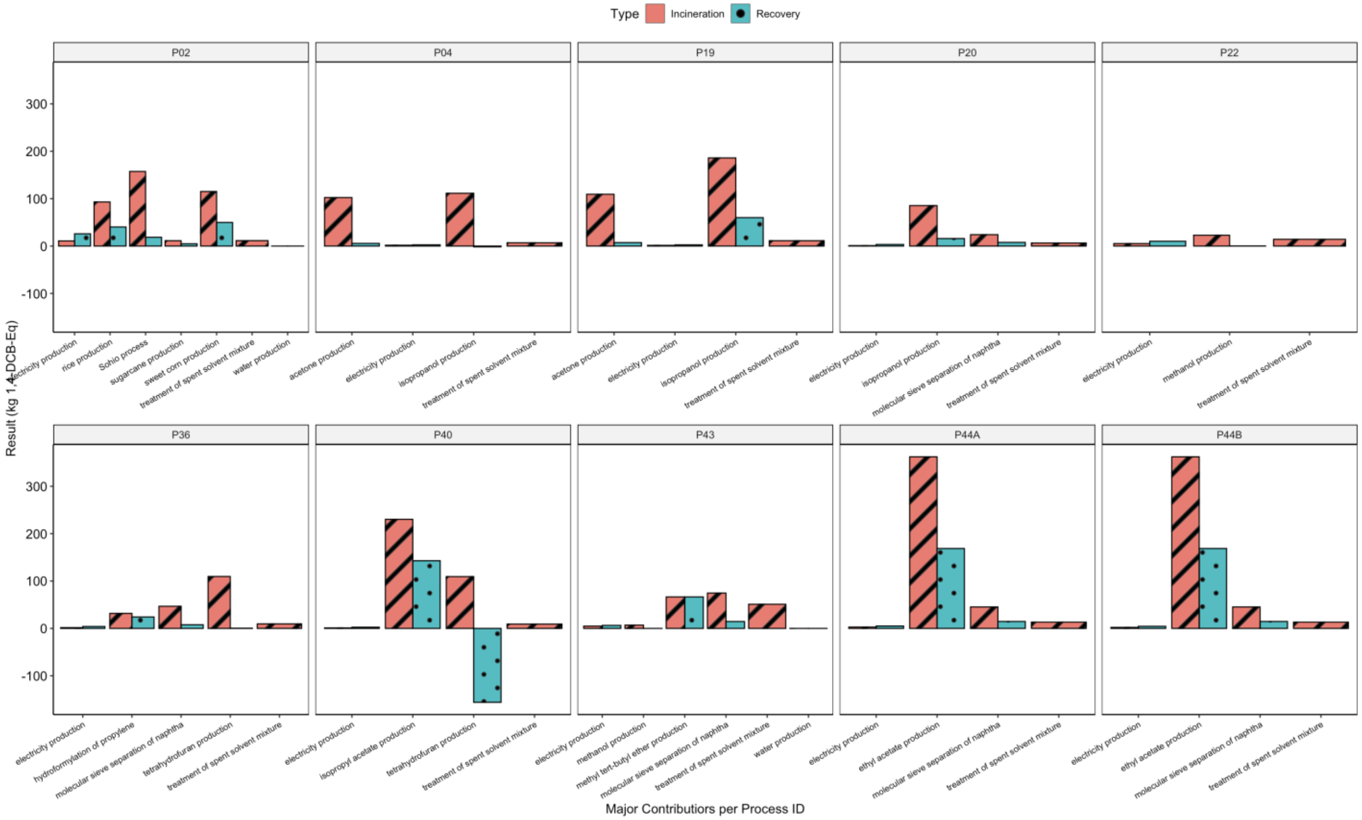

Figure 5-99. Major contributors for each evaporative crystallization process for terrestrial ecotoxicity potential (TETP).

5.6.3.6 Fossil Fuel Potential (FFP) Contributors for Evaporative Processes

Fossil fuel potential (FFP) major contributors for evaporative processes can be found in Figure 5-100. For the incineration option, solvent production showed the largest impacts while treatment of spent solvent mixture and electricity production impacts were smaller and similar. Electricity production impacts increased, solvent production impacts decreased, and treatment of spent solvent mixture impacts were eliminated in the recovery option with the implementation of the solvent recovery systems. Tetrahydrofuran production produced a negative impact result for P40 in the recovery option.

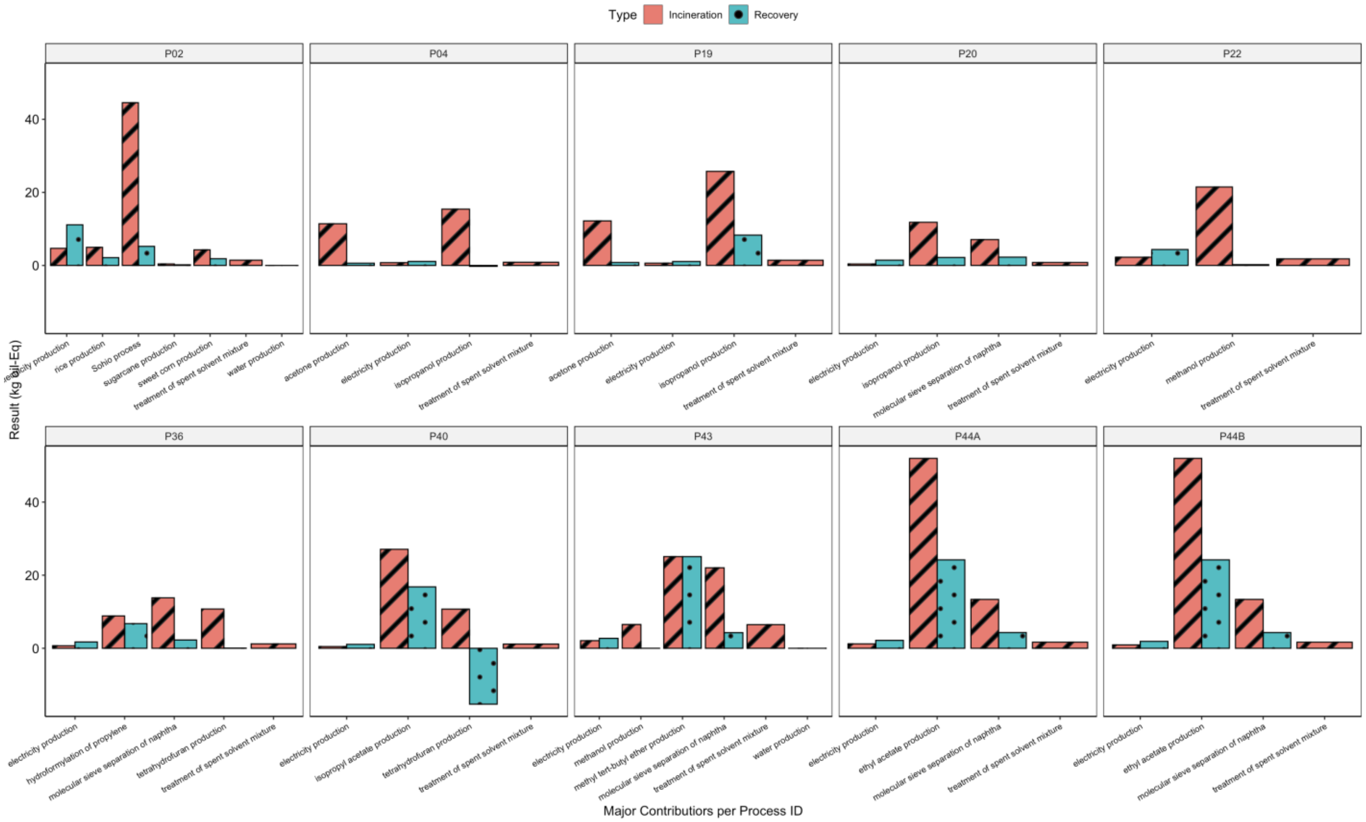

Figure 5-100. Major contributors for each evaporative crystallization process for fossil fuel potential (FFP).

5.6.3.7 Freshwater Eutrophication Potential (FEP) Contributors for Evaporative Processes

Freshwater eutrophication potential (FEP) major contributors for evaporative processes can be found in Figure 5-101. Solvent production had the largest impacts in the incineration option and was then followed by treatment of spent solvent mixture. Electricity production impacts increased from the incineration option to the recovery option with the implementation of the solvent recovery systems. Treatment of spent solvent mixture impact was eliminated in the recovery option and solvent production impacts were significantly decreased. Results also show that tetrahydrofuran production shows a positive effect of FEP impacts for P40 in the recovery option.

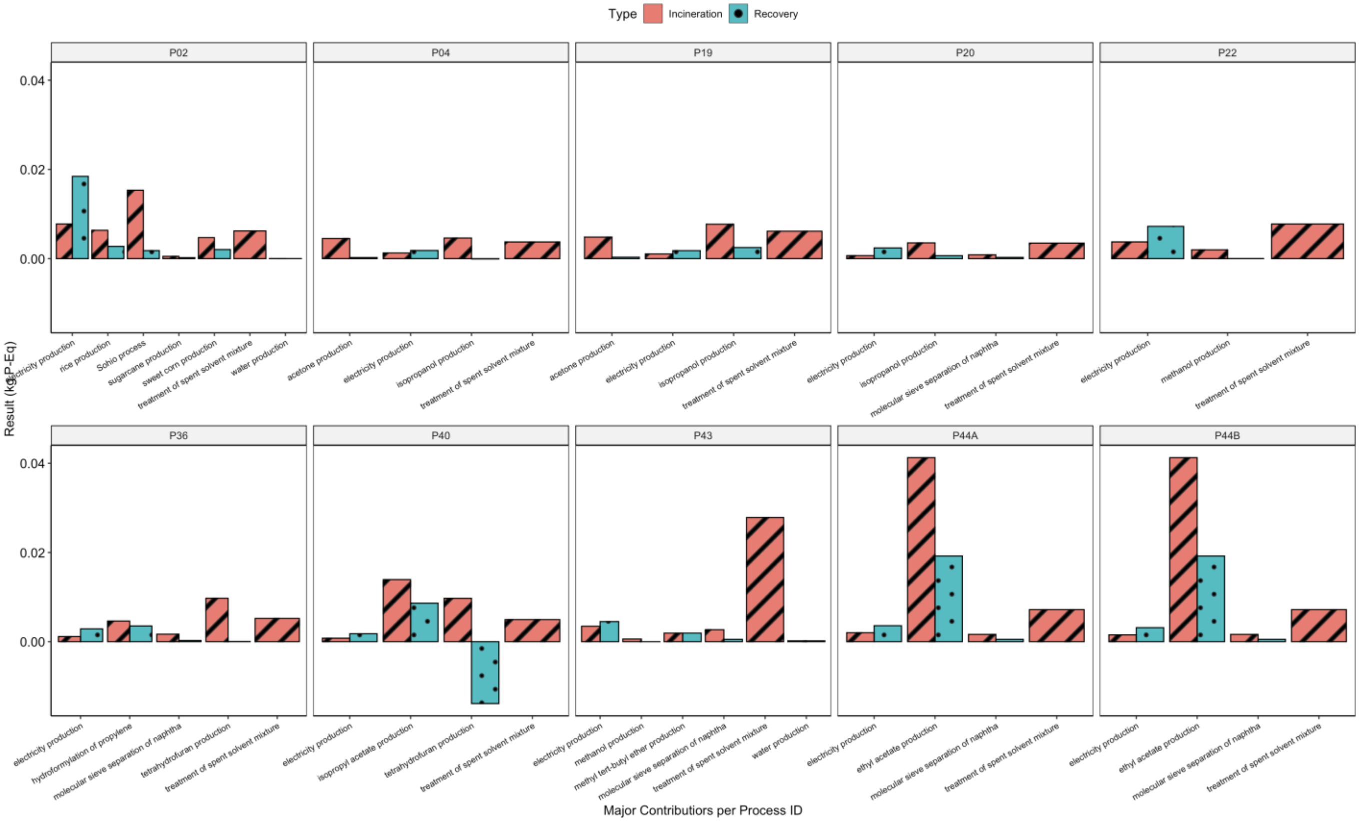

Figure 5-101. Major contributors for each evaporative crystallization process for freshwater eutrophication potential (FEP).

5.6.3.8 Marine Eutrophication Potential (MEP) Contributors for Evaporative Processes

Marine eutrophication potential (MEP) major contributors for evaporative processes can be found in Figure 5-102. Impacts were largest for the solvent production but were most elevated in P02. All other cooling processes had small impacts. Treatment of spent solvent mixture impacts were eliminated in the recovery option.

Figure 5-102. Major contributors for each evaporative crystallization process for marine eutrophication potential (MEP).

5.6.3.9 Human Toxicity Potential – Carcinogenic (HTPc) Contributors for Evaporative Processes

Human toxicity potential – carcinogenic (HTPc) major contributors for evaporative processes can be found in Figure 5-103. For the incineration option, solvent production had the largest impacts, then followed by treatment of spent solvent mixture impacts. Electricity production impacts were larger for the incineration option than for the recovery option because of the implementation of the solvent recovery systems. Solvent production impacts were reduced in the recovery option and the treatment of spent solvent production impacts were eliminated. In P40, tetrahydrofuran production showed a positive effect on HTPc impacts for the recovery option.

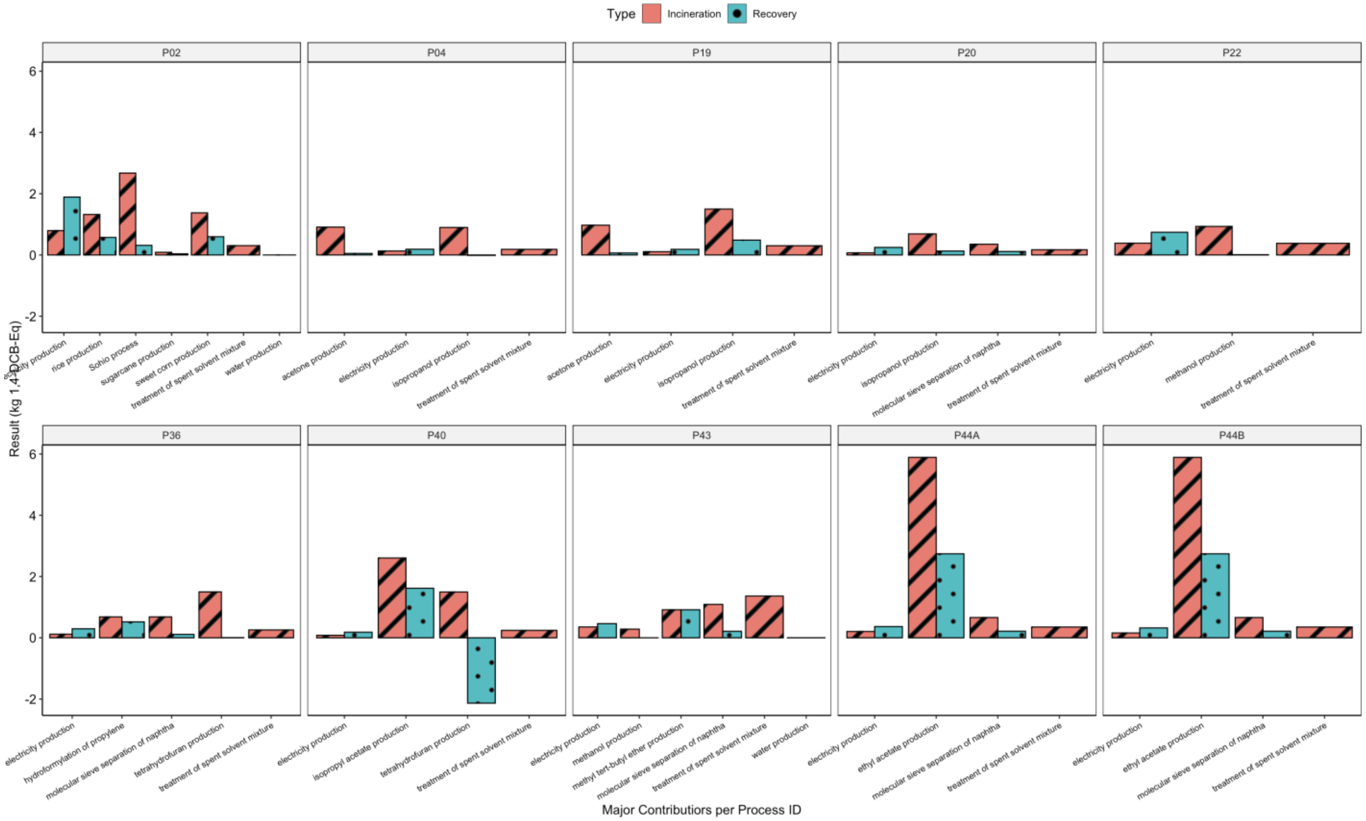

Figure 5-103. Major contributors for each evaporative crystallization process for human toxicity potential – carcinogenic (HTPc).

5.6.3.10 Human Toxicity Potential – Non-Carcinogenic (HTPnc) Contributors for Evaporative Processes

Human toxicity potential – non-carcinogenic (HTPnc) major contributors for evaporative processes can be found in Figure 5-104. Solvent production impacts were largest in the incineration option and significantly reduced in the recovery option. Treatment of spent solvent mixture impacts and electricity production were similar for the incineration option but electricity production impacts increased in the recovery option while treatment of spent solvent mixture impacts were eliminated. Rice production had a positive effect on HTPnc impacts for both the incineration and recovery options. Further, tetrahydrofuran production also had a positive effect on HTPnc impacts in the recovery option.

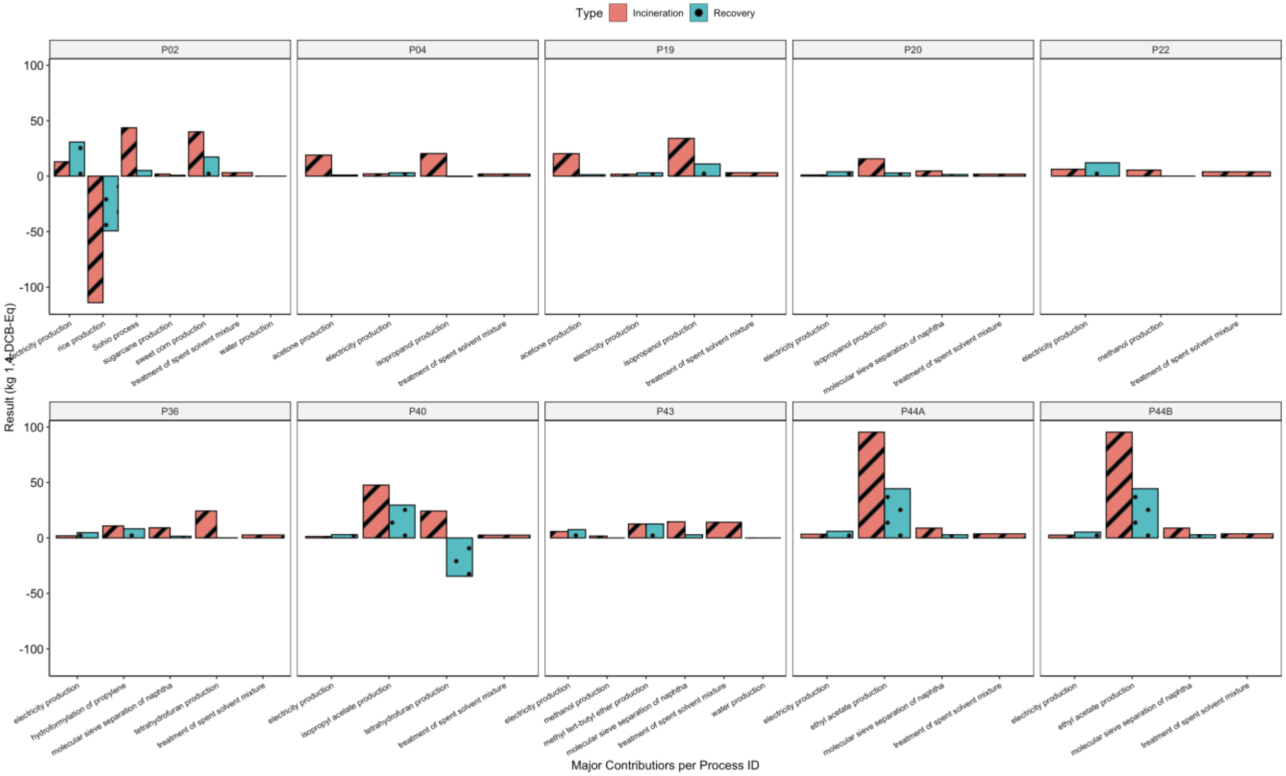

Figure 5-104. Major contributors for each evaporative crystallization process for human toxicity potential – non-carcinogenic (HTPnc).

5.6.3.11 Ionising Radiation Potential (IRP) Contributors for Evaporative Processes

Ionising radiation potential (IRP) major contributors for evaporative processes can be found in Figure 5-105. For the incineration option, the solvent production impacts were the largest contributors. They were significantly decreased in the recovery option. Treatment of spent solvent mixture impacts were the next largest impact in the incineration option, but were eliminated in the recovery option. Electricity production increased in the recovery option due to the implementation of the solvent recovery systems. In P40, tetrahydrofuran had a positive effect on the IRP impact in the recovery option.

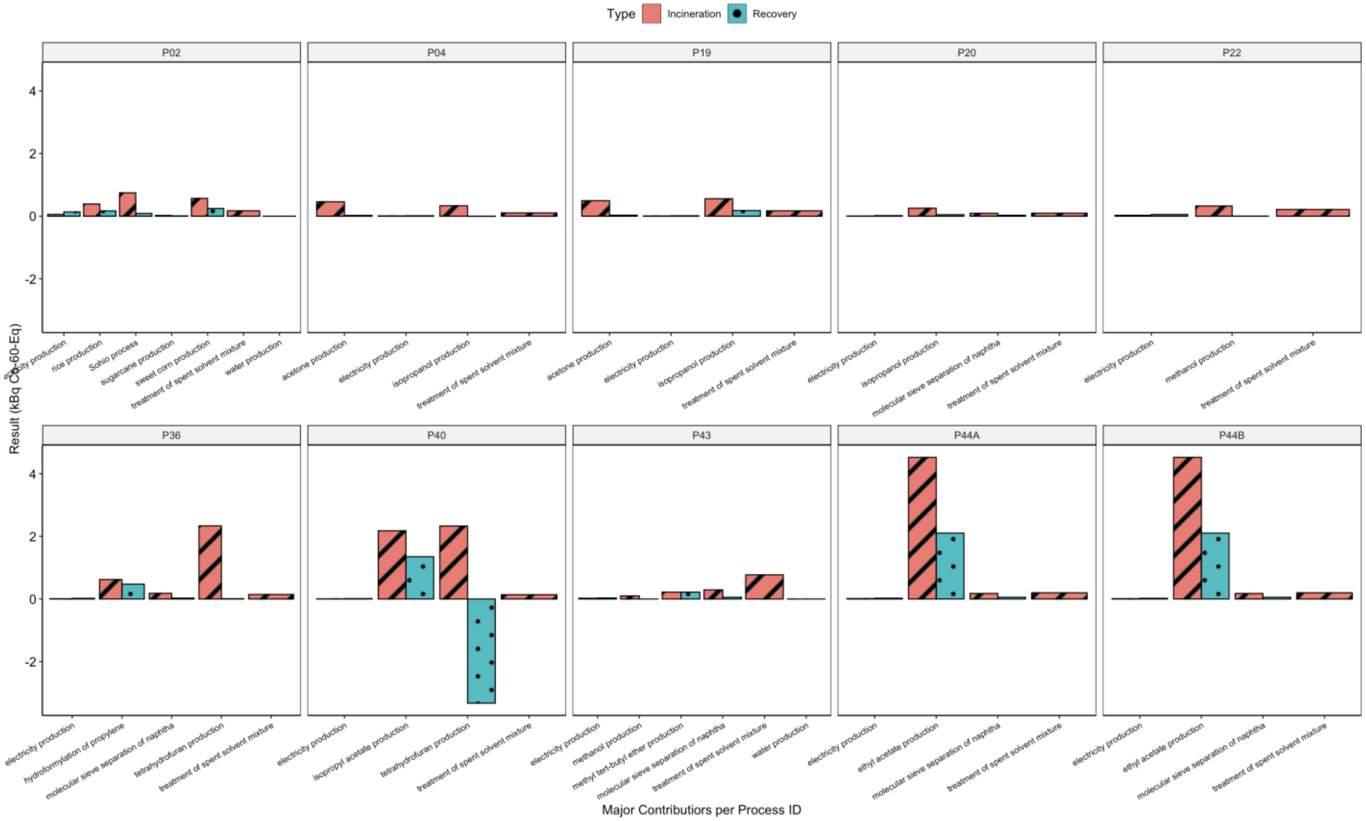

Figure 5-105. Major contributors for each evaporative crystallization process for ionising radiation potential (IRP).

5.6.3.12 Agricultural Land Occupation (LOP) Contributors for Evaporative Processes

Agricultural land occupation (LOP) major impacts for evaporative processes can be found in Figure 5-106. Impacts were largest for the production of sugarcane, rice, and corn due to the large land area required for these crops. These impacts were reduced for the recovery option due to the reuse of 2-MeTHF. All other contributors showed small impacts for both incineration and recovery options.

Figure 5-106. Major contributors for each evaporative crystallization process for agricultural land occupation (LOP)

5.6.3.13 Surplus Ore Potential (SOP) Contributors for Evaporative Processes

Surplus ore potential (SOP) major contributors for evaporative processes can be found in Figure 5-107. The major contributors in the incineration option were solvent production and treatment of spent solvent mixtures. Solvent production impacts were significantly reduced for the recovery option and treatment of spent solvent mixture impacts were eliminated. Electricity production was increased from the incineration option to the recovery option with the added energy requirement from solvent recovery systems. In P40, tetrahydrofuran production showed a positive effect on SOP impacts in the recovery option.

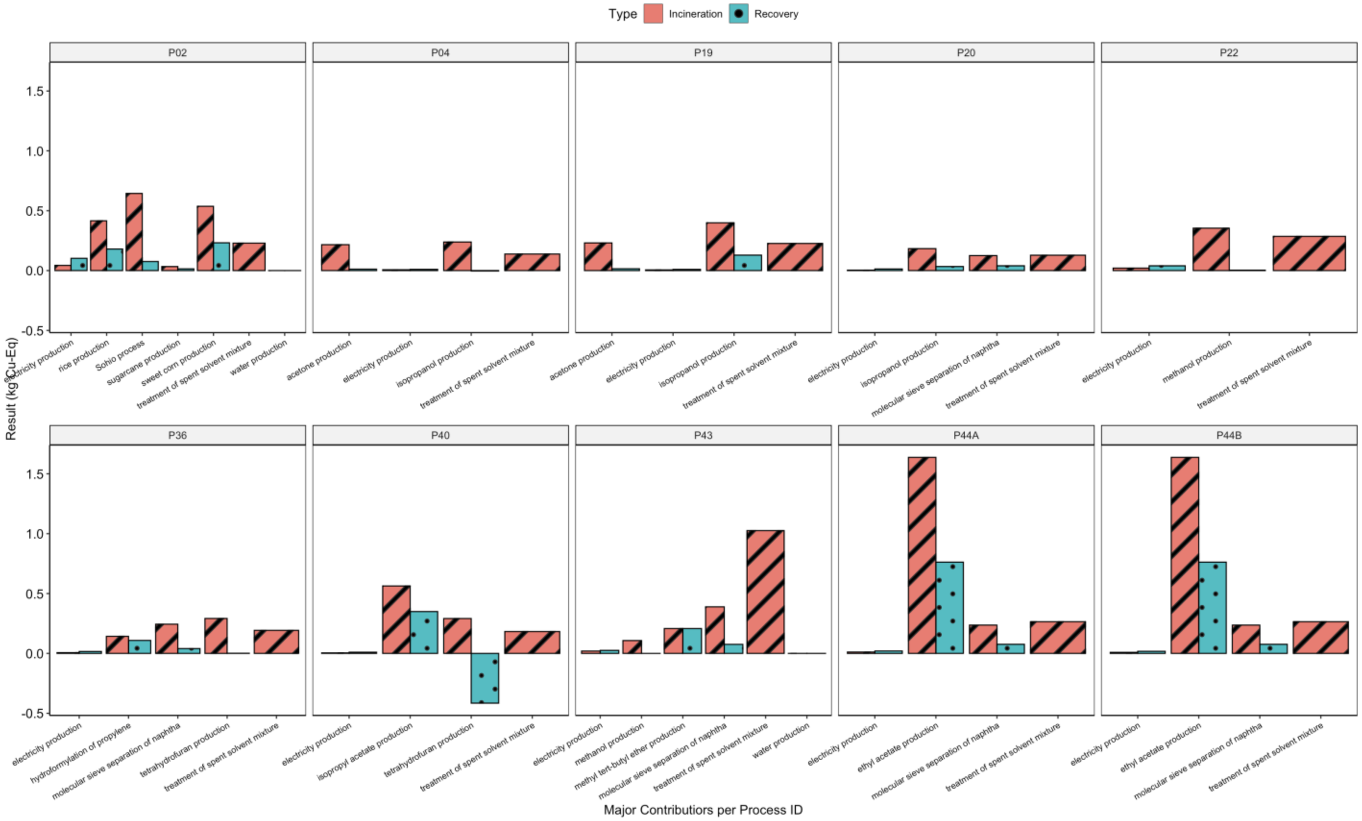

Figure 5-107. Major contributors for each evaporative crystallization process for surplus ore potential (SOP).

5.6.3.14 Ozone Depletion Potential ($ODP_{infinite}$) Contributors for Evaporative Processes

Ozone depletion potential ($ODP_{infinite}$) major contributors for evaporative processes can be found in Figure 5-108. The major contributors were solvent production related. Specifically, agricultural crop production (rice, corn, and sugarcane) had the largest results. Solvent production impacts were reduced in the recovery option but electricity production impacts were increased. Treatment of spent solvent mixture impacts were eliminated in the recovery option.

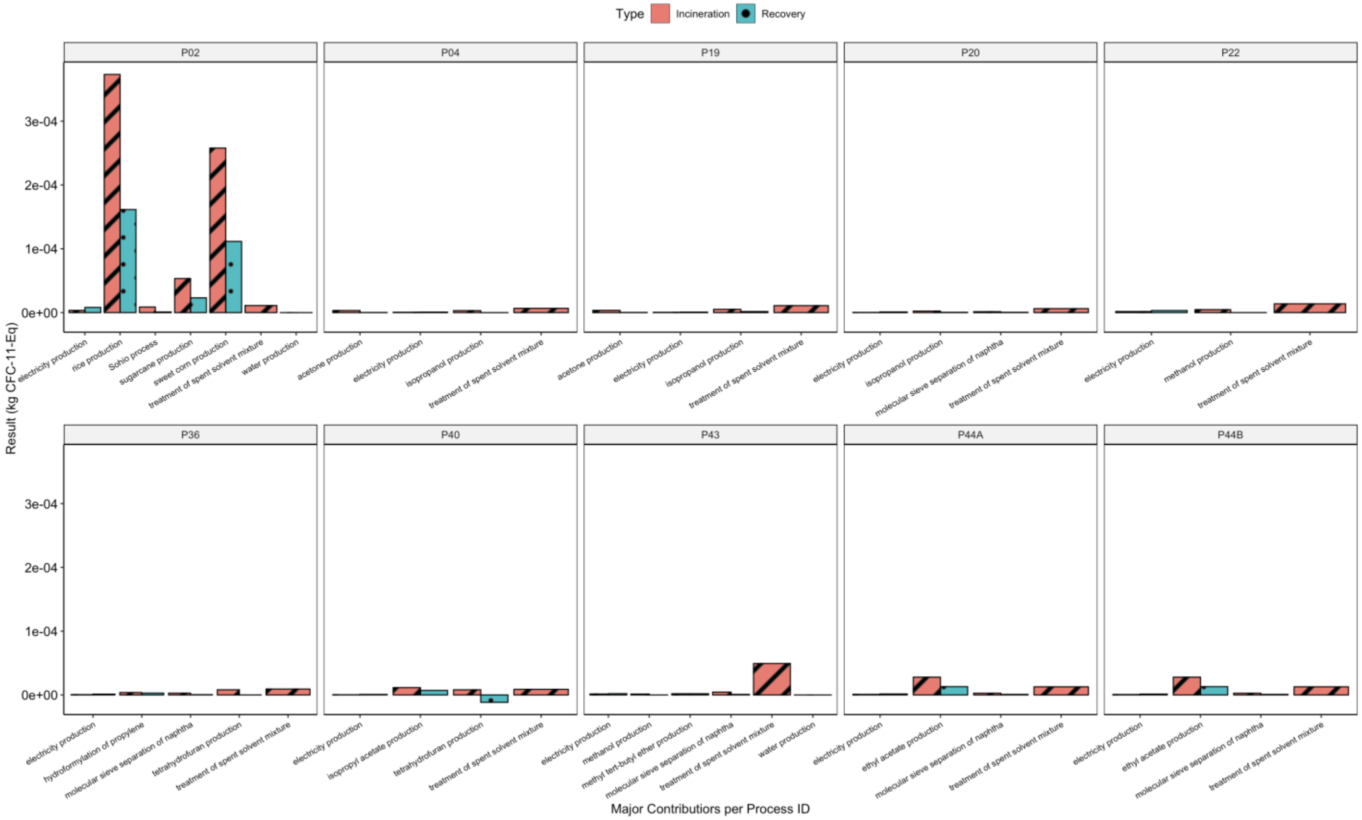

Figure 5-108. Major contributors for each evaporative crystallization process for ozone depletion potential ($ODP_{infinite}$).

5.6.3.15 Particulate Matter Formation Potential (PMFP) Contributors for Evaporative Processes

Particulate matter formation potential (PMFP) major contributors for evaporative processes can be found in Figure 5-109. For the incineration option, solvent production had the largest impacts. Electricity production and treatment of spent solvent mixture impacts were similar for the incineration option. Electricity production impacts increased with the recovery option and treatment of spent solvent mixture impacts were eliminated. Tetrahydrofuran production showed a positive effect on the PMFP impacts for the recovery option.

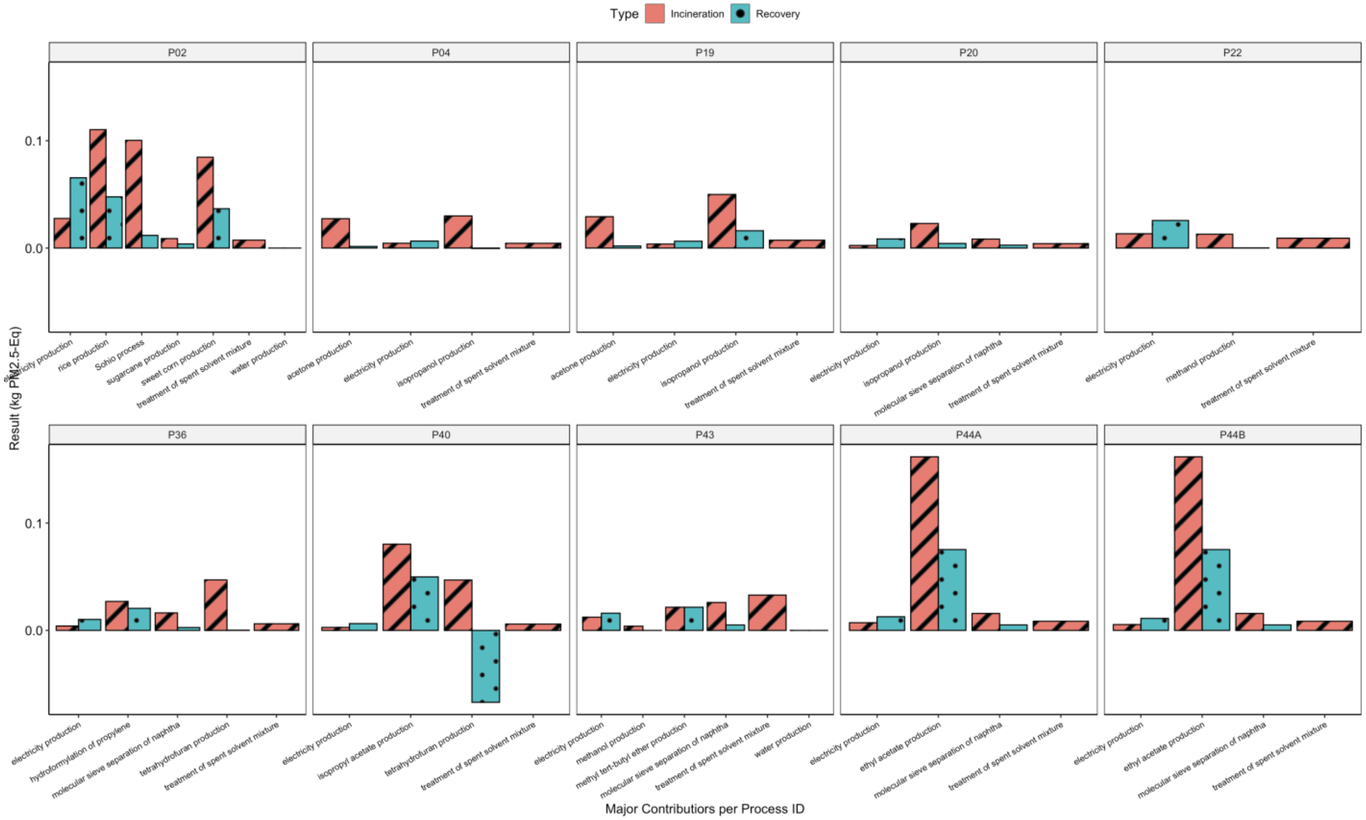

Figure 5-109. Major contributors for each evaporative crystallization process for particulate matter formation potential (PMFP).

5.6.3.16 Photochemical Oxidant Formation Potential – Humans (HOFP) Contributors for Evaporative Processes

Photochemical oxidant formation potential – humans (HOFP) major contributors for evaporative processes can be found in Figure 5-110. Impacts were largest for solvent production in the incineration option. However, there was a significant decrease of solvent production in the recovery option. Electricity production and treatment of spent solvent mixture impacts were similar in the incineration option, and electricity production impacts increased in the recovery option and the treatment of spent solvent mixture impacts was eliminated. Tetrahydrofuran production had a positive effect on the HOFP impacts for the recovery option in P40.

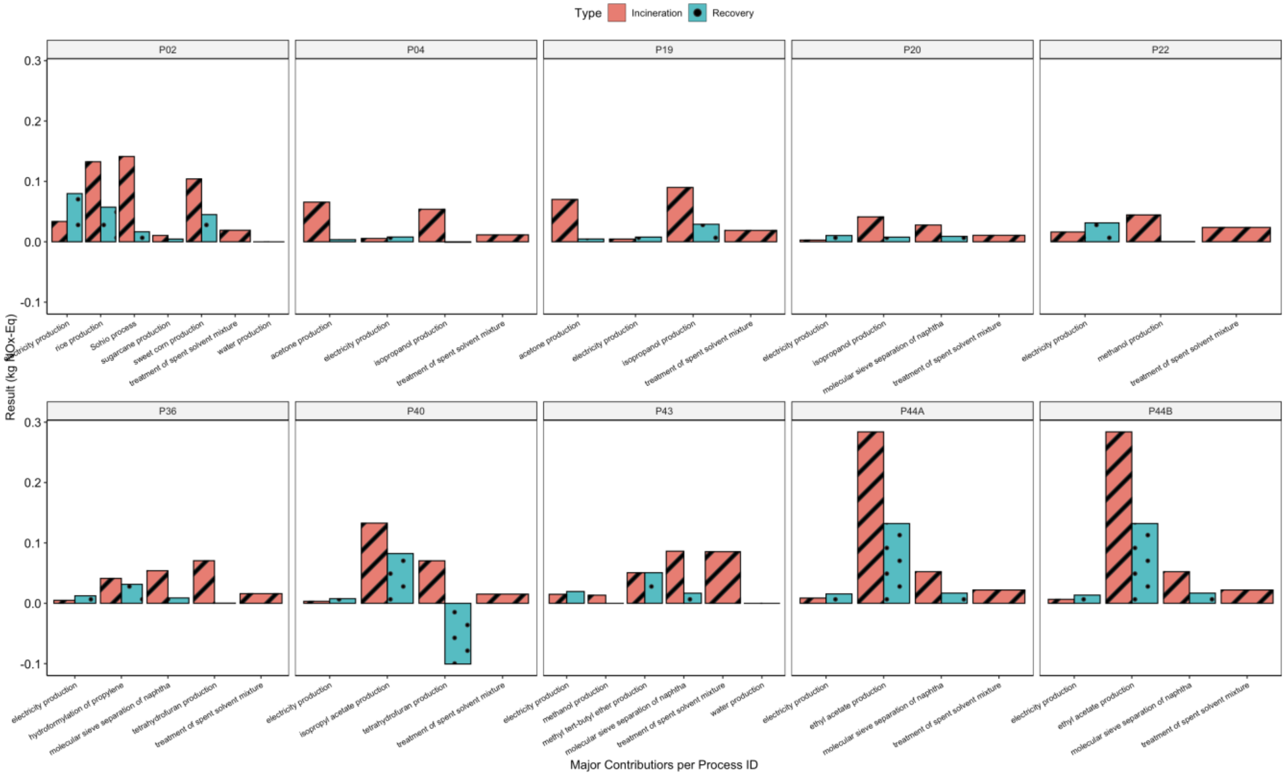

Figure 5-110. Major contributors for each evaporative crystallization process for photochemical oxidant formation potential – humans (HOFP).

5.6.3.17 Photochemical Oxidant Formation Potential – Ecosystems (EOFP) Contributors for Evaporative Processes

Photochemical oxidant formation potential – ecosystems (EOFP) major contributors for evaporative processes can be found in Figure 5-111. Results were like those of HOFP. Electricity production increased with the recovery option and solvent production showed the largest impacts in the incineration option but was significantly reduced in the recovery option. For P40, tetrahydrofuran production had a positive effect on EOFP impacts for the recovery option.

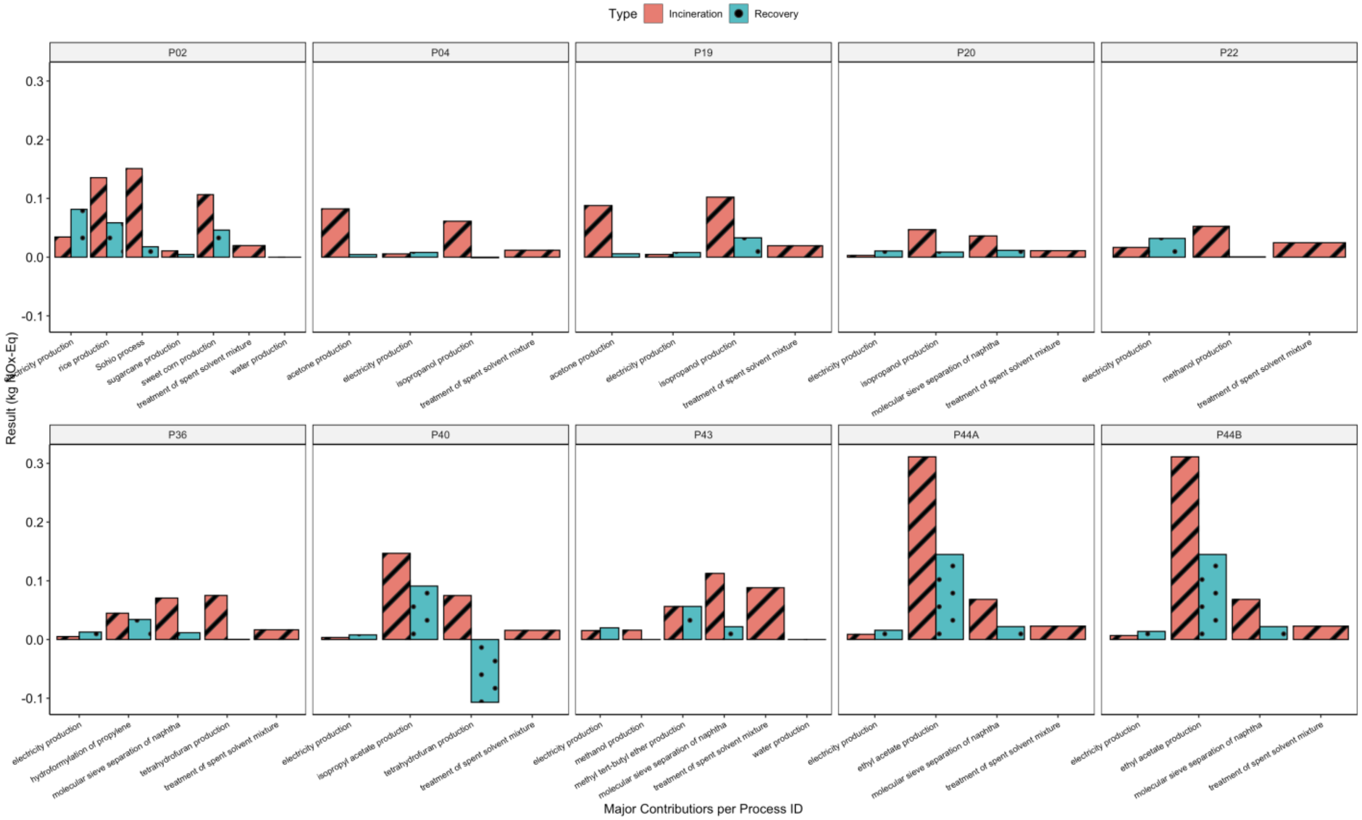

Figure 5-111. Major contributors for each evaporative crystallization process for photochemical oxidant formation potential – ecosystems (EOFP).

5.6.3.18 Water Consumption Potential (WCP) Contributors for Evaporative Processes

Water consumption potential (WCP) major contributors for evaporative processes can be found in Figure 5-112. Water consumption's largest contributor came from the production of 2-MeTHF due to the large agricultural crop requirement for its production. Overall, solvent production still showed the largest impacts for the incineration process and was decreased during the recovery option. Electricity production increased with the recovery option. Tetrahydrofuran production had a positive effect on WCP impacts for the recovery option.

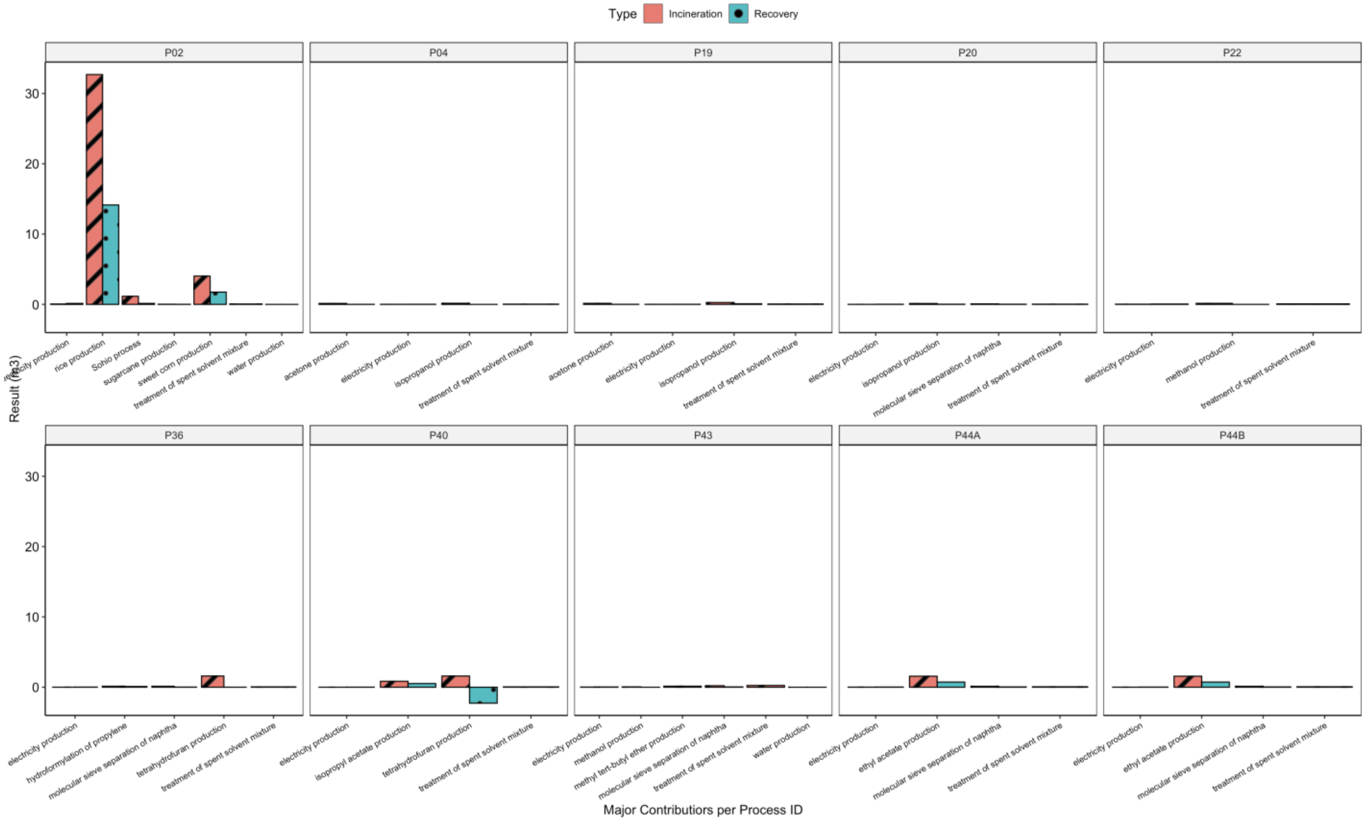

Figure 5-112. Major contributors for each evaporative crystallization process for water consumption potential (WCP).

Overall, for the evaporative processes, the major contributors were the solvent production and then usually followed by treatment of spent solvent mixtures for the incineration option. Electricity production impacts increased from the incineration option to the recovery option due to the additional energy requirement from the implementation of the solvent recovery options. Agricultural crops produced elevated impacts in several categories and led to 2-MeTHF having elevated impacts. Tetrahydrofuran production, in P40, had a positive effect on all impact categories for the recovery option.

5.6.4 Major Reactive Crystallization Environmental Impact Contributors

The major contributors for reactive crystallization processes are discussed below. Processes P21 and P32 had much greater results than the other reactive processes and were included in separate figures.

5.6.4.1 Terrestrial Acidification Potential (TAP) Contributors for Reactive Processes

Terrestrial acidification potential (TAP) major contributors for reactive processes can be found in Figure 5-113 and Figure 5-114 (P21 & P32). Solvent production showed the largest impacts in the incineration option, which were significantly reduced in the recovery option. Electricity production and treatment of spent solvent mixtures showed similar impacts for the incineration option. Electricity production increased in the recovery option while the treatment of spent solvent mixture impacts were eliminated. For the recovery option, ethyl acetate in P22 showed a positive effect on the TAP impact.

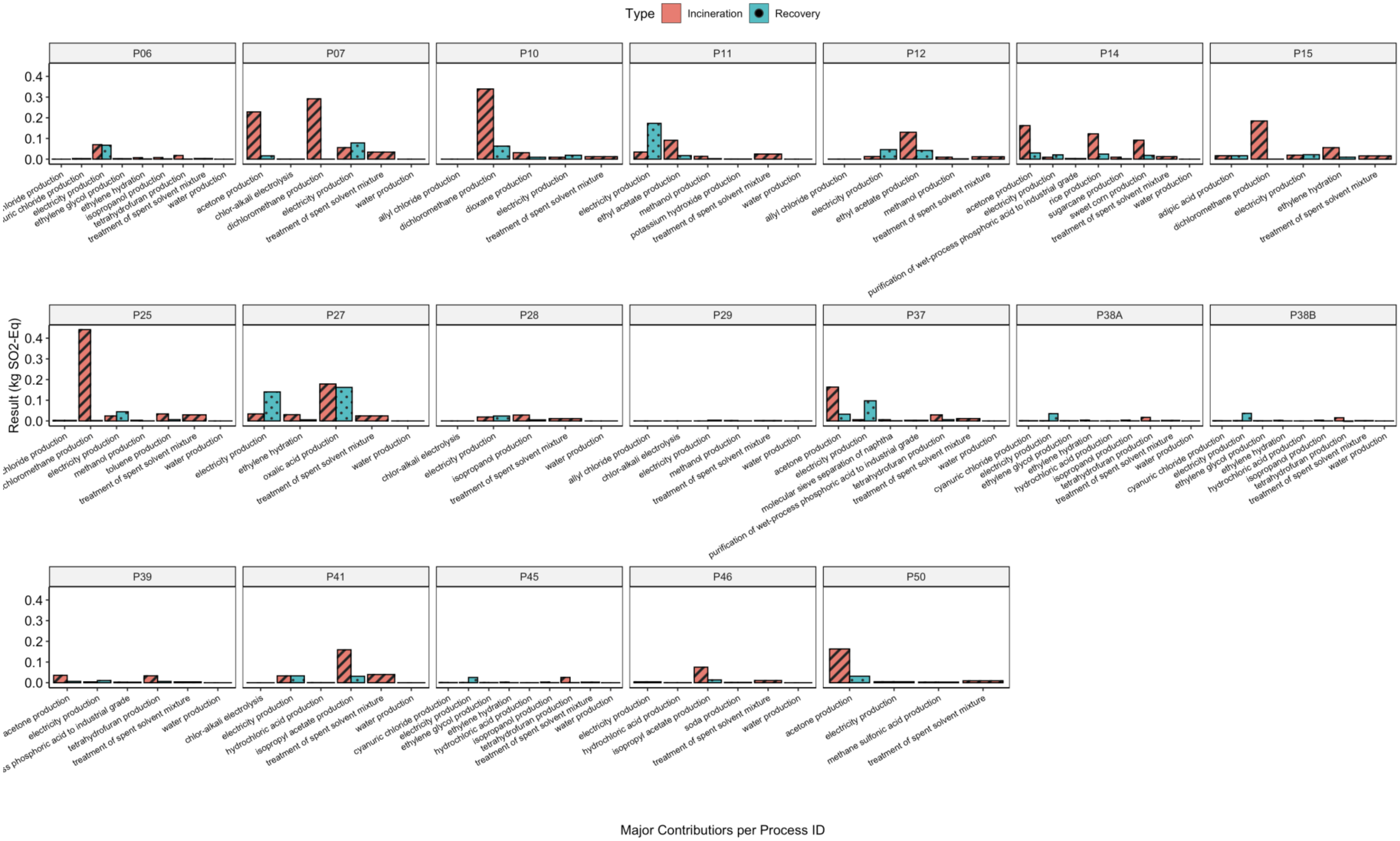

Figure 5-113. Major contributors for each reactive crystallization process for terrestrial acidification potential (TAP).

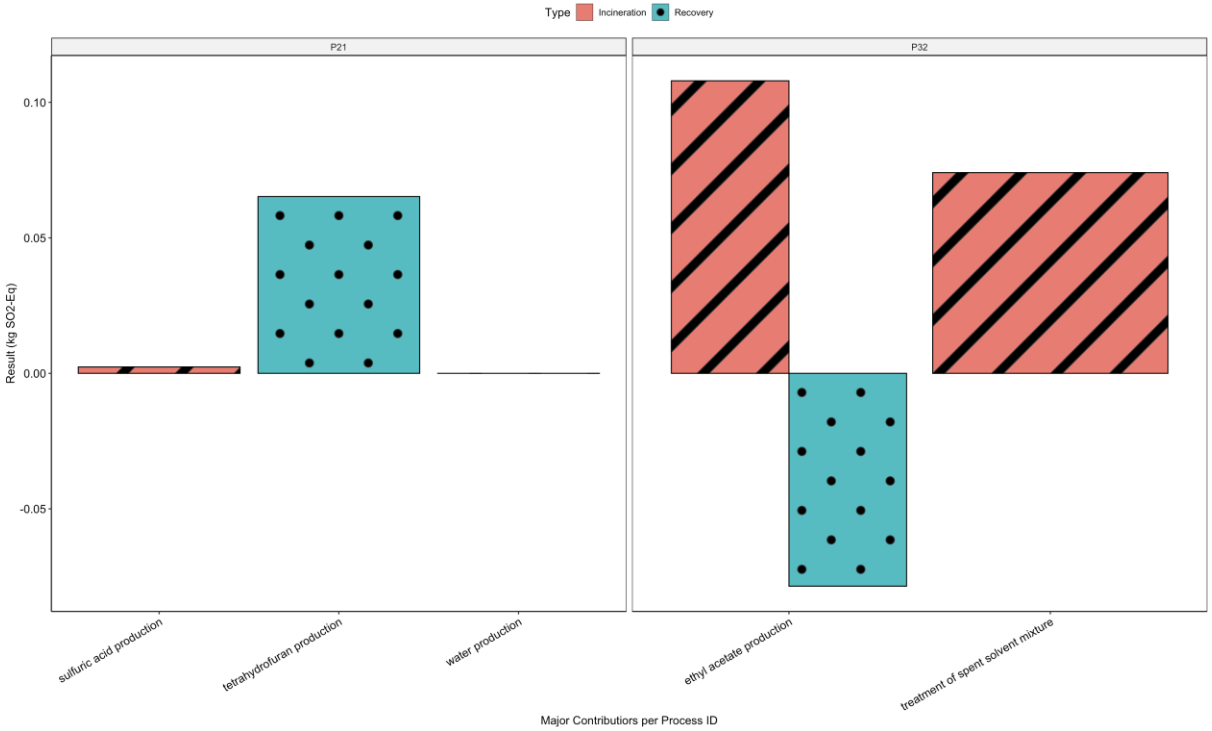

Figure 5-114. Major contributors for Processes 21 and 32 for terrestrial acidification potential (TAP).

5.6.4.2 Global Warming Potential (GWP100) Contributors for Reactive Processes

Global warming potential (GWP100) major contributors for reactive processes can be found in Figure 5-115 and Figure 5-116 (P21 & P32). Treatment of spent solvent mixture impacts and solvent production had the largest impacts in the incineration option. Electricity showed a much more minimal impact in the incineration option. Electricity did increase in the recovery option with the implementation of the solvent recovery systems. Treatment of spent solvent mixture impacts were eliminated in the recovery option while the solvent production impacts were significantly reduced.

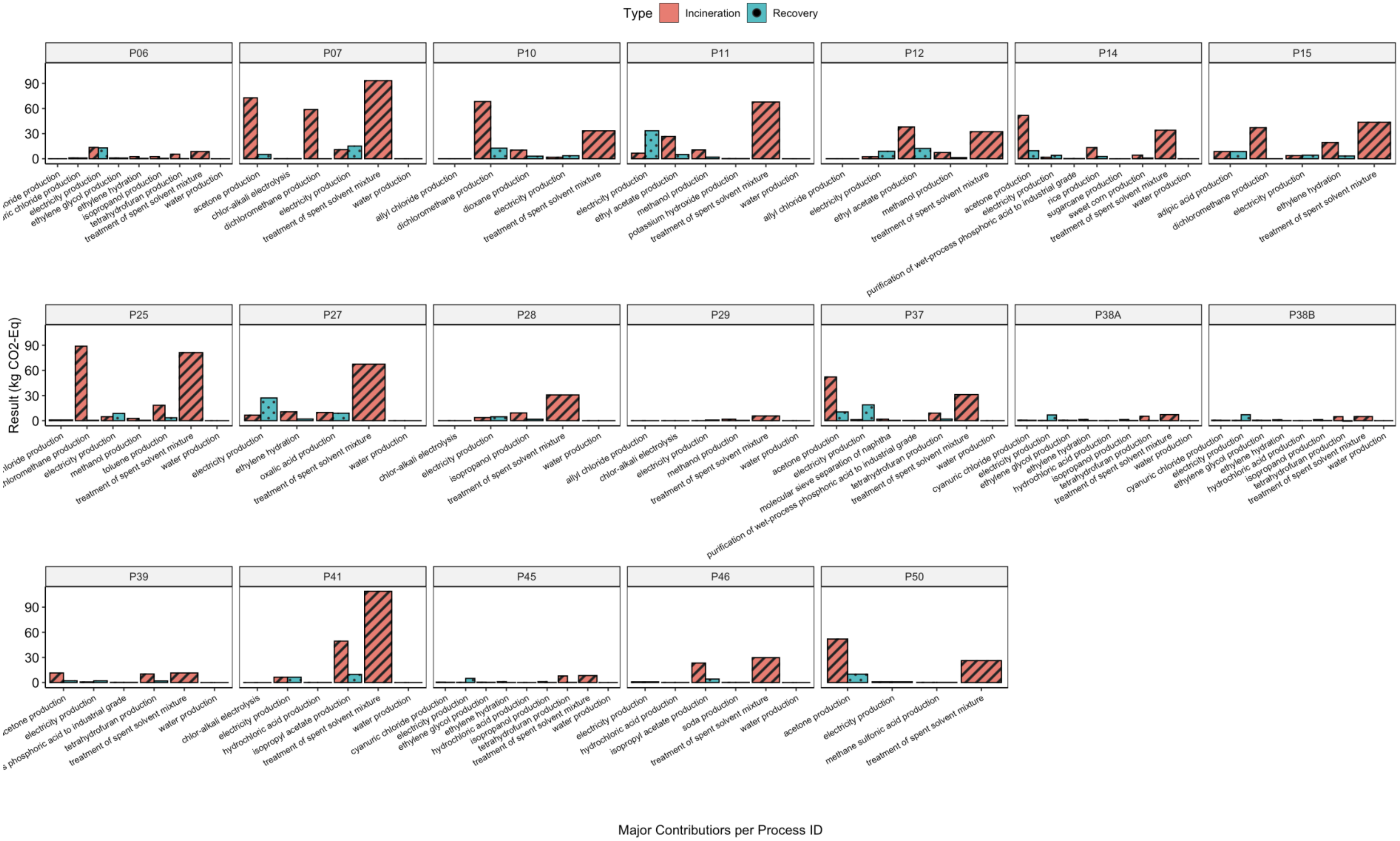

Figure 5-115. Major contributors for each reactive crystallization process for global warming potential (GWP100).

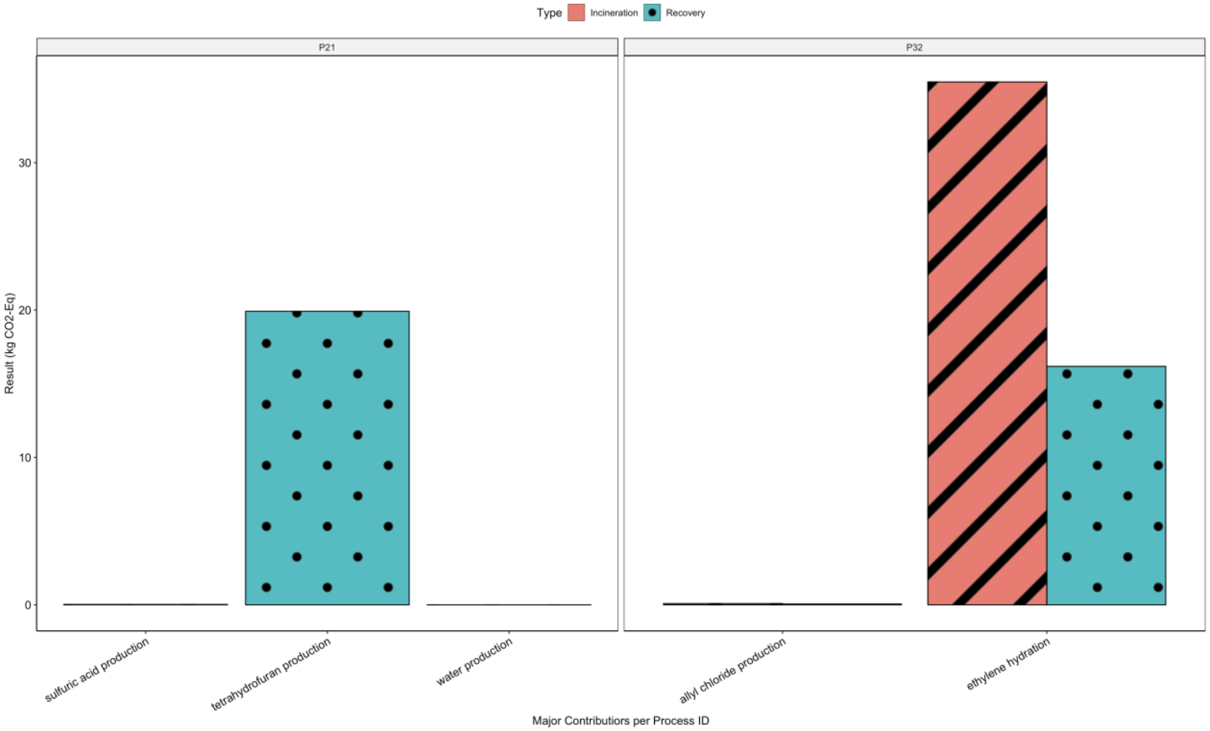

Figure 5-116. Major contributors for Processes 21 and 32 for global warming potential (GWP100).

5.6.4.3 Freshwater Ecotoxicity Potential (FETP) Contributors for Reactive Processes

Freshwater ecotoxicity potential (FETP) major contributors for reactive processes can be found in Figure 5-117 and Figure 5-118 (for P21 and P32). For the incineration option, solvent production impacts were largest. Treatment of spent solvent mixtures and electricity production impacts showed similar results in the incineration option but electricity production impacts increased in the recovery option and treatment of spent solvent mixture impacts were eliminated. Solvent production impacts were significantly decreased in the recovery option.

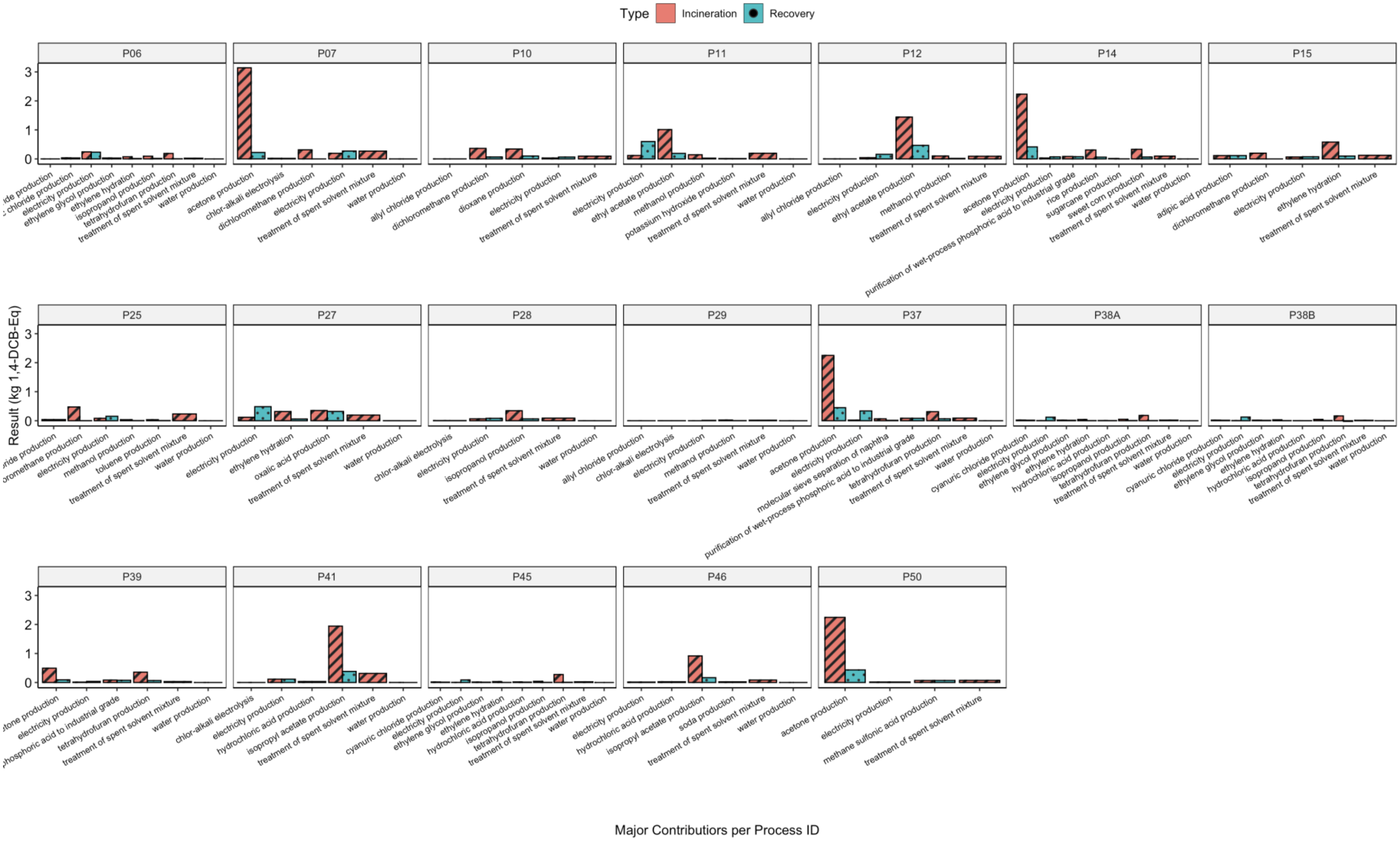

Figure 5-117. Major contributors for each reactive crystallization process for freshwater ecotoxicity potential (FETP).

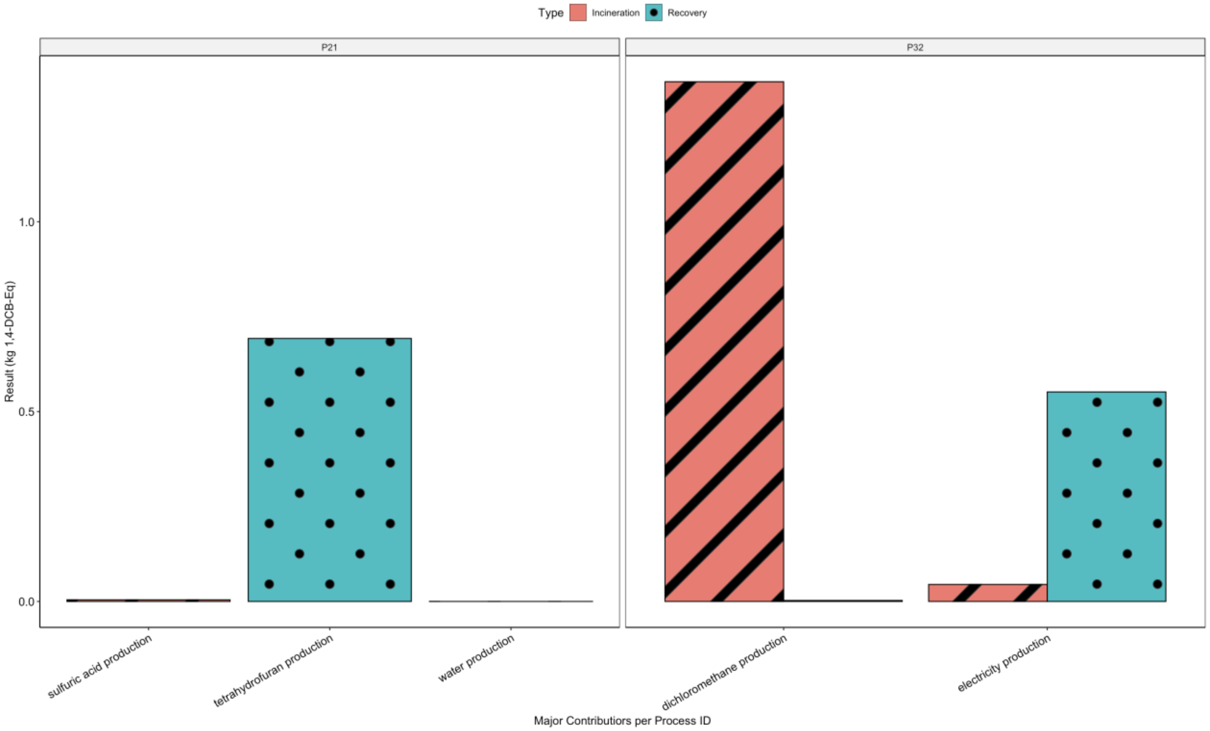

Figure 5-118. Major contributors for Processes 21 and 32 for freshwater ecotoxicity potential (FETP).

5.6.4.4 Marine Ecotoxicity Potential (METP) Contributors for Reactive Processes

Marine ecotoxicity potential (METP) major contributors for reactive processes can be found in Figure 5-119 and Figure 5-120 (for P21 & P32). Solvent production was the largest contributor in the incineration option but significantly decreased for the recovery option. Treatment of spent solvent mixture impacts were eliminated in the recovery option. Electricity production was higher than the incineration option than it was in the recovery option. In P32, ethyl acetate production had a positive effect on METP impacts for the recovery option.

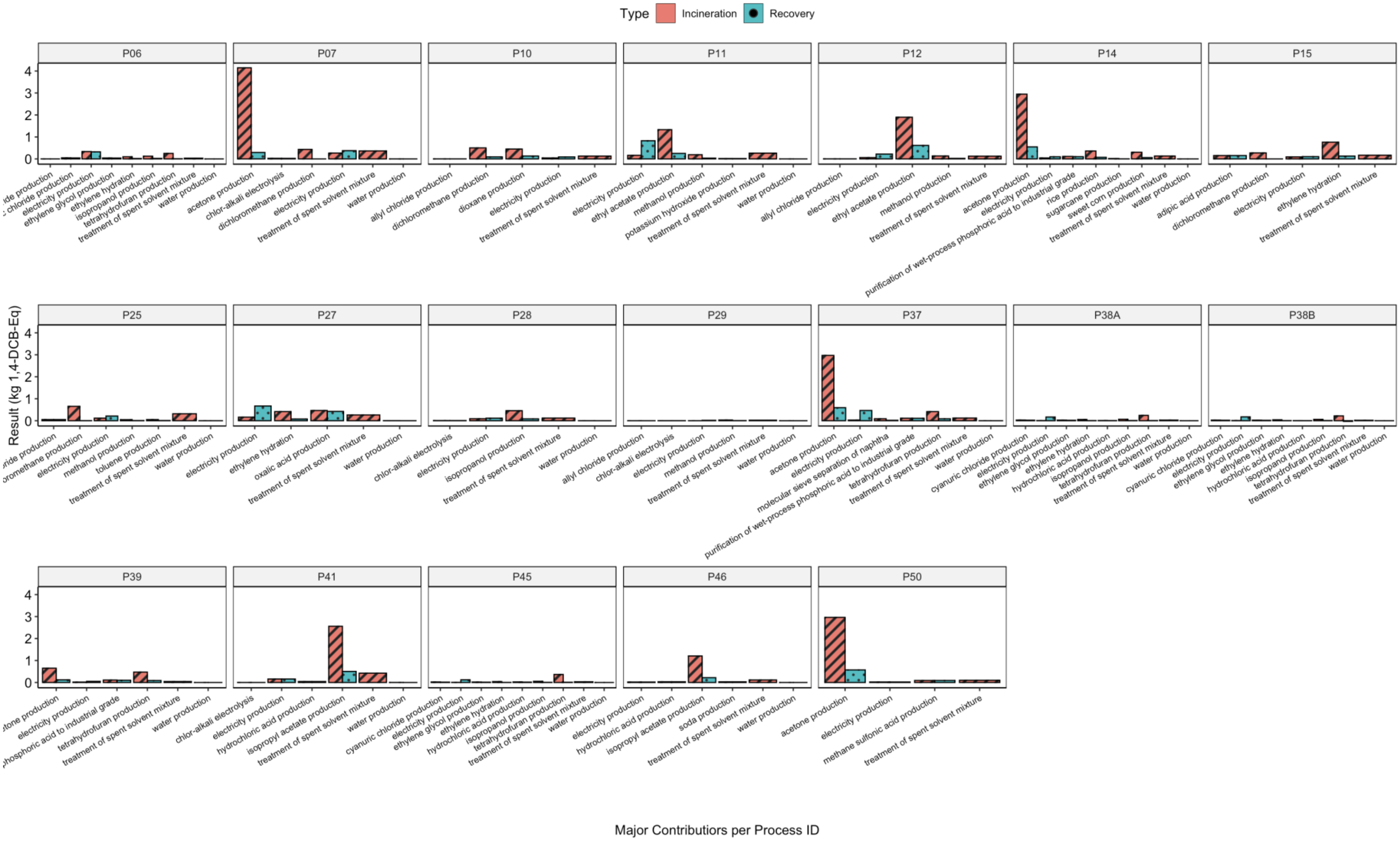

Figure 5-119. Major contributors for each reactive crystallization process for marine ecotoxicity potential (METP).

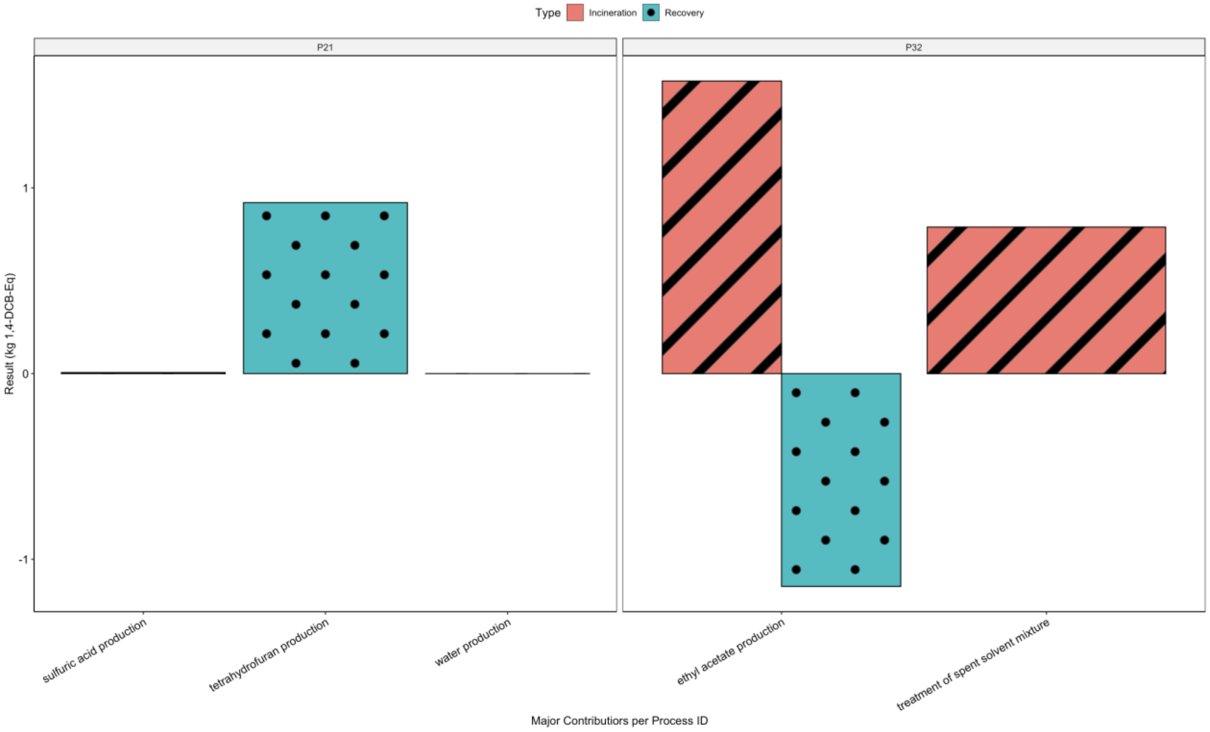

Figure 5-120. Major contributors for Processes 21 and 32 for marine ecotoxicity potential (METP).

5.6.4.5 Terrestrial Ecotoxicity Potential (TETP) Contributors for Reactive Processes

Terrestrial ecotoxicity potential (TETP) major contributors for reactive processes can be found in Figure 5-121 and Figure 5-122 (for P21 & P32). Solvent production produced the largest impacts in the incineration option which decreased significantly for the recovery option. Electricity impacts were increased during the recovery option with the implementation of the solvent recovery systems. Treatment of spent solvent mixture impacts were eliminated in the recovery option.

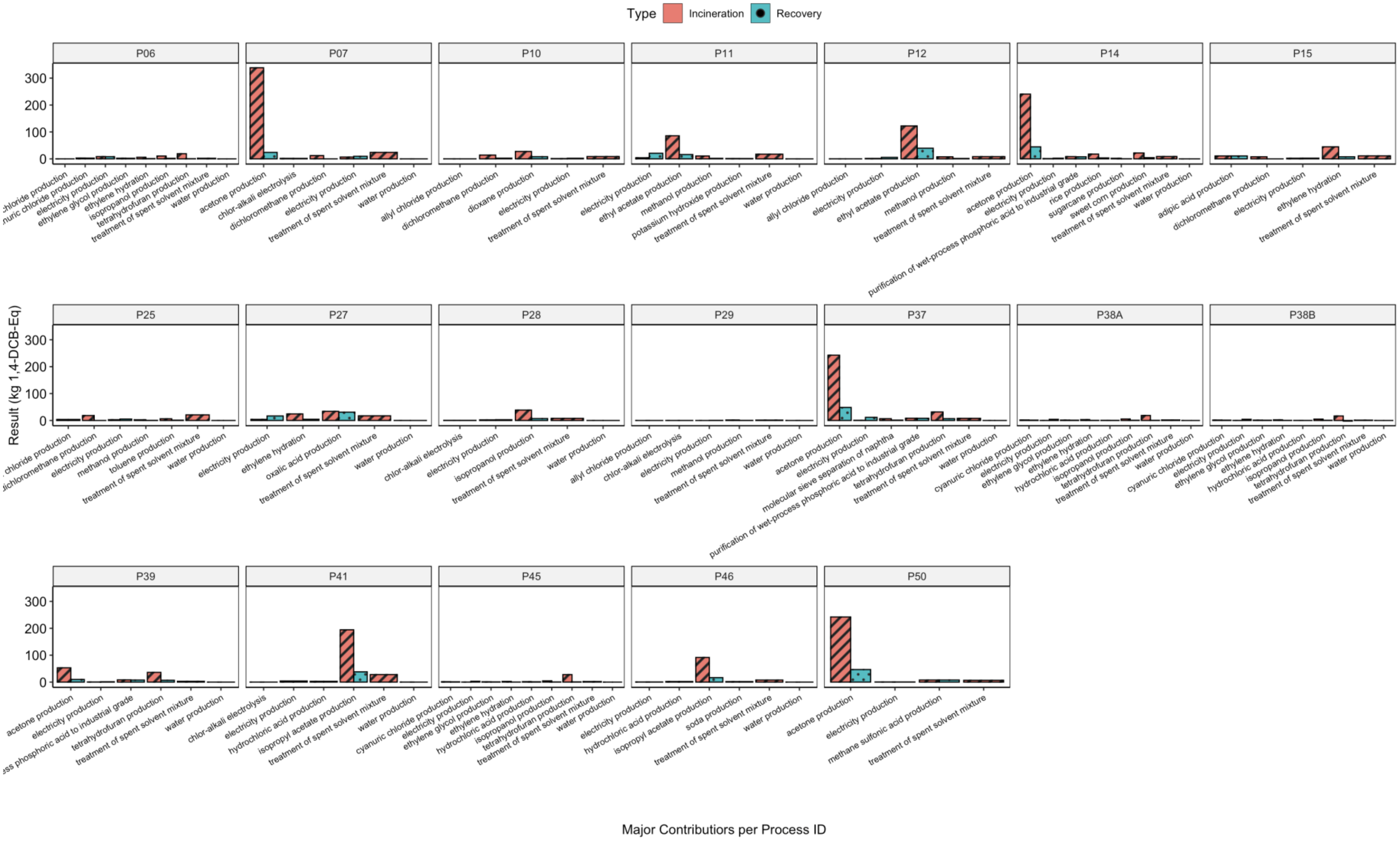

Figure 5-121. Major contributors for each reactive crystallization process for terrestrial ecotoxicity potential (TETP).

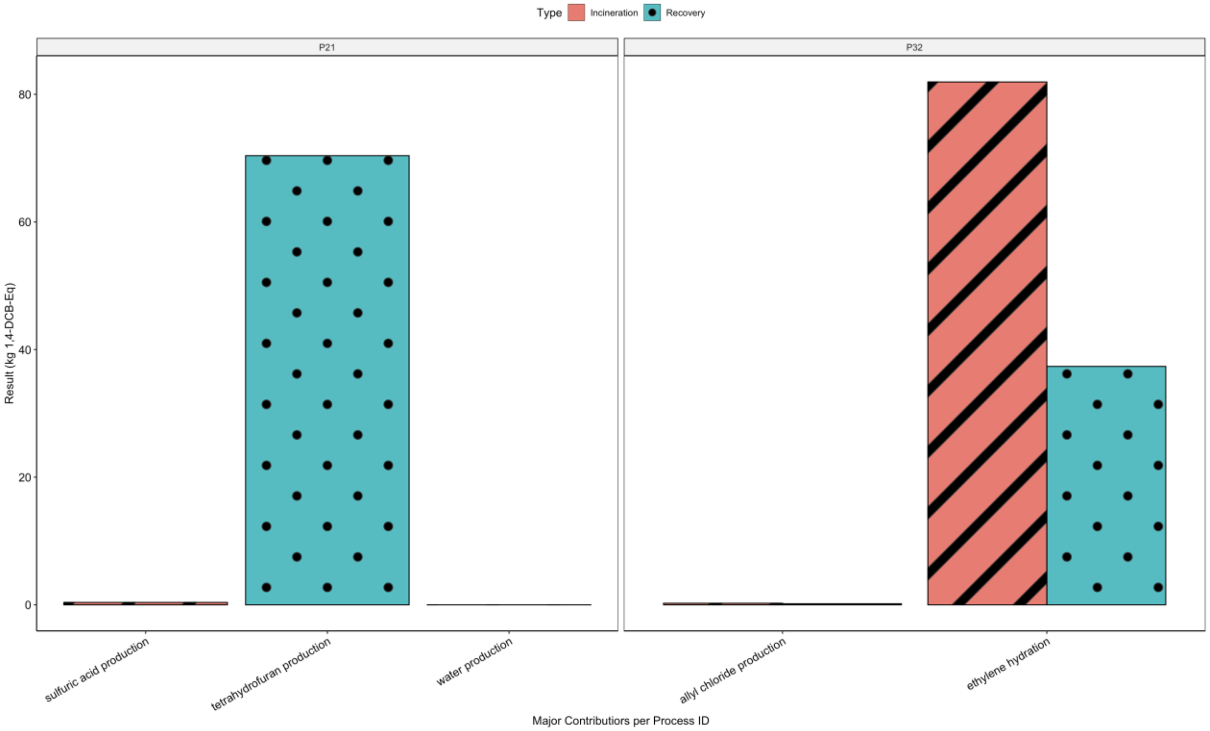

Figure 5-122. Major contributors for Processes 21 and 32 for terrestrial ecotoxicity potential (TETP).

5.6.4.6 Fossil Fuel Potential (FFP) Contributors for Reactive Processes

Fossil fuel potential (FFP) major contributors for reactive processes can be found in Figure 5-123 and Figure 5-124 (for P21 and P32). Solvent production was largest in the incineration option. Treatment of spent solvent mixture and electricity production impacts were similar in the incineration option. Electricity production impacts increased with the recovery option while treatment of spent solvent mixture impacts were eliminated. Reactant production was a minimal contributor to the FFP impacts.

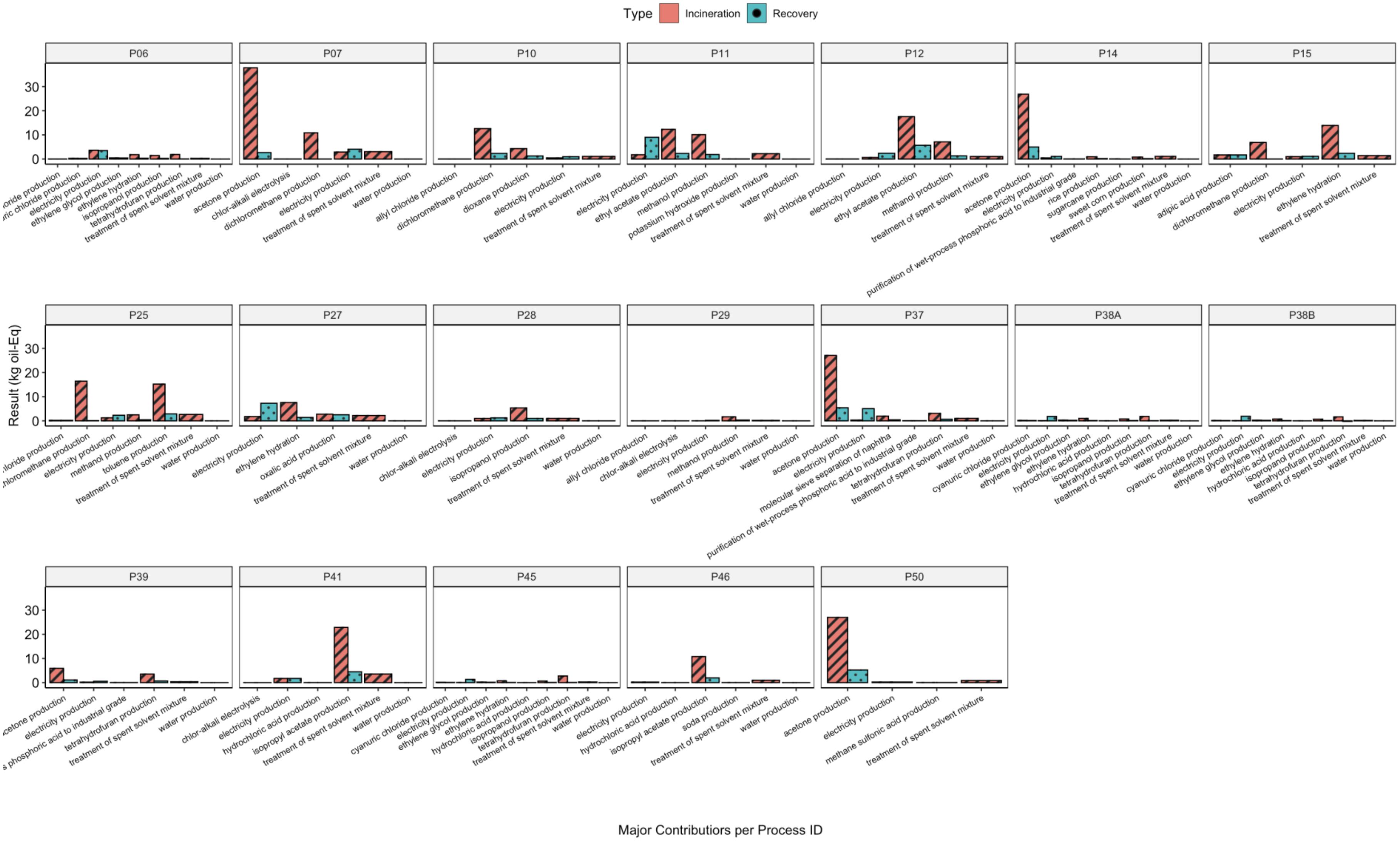

Figure 5-123. Major contributors for each reactive crystallization process for fossil fuel potential (FFP).

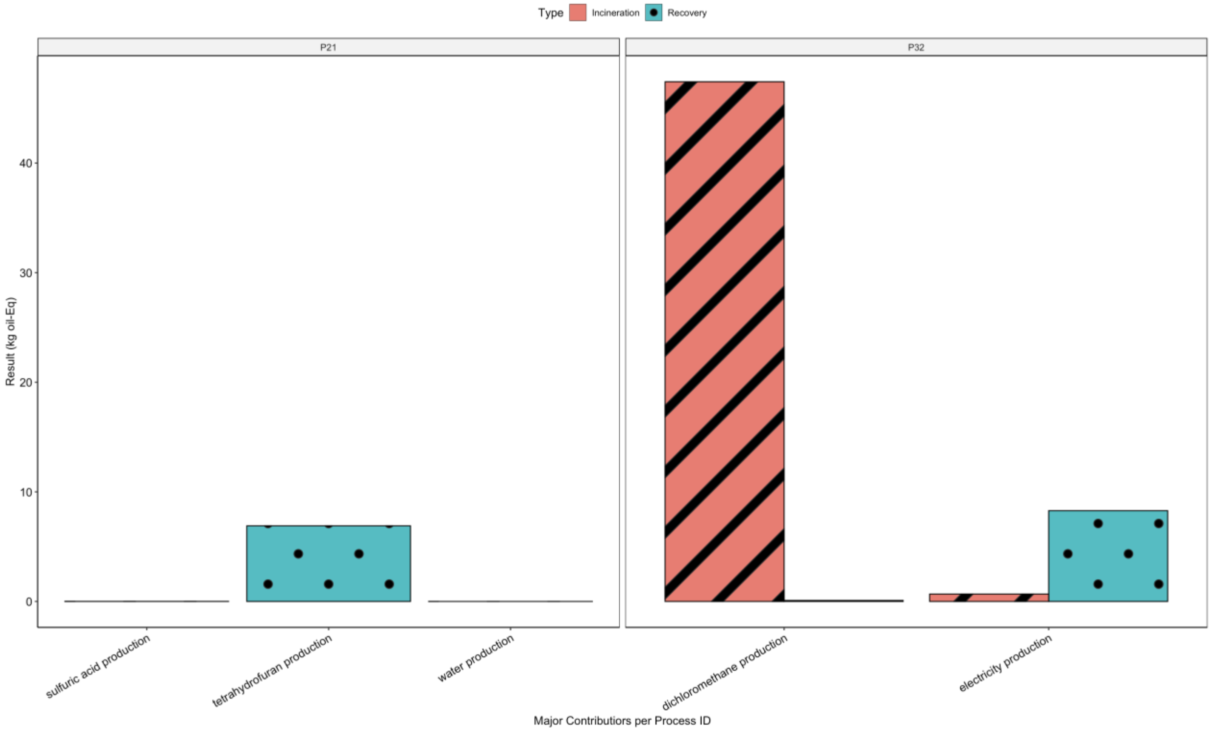

Figure 5-124. Major contributors for Processes 21 and 32 for fossil fuel potential (FFP).

5.6.4.7 Freshwater Eutrophication Potential (FEP) Contributors for Reactive Processes

Freshwater eutrophication potential (FEP) major contributors for reactive processes can be found in Figure 5-125 and Figure 5-126 (for P21 and P32). Solvent production and treatment of spent solvent mixtures had the largest impacts in the incineration option. Reactant production impacts were minimal when compared to those of the other contributors. Electricity production impacts were increased from the incineration option to the recovery option. Treatment of spent solvent mixture impacts were eliminated in the recovery option. Ethyl acetate had a positive effect on the FEP impacts for the recovery option of P32.

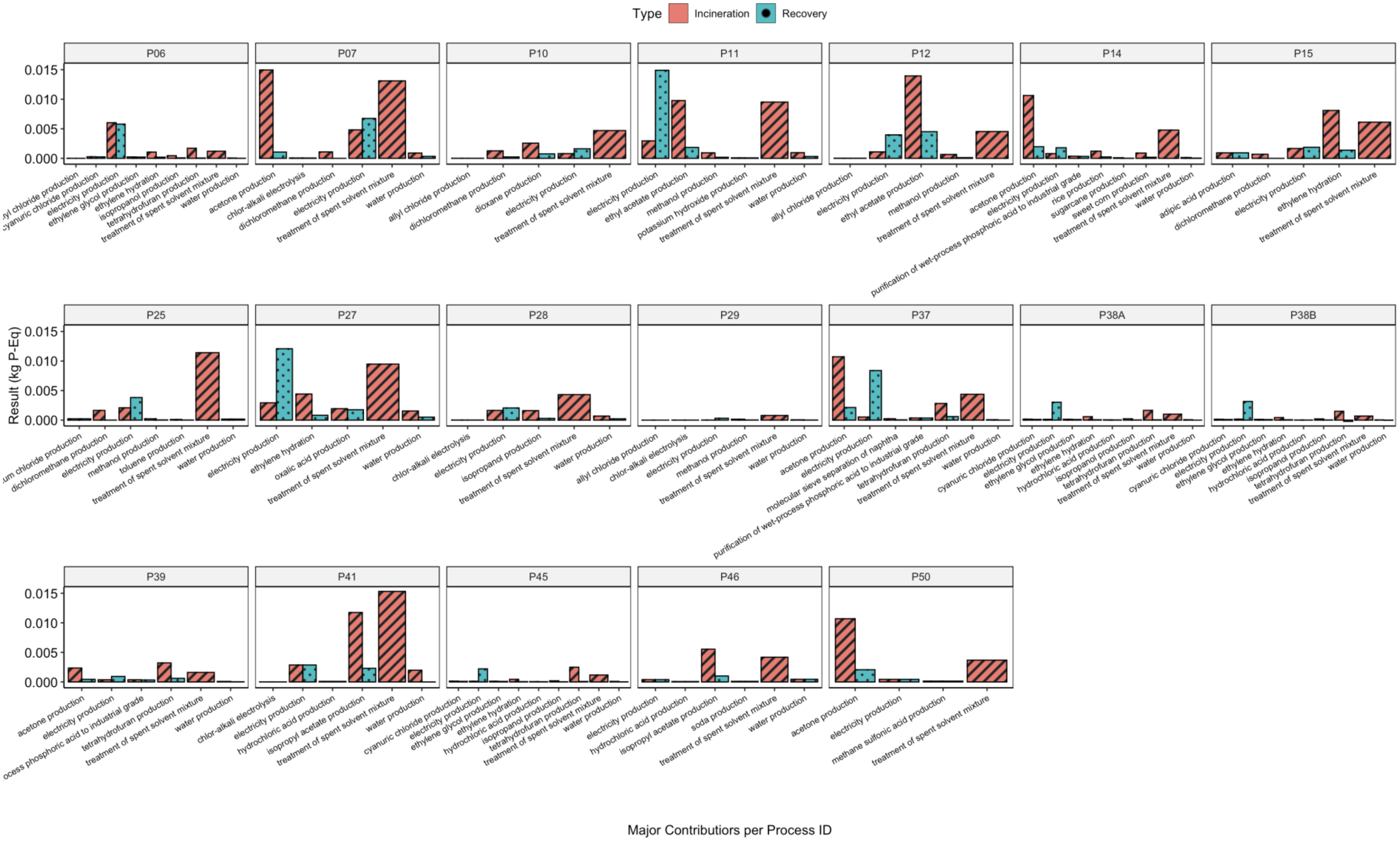

Figure 5-125. Major contributors for each reactive crystallization process for freshwater eutrophication potential (FEP).

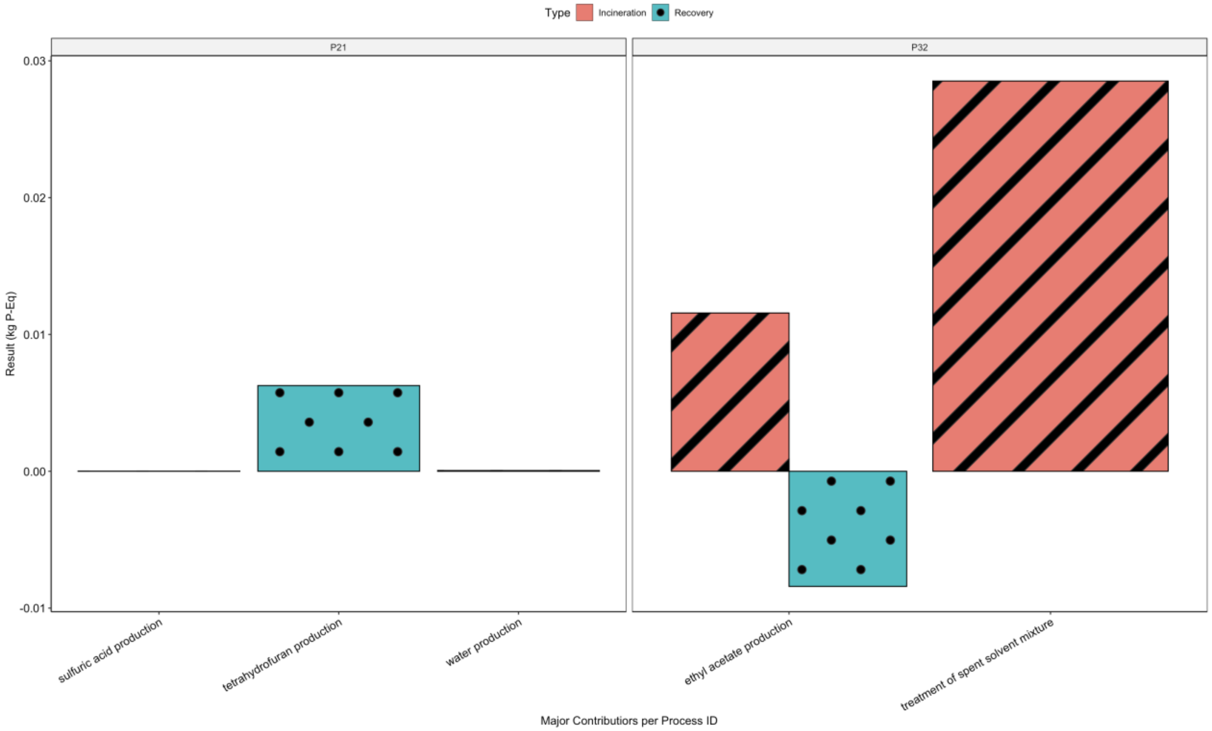

Figure 5-126. Major contributors for Processes 21 and 32 for freshwater eutrophication potential (FEP).

5.6.4.8 Marine Eutrophication Potential (MEP) Contributors for Reactive Processes

Marine eutrophication potential (MEP) major contributors for reactive processes can be found in Figure 5-127 and Figure 5-128 (for P21 and P32). Treatment of spent solvent mixtures was a large contributor to MEP impacts as well as solvent production. Solvent production of 2-MeTHF (i.e., agricultural crops) had larger impacts than the production of solvent. Treatment of spent solvent mixture impacts were eliminated in the recovery option while the solvent production impacts were significantly decreased. Electricity production increased with the recovery option due to the implementation of solvent recovery systems.

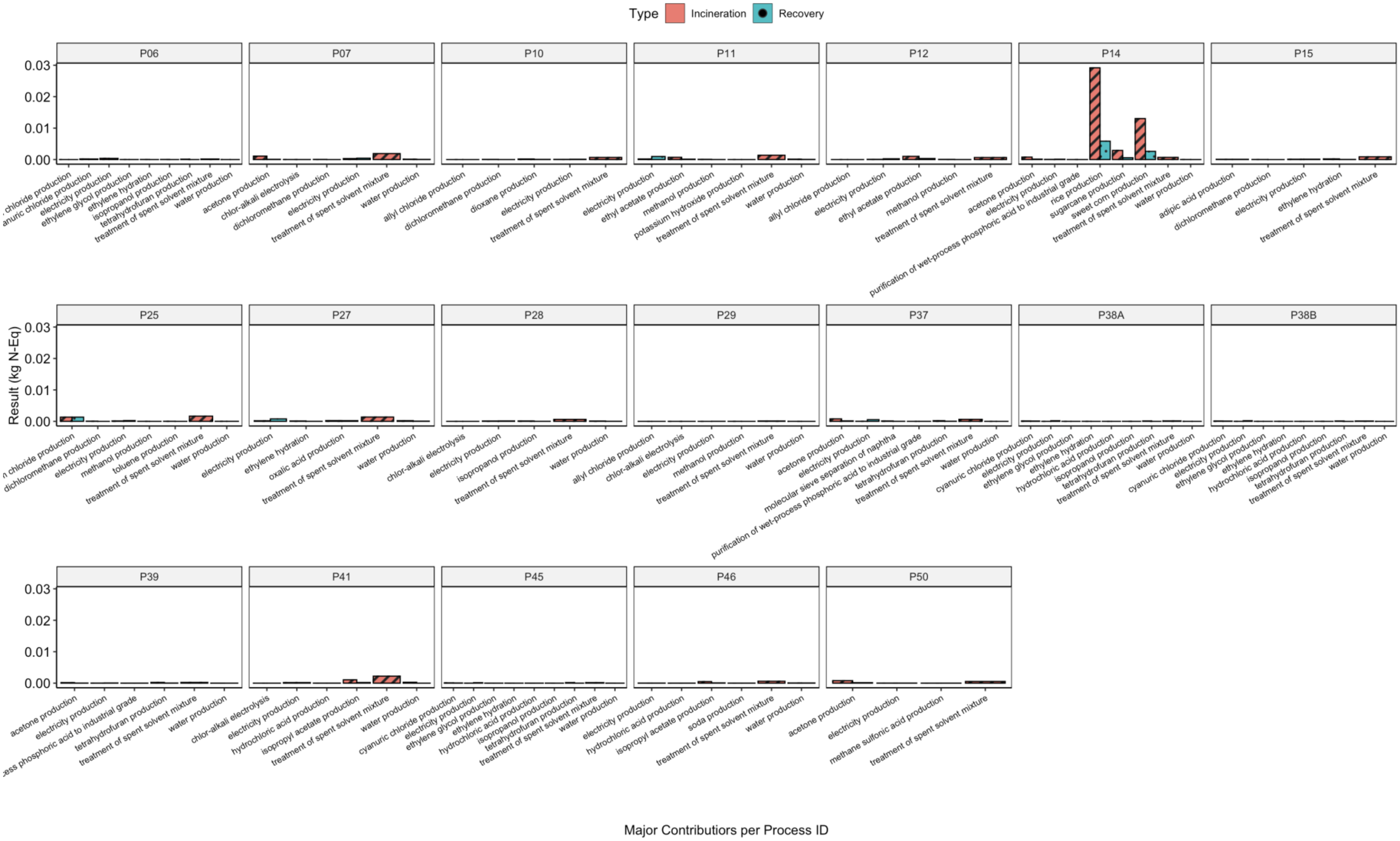

Figure 5-127. Major contributors for each reactive crystallization process for marine eutrophication potential (MEP).

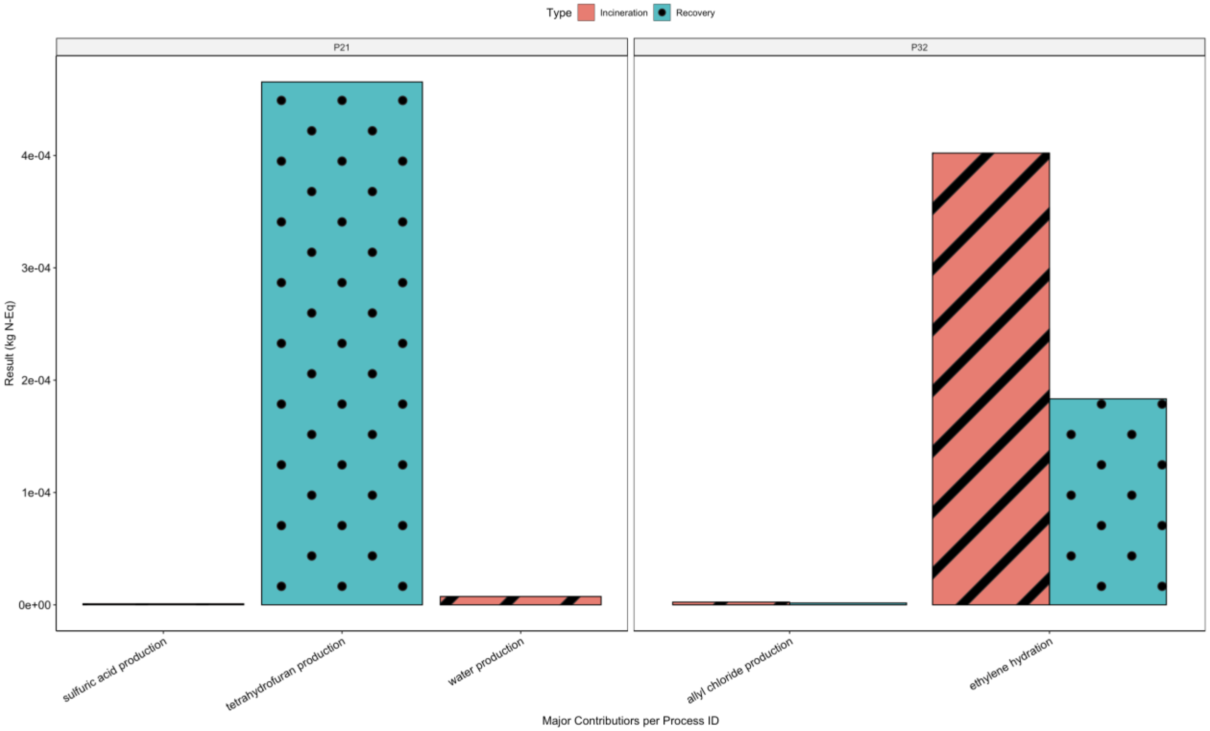

Figure 5-128. Major contributors for Processes 21 and 32 for marine eutrophication potential (MEP).

5.6.4.9 Human Toxicity Potential – Carcinogenic (HTPc) Contributors for Reactive Processes

Human toxicity potential – carcinogenic (HTPc) major contributors for reactive processes can be found in Figure 5-129 and Figure 5-130 (for P21 & P32). The largest contributor in the incineration option was from solvent production. Treatment of spent solvent mixtures was also a large contributor but was eliminated in the recovery option. Solvent production was significantly decreased in the recovery option. Electricity production increased with the implementation of the solvent recovery system for the recovery option and reactant production did not have a large impact for either option.

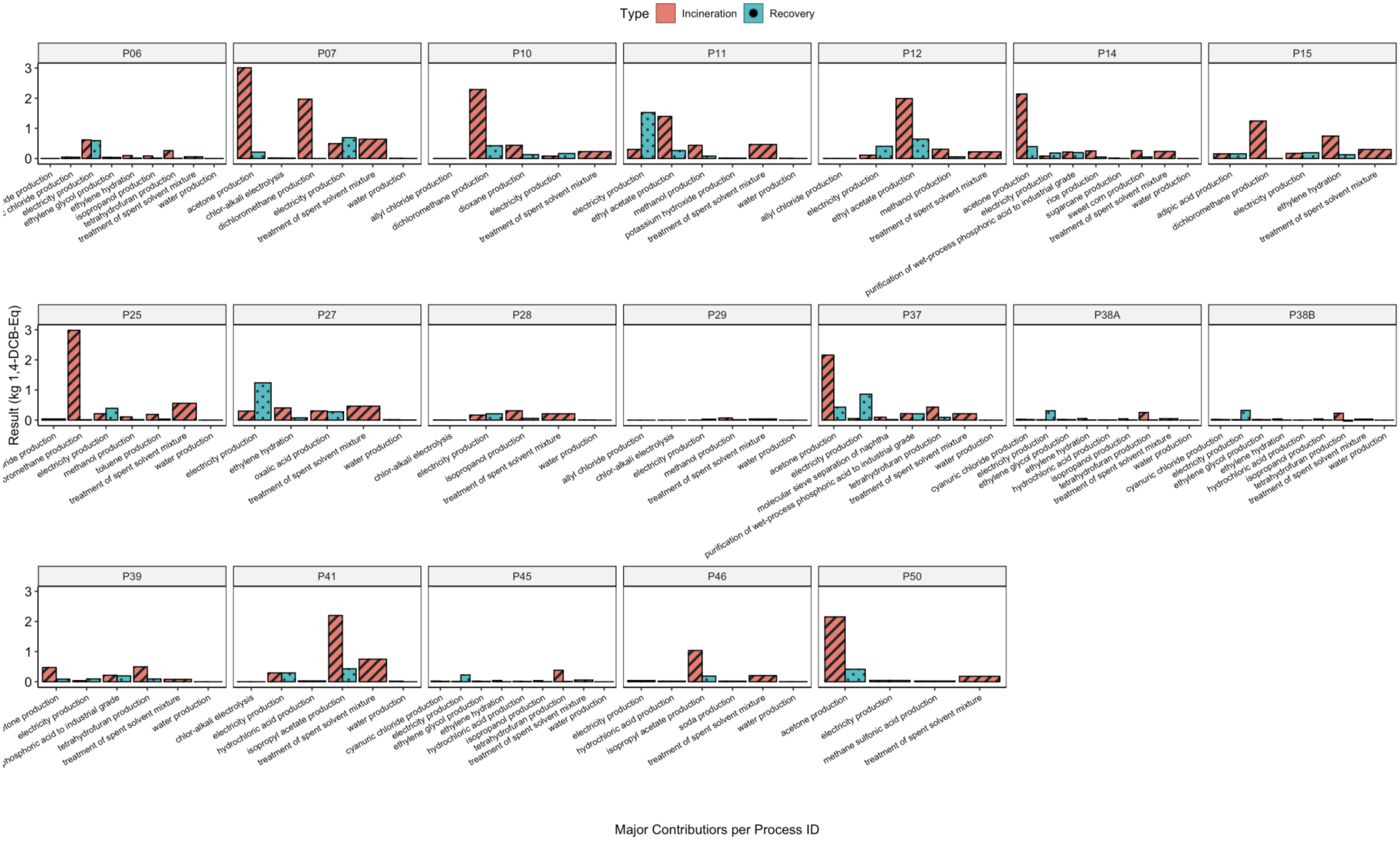

Figure 5-129. Major contributors for each reactive crystallization process for human toxicity potential – carcinogenic (HTPc).

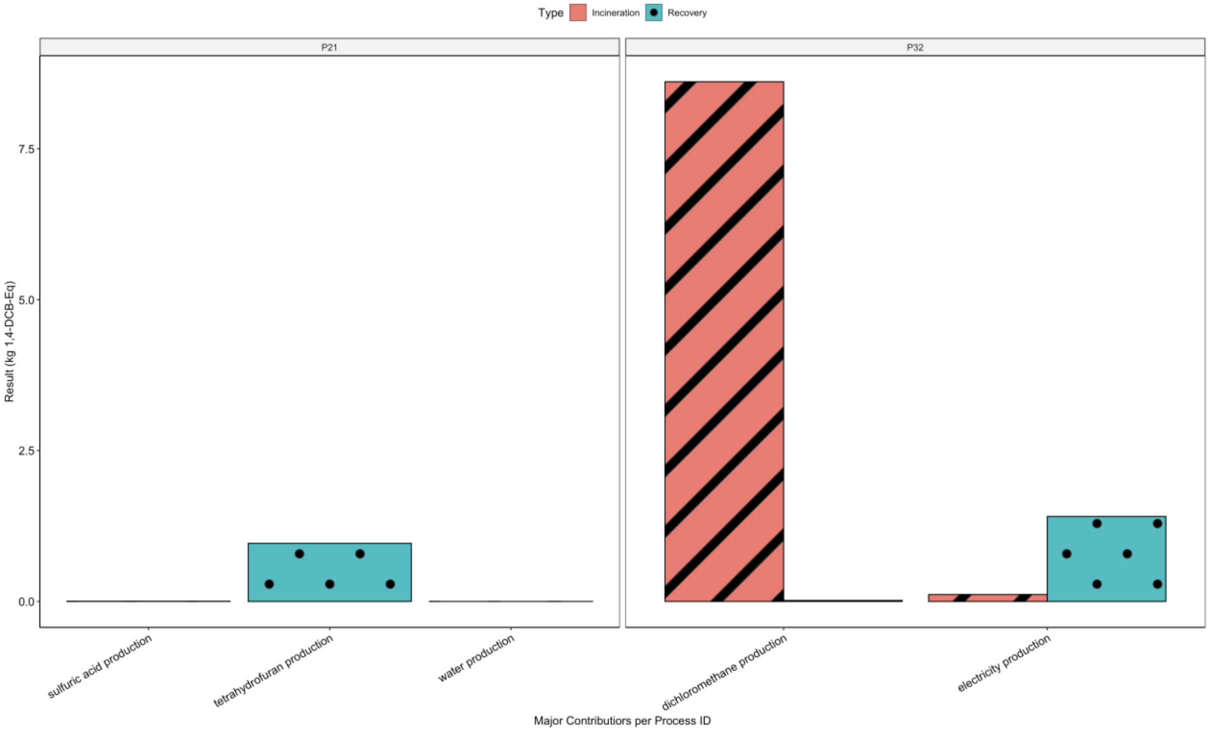

Figure 5-130. Major contributors for Processes 21 and 32 for human toxicity potential – carcinogenic (HTPc).

5.6.4.10 Human Toxicity Potential – Non-Carcinogenic (HTPnc) Contributors for Reactive Processes

Human toxicity potential – non-carcinogenic (HTPnc) major contributors for reactive processes can be found in Figure 5-131 and Figure 5-132 (for P21 & P32). Solvent production had the largest impact in the incineration option but was significantly decreased in the recovery option. Rice production in the P14 had a positive effect on HTPnc impacts for both the incineration and recovery options. Treatment of spent solvent mixture impacts were similar to those of electricity production impacts for the incineration option but were eliminated in the recovery option while electricity production impacts increased. Ethyl acetate had a positive effect on the HTPnc impacts for P32 in the recovery option.

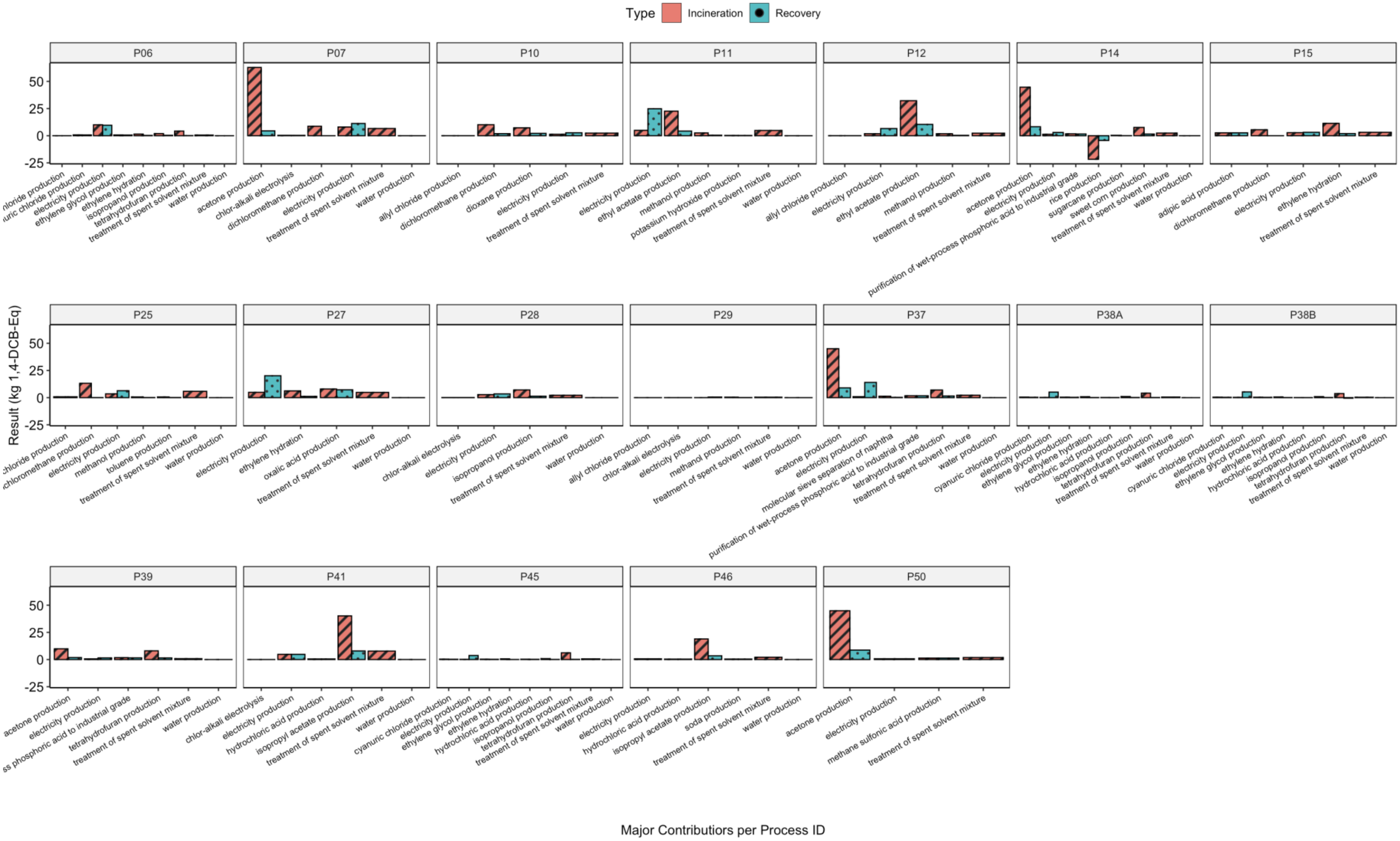

Figure 5-131. Major contributors for each reactive crystallization process for human toxicity potential – non-carcinogenic (HTPnc).

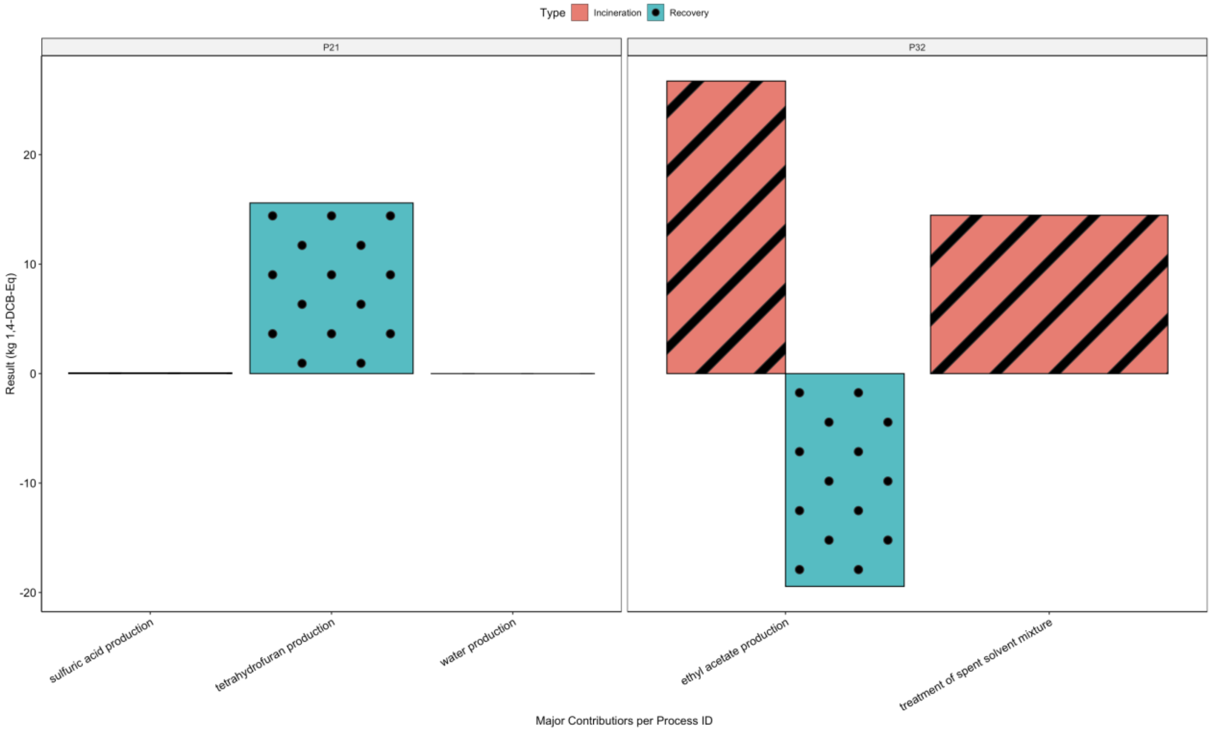

Figure 5-132. Major contributors for Processes 21 and 32 for human toxicity potential – non-carcinogenic (HTPnc).

5.6.4.11 Ionising Radiation Potential (IRP) Contributors for Reactive Processes

Ionising radiation potential (IRP) major contributors for reactive processes can be found in Figure 5-132 and Figure 5-133 (for P21 & P32). The major contributor in the incineration option was solvent production, then followed by treatment of spent solvent mixtures. Electricity production was lower in the incineration option but increased in the recovery option with the implementation of the solvent recovery systems. Solvent production impacts were reduced in the recovery option and treatment of spent solvent mixtures were eliminated. Reactant production impacts were minimal compared to those of the other contributors.

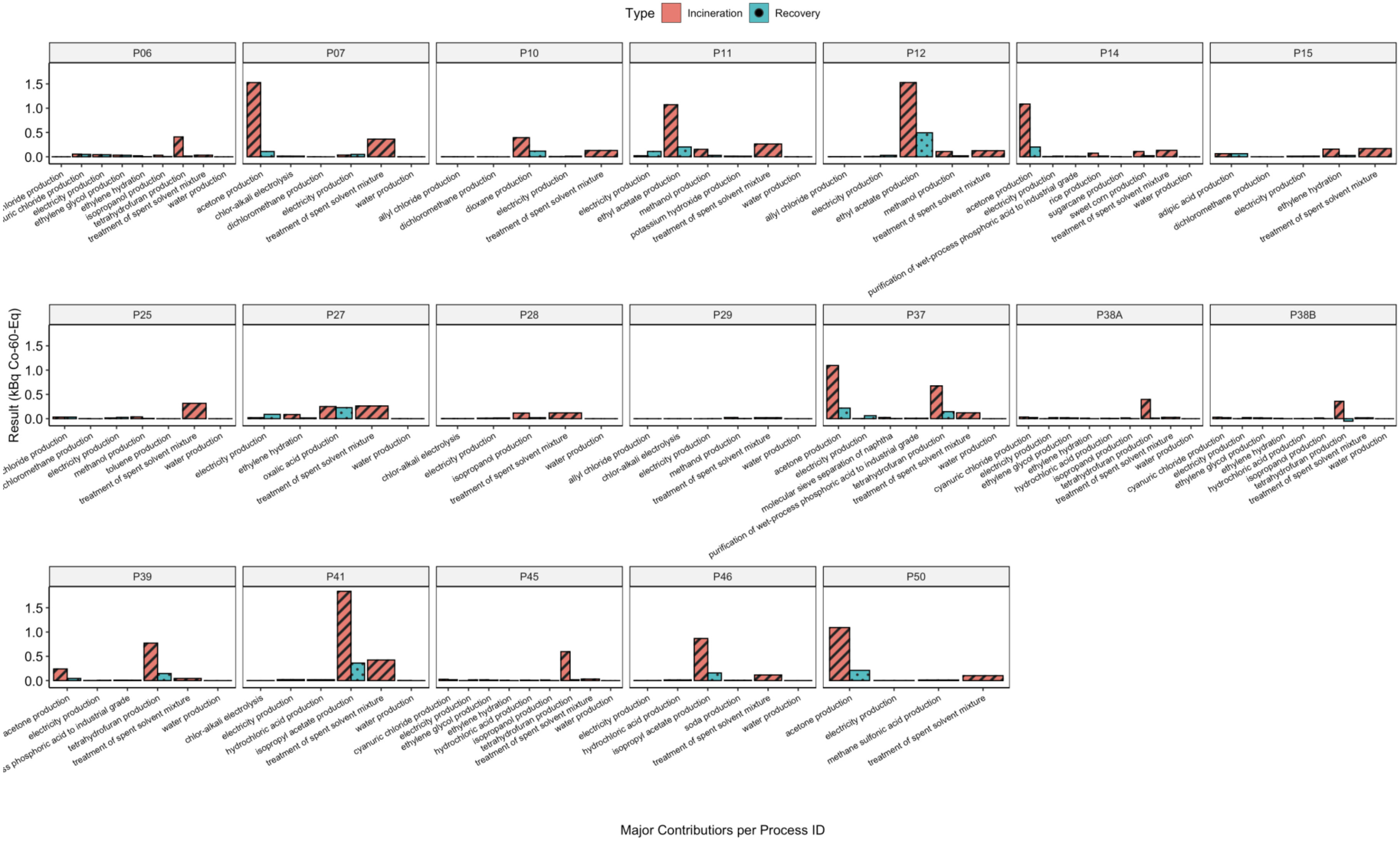

Figure 5-133. Major contributors for each reactive crystallization process for ionising radiation potential (IRP).

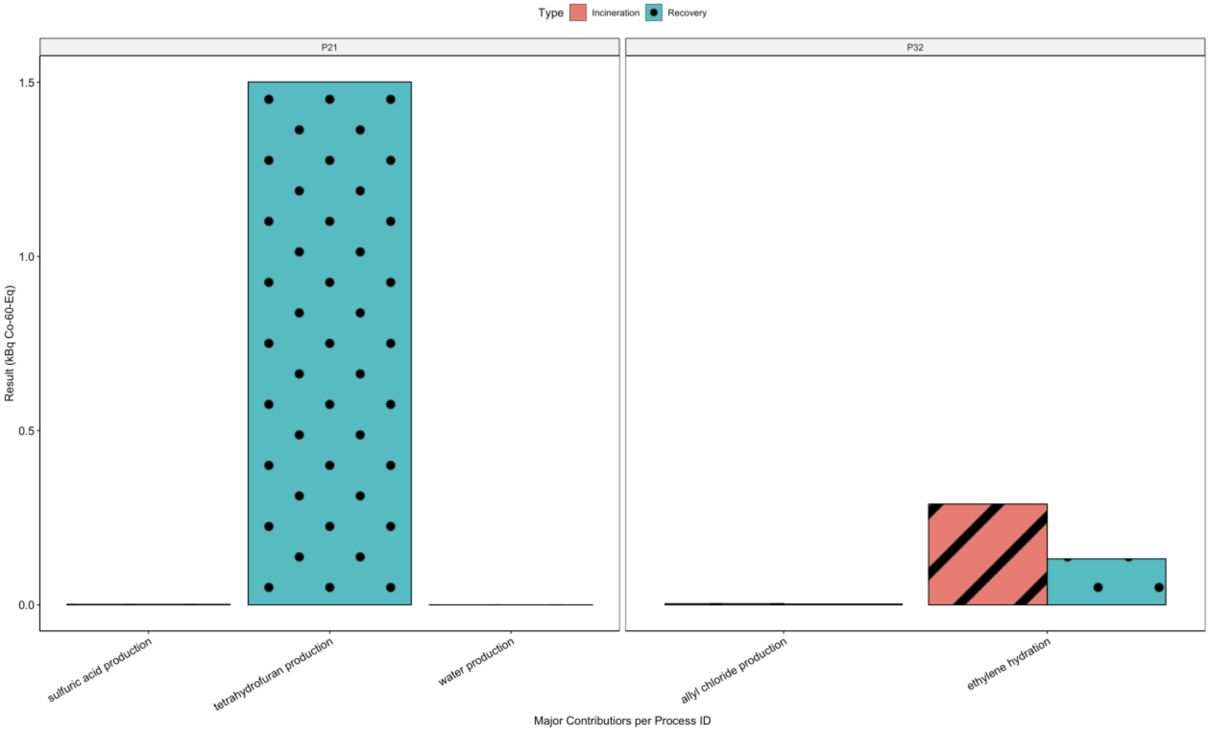

Figure 5-134. Major contributors for Processes 21 and 32 for ionising radiation potential (IRP).

5.6.4.12 Agricultural Land Occupation (LOP) Contributors for Reactive Processes

Agricultural land occupation (LOP) major contributors for reactive processes can be found in Figure 5-135 and Figure 5-136 (for P21 & P32). The major contributors to LOP came from the production of 2-MeTHF. Rice, corn, and sugarcane require a large amount of agricultural land to produce 2-MeTHF. All other contributors had much smaller impacts but displayed similar patterns when compared to the other impact categories.

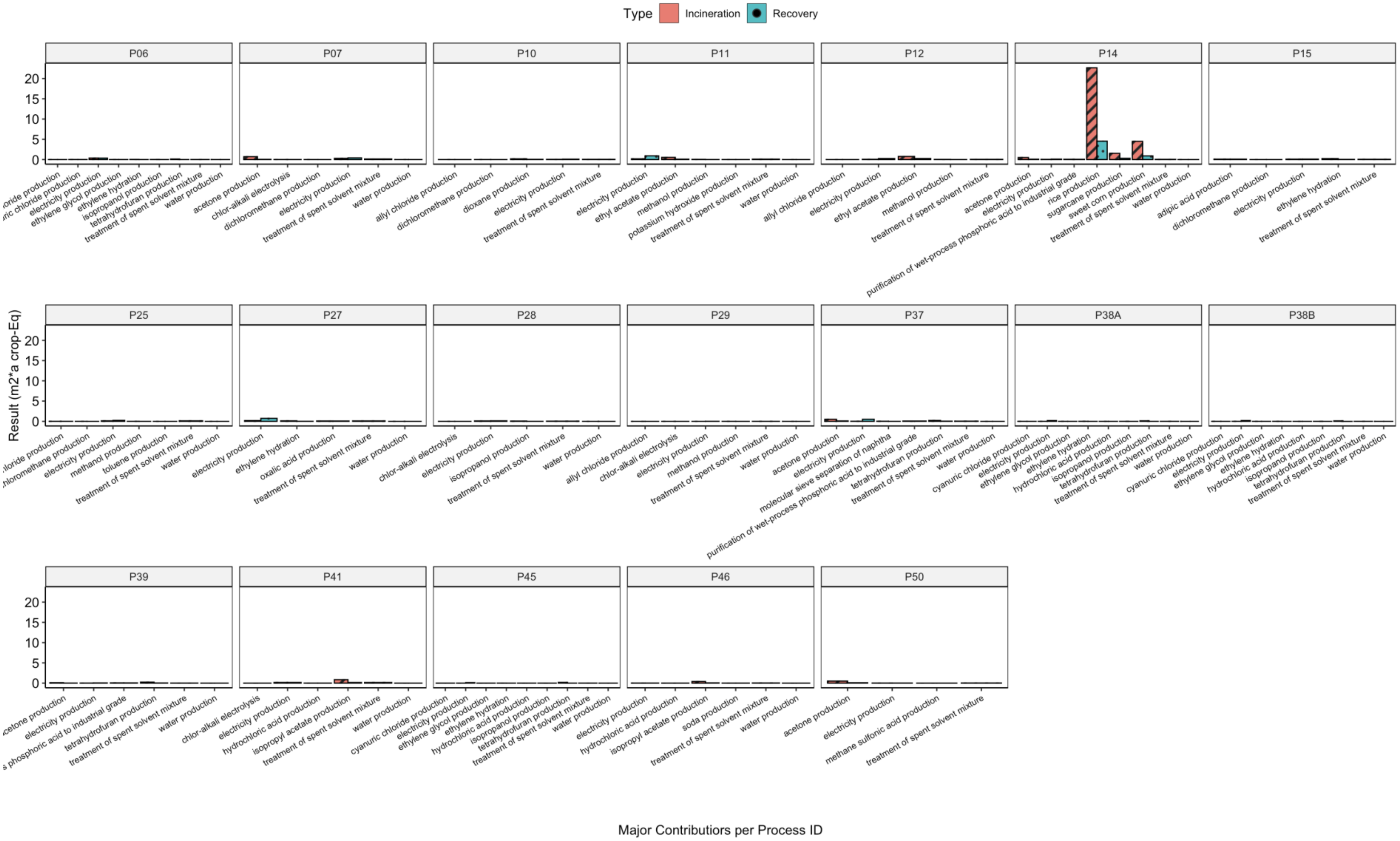

Figure 5-135. Major contributors for each reactive crystallization process for agricultural land occupation (LOP).

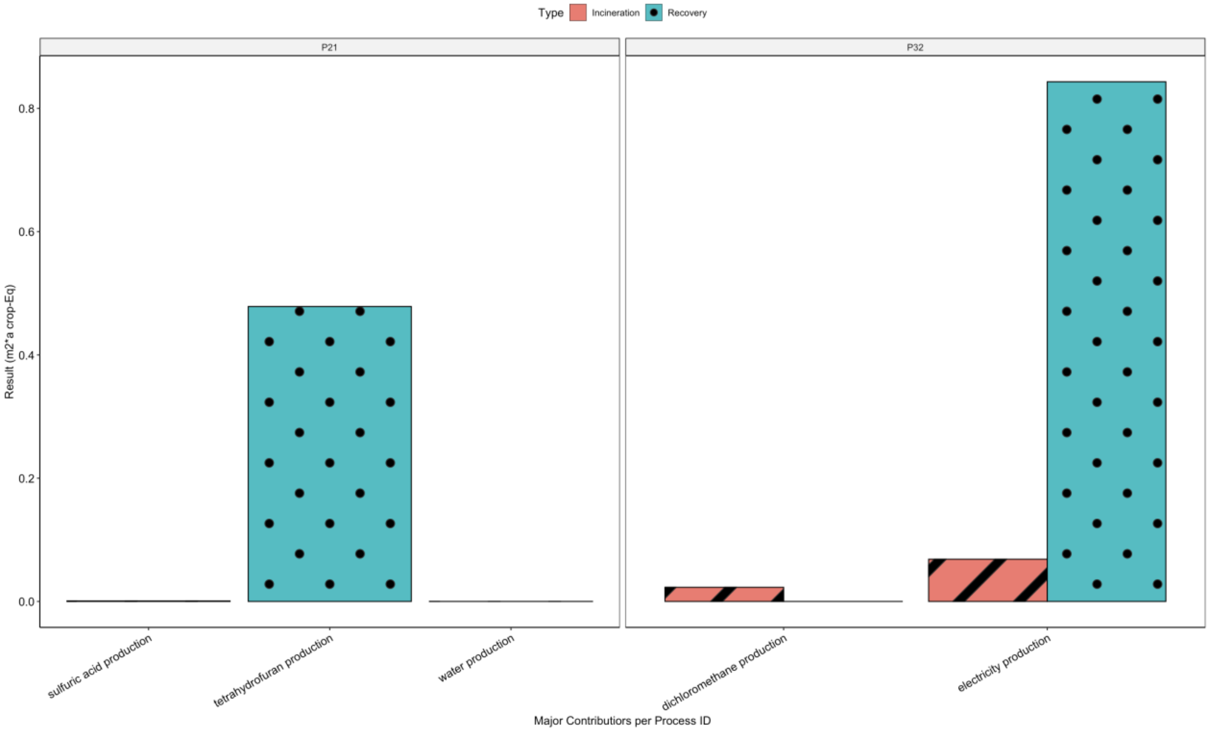

Figure 5-136. Major contributors for Processes 21 and 32 for agricultural land occupation (LOP).

5.6.4.13 Surplus Ore Potential (SOP) Contributors for Reactive Processes

Surplus ore potential (SOP) major contributors for reactive processes can be found in Figure 5-137 and Figure 5-138 (for P21 & P32). The largest contributors, in the incineration option, came from solvent production and treatment of spent solvent mixtures. The solvent production impacts were significantly reduced in the recovery option and treatment of spent solvent mixture impacts were eliminated. Electricity production resulted in smaller impacts in the incineration option but were increased in the recovery option with the implementation of the solvent recovery systems. Reactant production was not a major contributor. For P32, ethyl acetate production showed a positive effect on the SOP impacts in the recovery option.

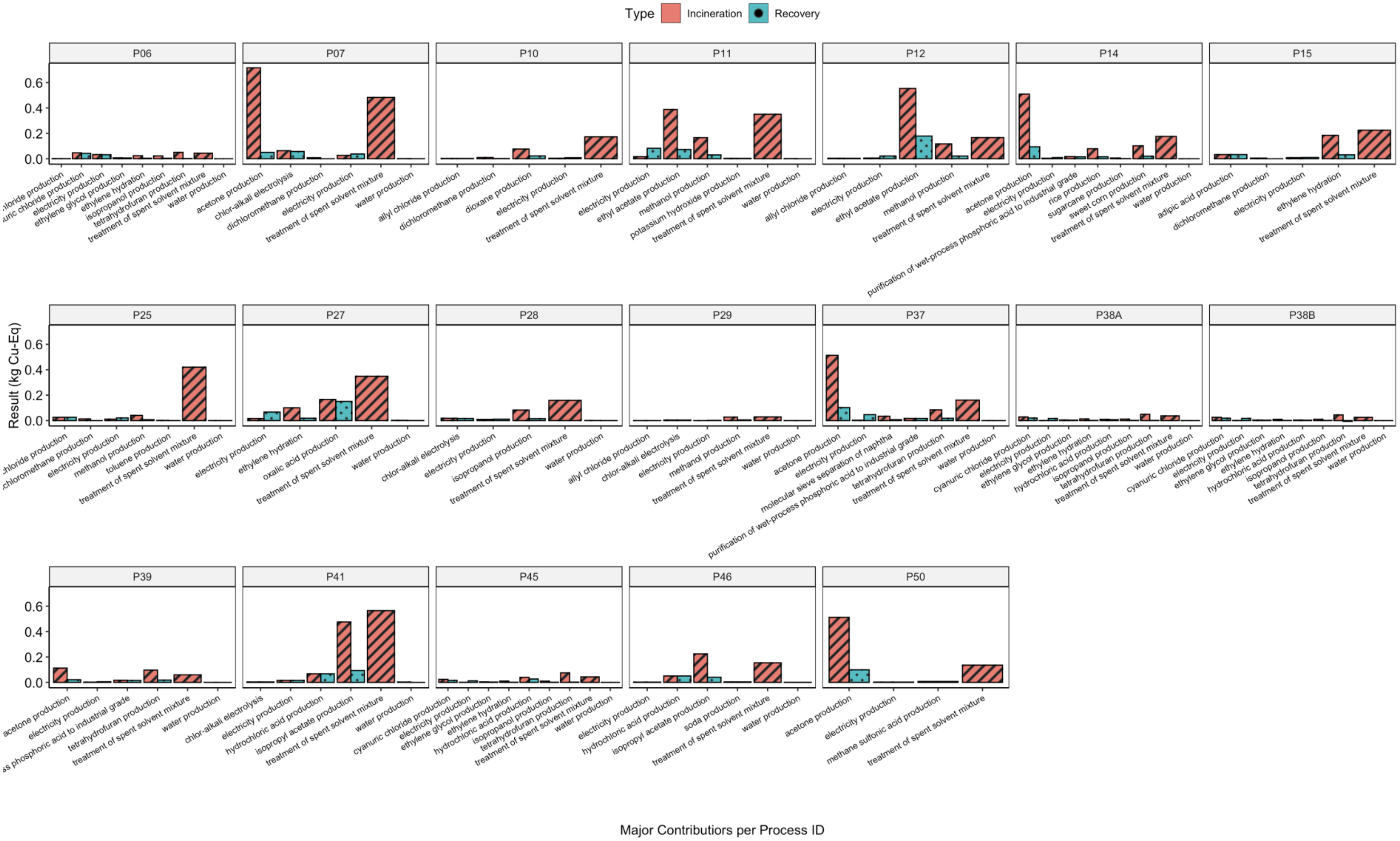

Figure 5-137. Major contributors for each reactive crystallization process for surplus ore potential (SOP).

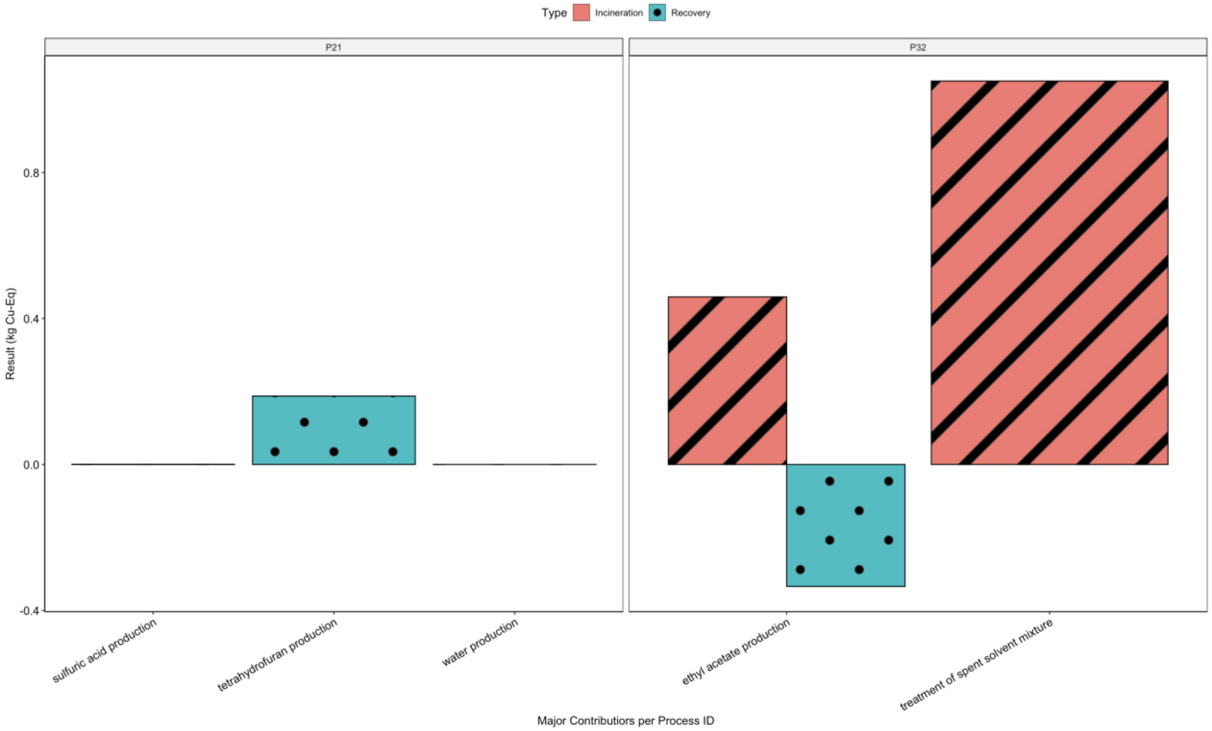

Figure 5-138. Major contributors for Processes 21 and 32 for surplus ore potential (SOP).

5.6.4.14 Ozone Depletion Potential ($ODP_{infinite}$) Contributors for Reactive Processes

Ozone depletion potential ($ODP_{infinite}$) major contributors for reactive processes can be found in Figure 5-139 and Figure 5-140 (for P21 & P32). The major contributor for this impact category came from dichloromethane production. This impact was significantly decreased in the recovery option with the reuse of solvents. All other contributors had much lower impacts but showed similar patterns observed in the other impact categories.

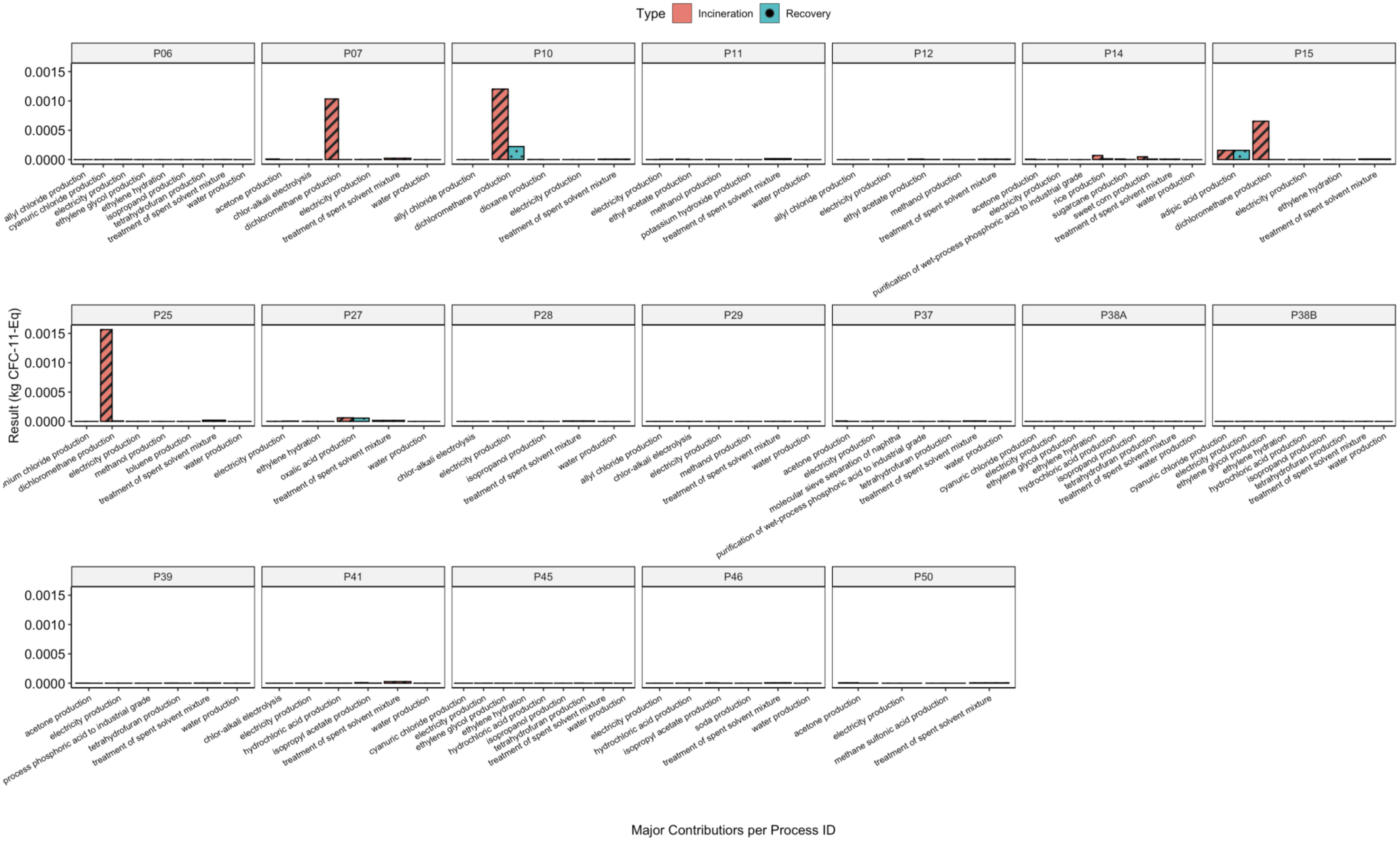

Figure 5-139. Major contributors for each reactive crystallization process for ozone depletion potential (ODP$_{\text{infinite}}$).

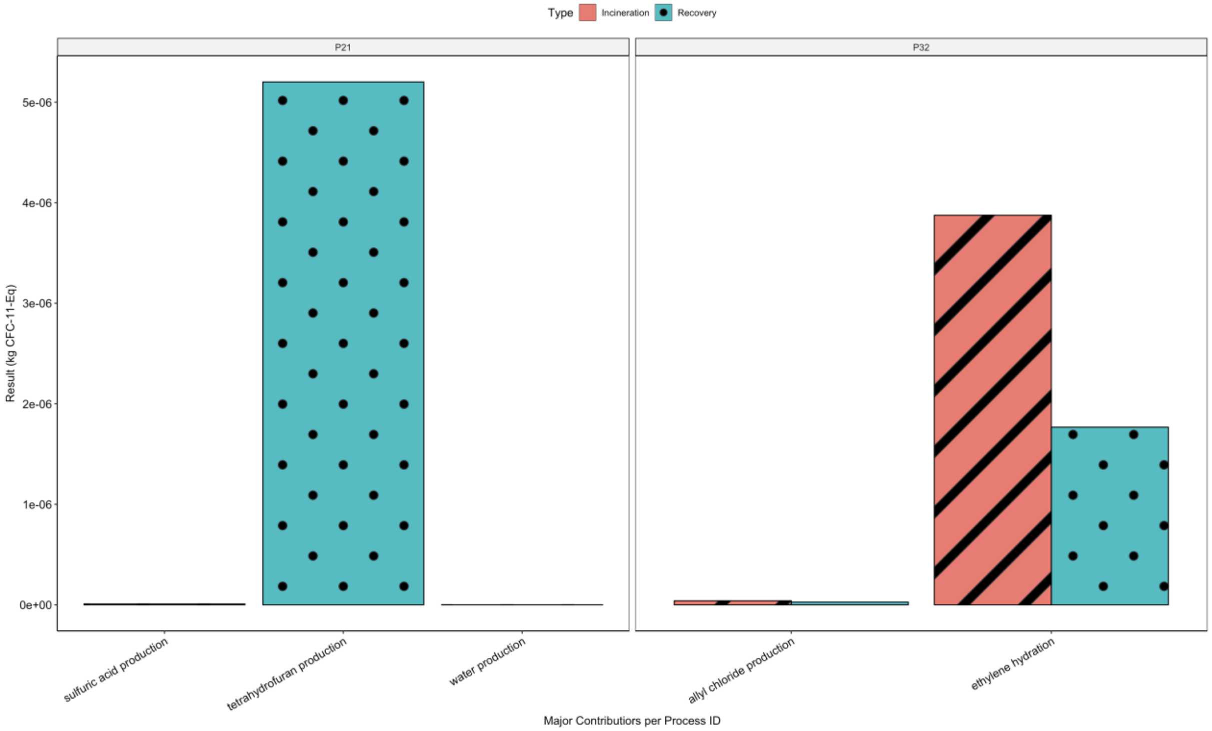

Figure 5-140. Major contributors for Processes 21 and 32 for ozone depletion potential ($\text{ODP}_{\text{infinite}}$).

5.6.4.15 Particulate Matter Formation Potential (PMFP) Contributors for Reactive Processes

Particulate matter formation potential (PMFP) major contributors for the reactive processes can be found in Figure 5-141 and Figure 5-142 (for P21 & P32). Solvent production showed the largest impacts in the incineration option. Electricity production and treatment of spent solvent mixture impacts showed similar results in the incineration option but electricity production impacts increased in the recovery option while treatment of spent solvent mixture impacts were eliminated. Reactant production impacts were low compared to the other contributors.

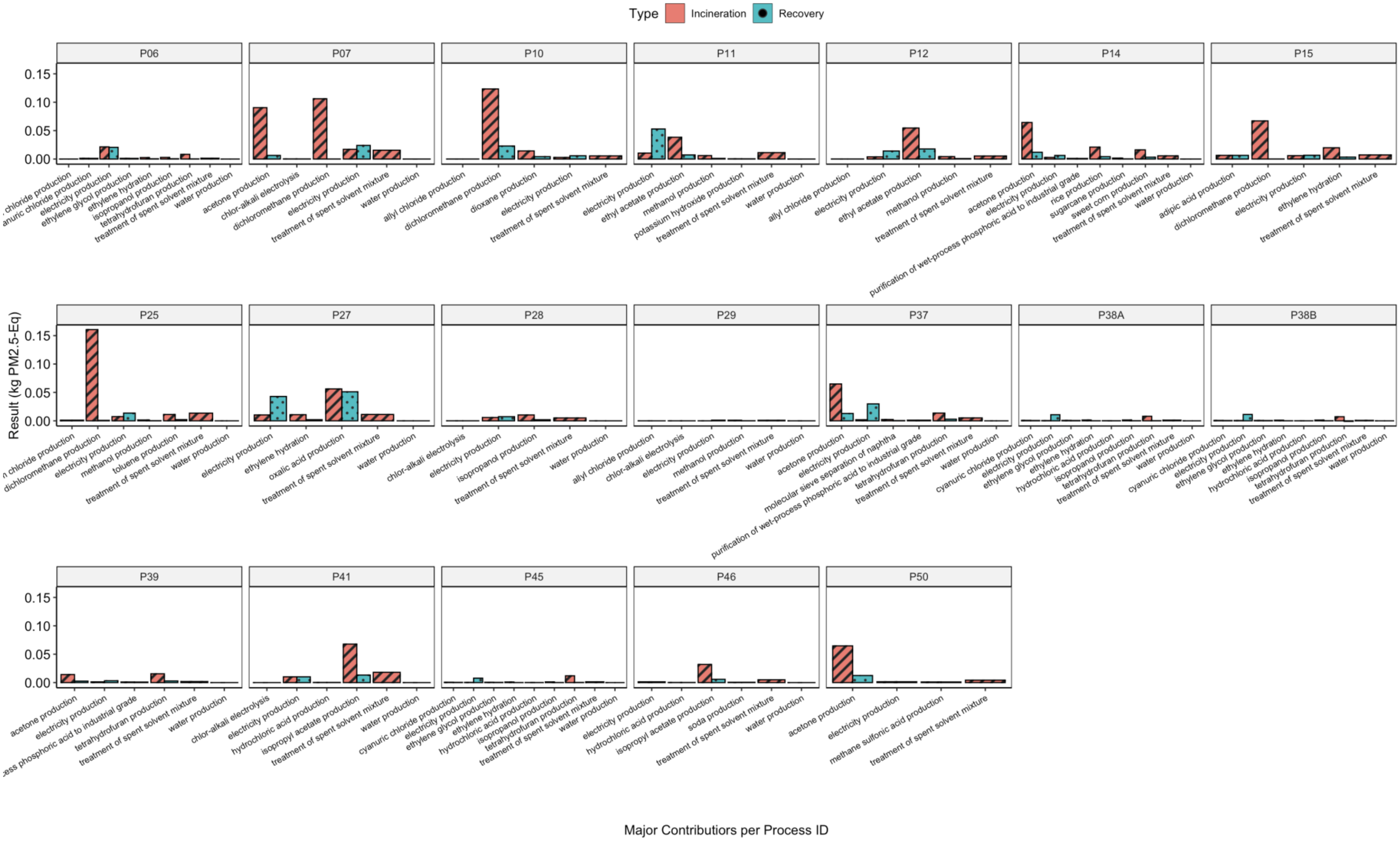

Figure 5-141. Major contributors for each reactive crystallization process for particulate matter formation potential (PMFP).

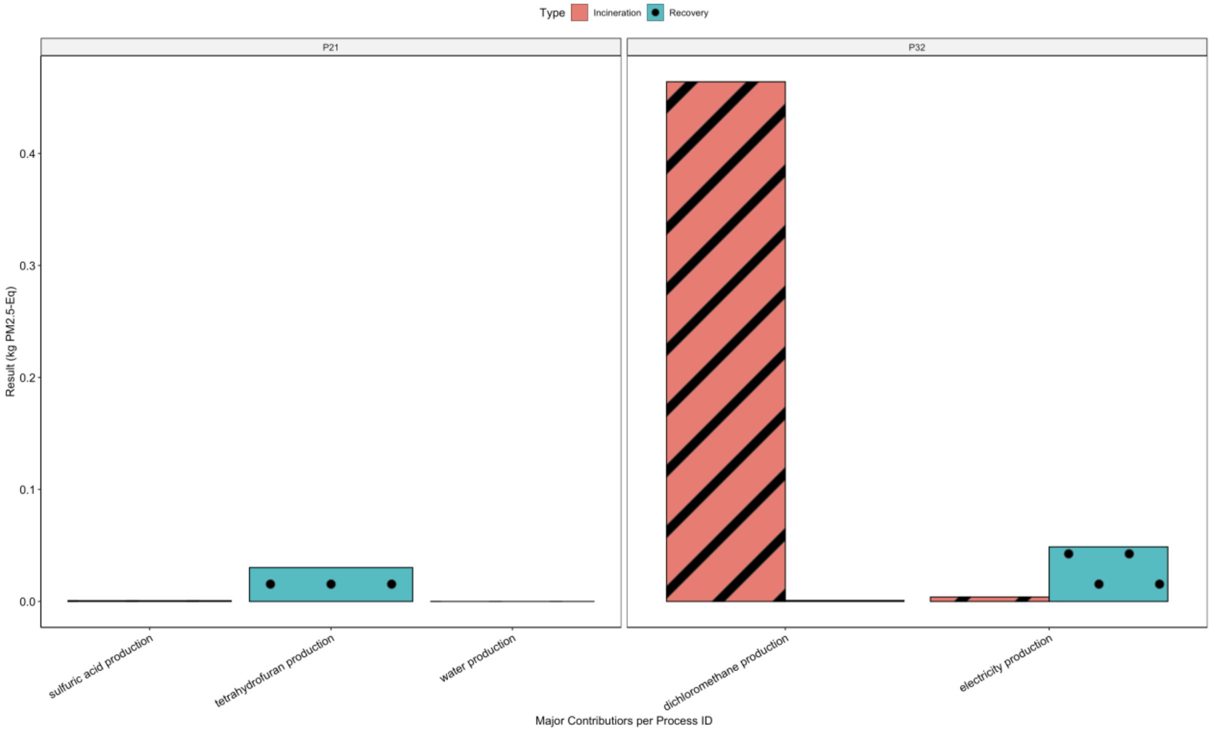

Figure 5-142. Major contributors for Process 21 and 32 for particulate matter formation potential (PMFP).

5.6.4.16 Photochemical Oxidant Formation Potential – Humans (HOFP) Contributors for Reactive Processes

Photochemical oxidant formation potential – humans (HOFP) major contributors for reactive processes can be found in Figure 5-143 and Figure 5-144 (for P21 & P32). Solvent production was the largest contributor for the incineration option, then followed by treatment of spent solvent mixture impacts. Treatment of spent solvent mixture impacts were eliminated in the recovery option and solvent production impacts were significantly decreased. Electricity production impacts were increased in the recovery option with the implementation of solvent recovery systems. Reactant production showed minimal impacts. For P32, ethyl acetate showed a positive effect on HOFP for the recovery option.

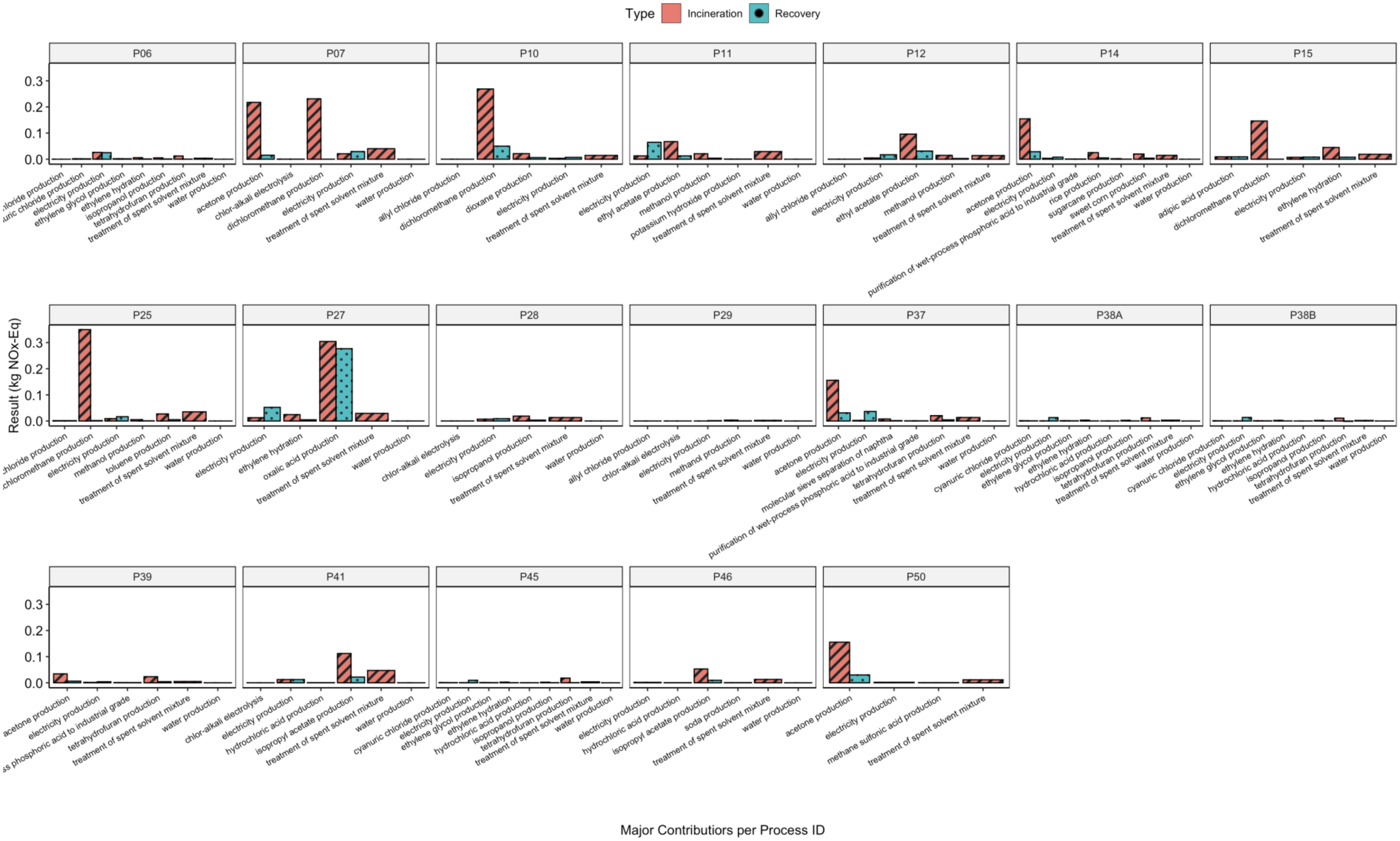

Figure 5-143. Major contributors for each reactive crystallization process for photochemical oxidant formation potential – humans (HOFP).

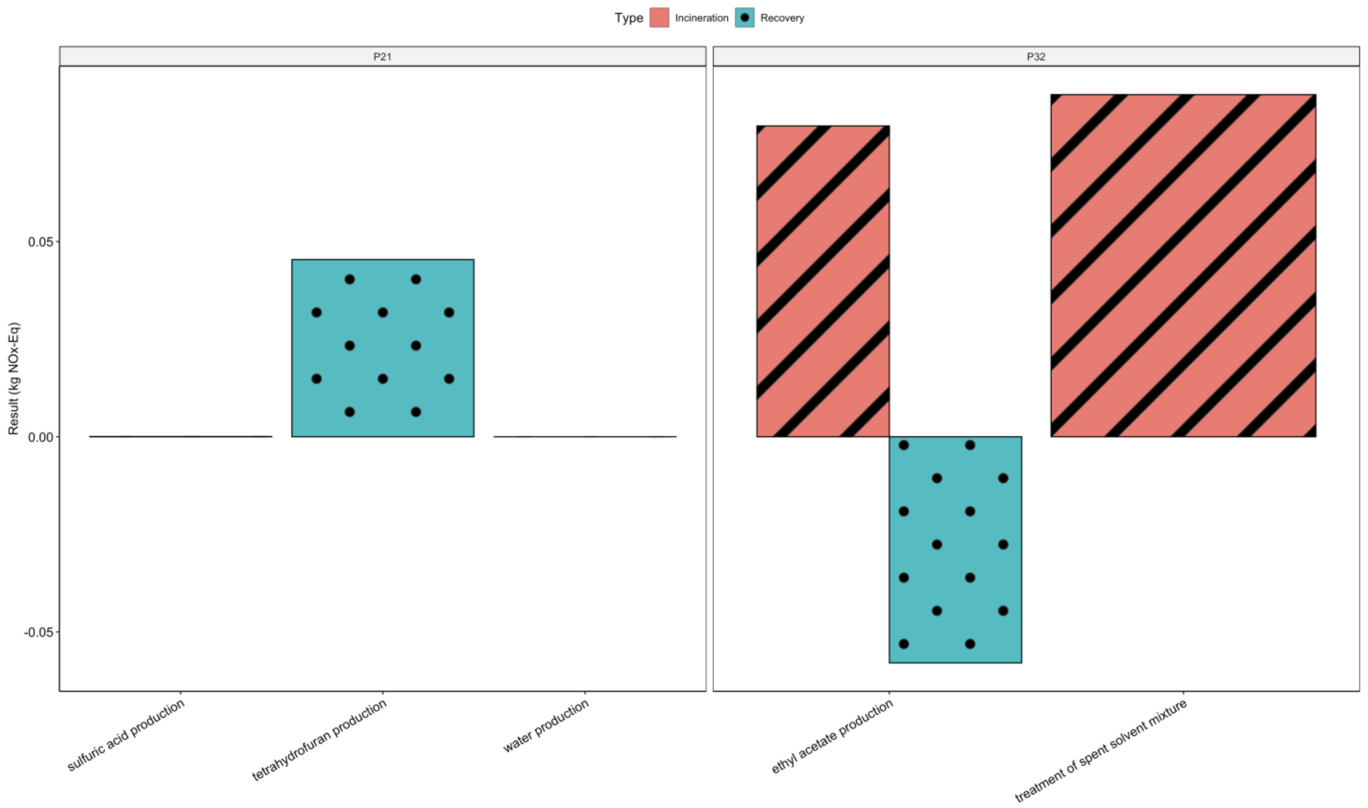

Figure 5-144. Major contributors for Process 21 and 32 for photochemical oxidant formation potential – humans (HOFP).

5.6.4.17 Photochemical Oxidant Formation Potential – Ecosystems (EOFP) Contributors for Reactive Processes

Photochemical oxidant formation potential – ecosystems (EOFP) major contributors for reactive processes can be found in Figure 5-145 and Figure 5-146 (for P21 & P32). EOFP results were similar to those of HOFP. Electricity production impacts increased with the recovery option, solvent production was largest in the incineration option but significantly decreased in the recovery option, and treatment of spent solvent mixture impacts were eliminated. Reactant production had minimal.

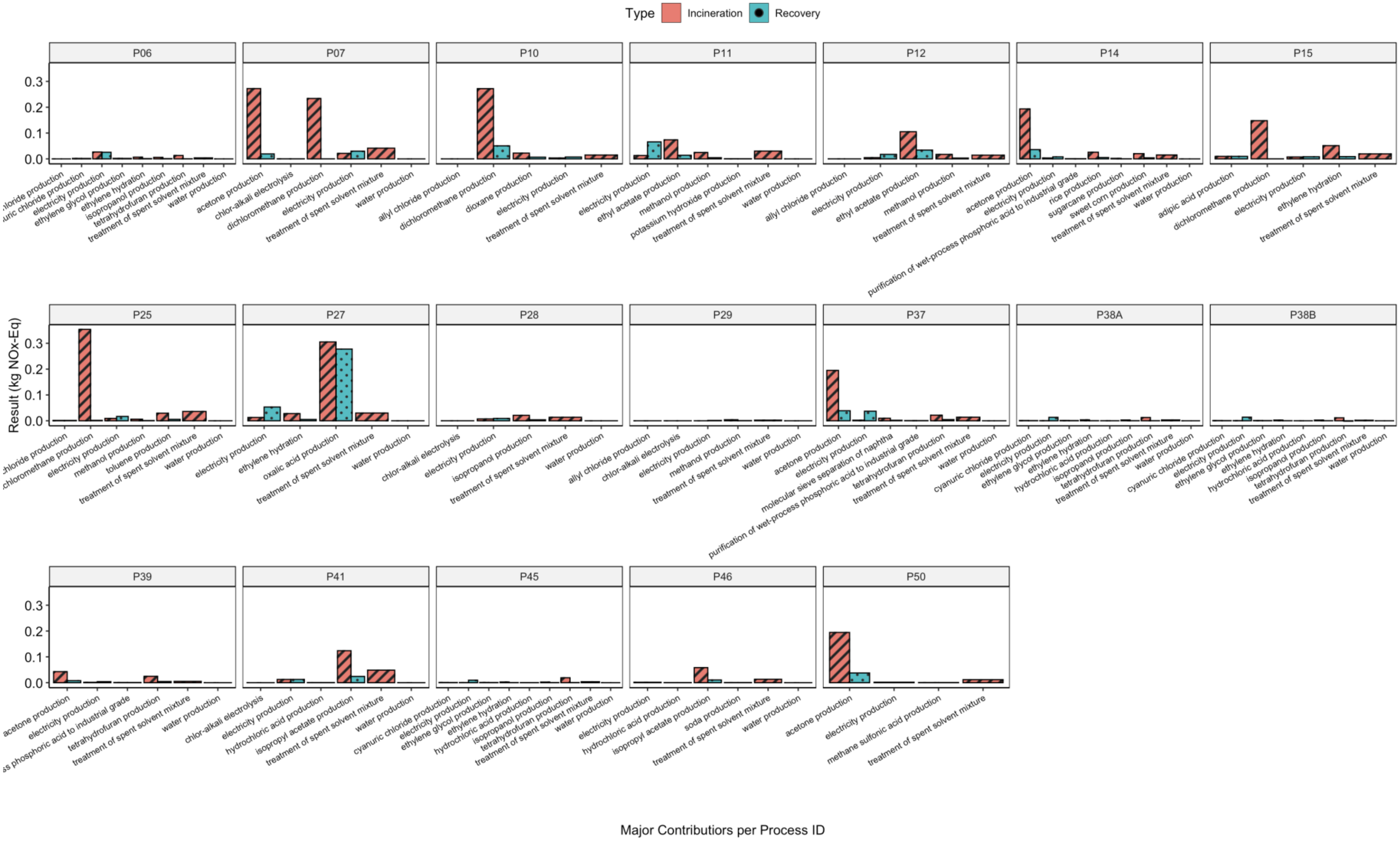

Figure 5-145. Major contributors for each reactive crystallization process for photochemical oxidant formation potential – ecosystems (EOFP).

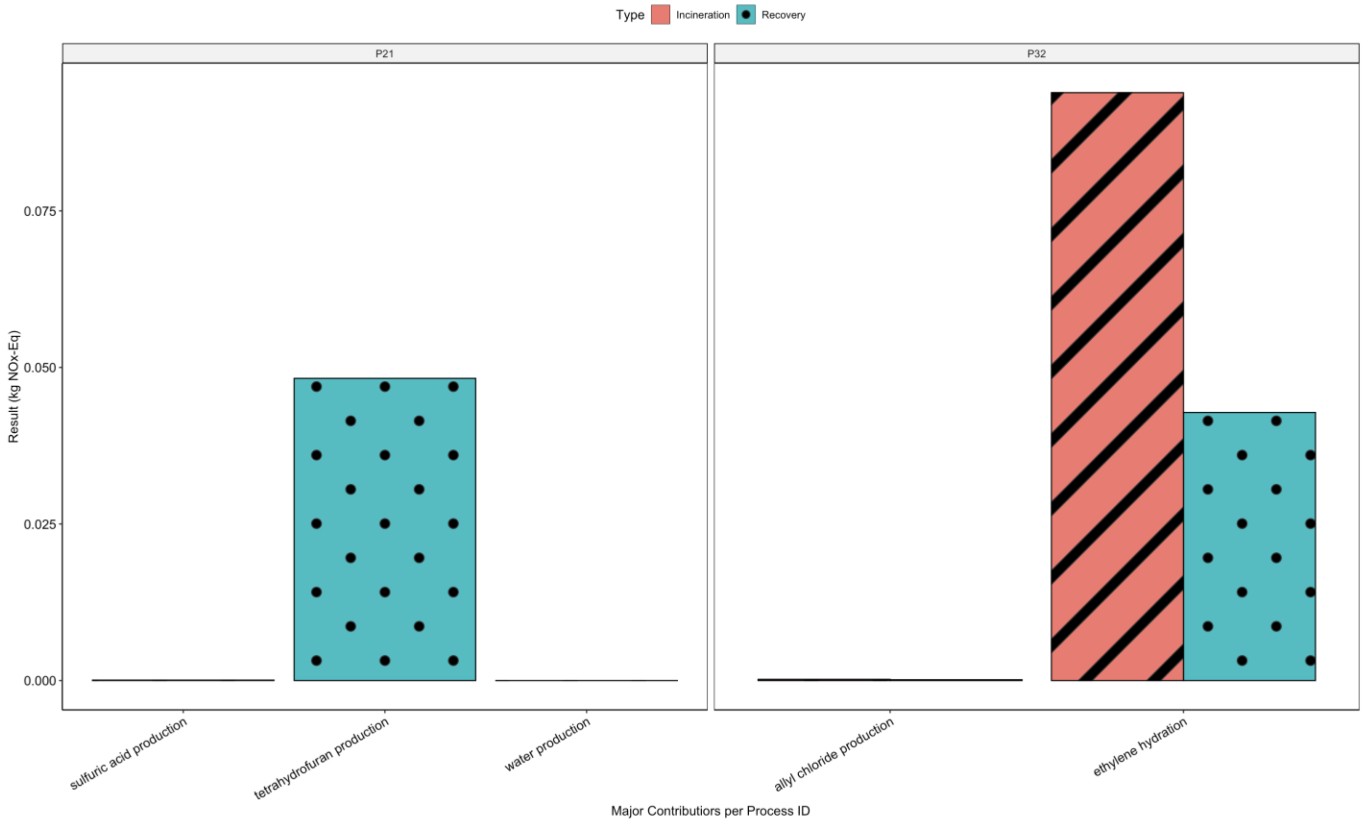

Figure 5-146. Major contributors for Process 21 and 32 for photochemical oxidant formation potential – ecosystems (EOFP).

5.6.4.18 Water Consumption Potential (WCP) Contributors for Reactive Processes

Water consumption potential (WCP) major contributors for reactive processes can be found in Figure 5-147 and Figure 5-148 (for P21 & P32). The largest contributors to this impact category were from the production of 2-MeTHF. This is due to the large water requirement needed to produce agricultural crops (i.e., corn, sugarcane, and rice). All other impacts were much lower but showed similar patterns to the other impact categories examined in this section.

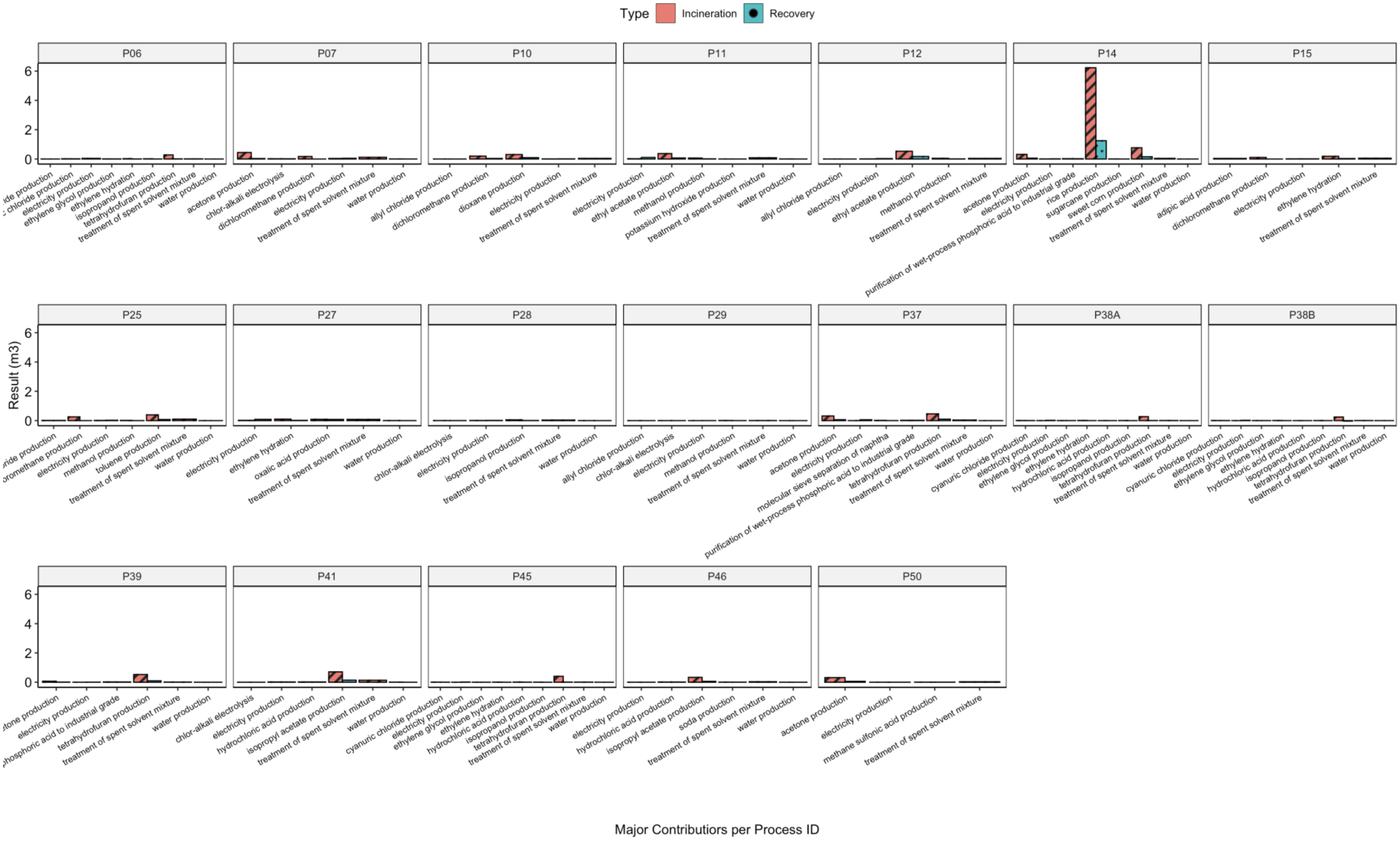

Figure 5-147. Major contributors for each reactive crystallization process for water consumption potential (WCP).

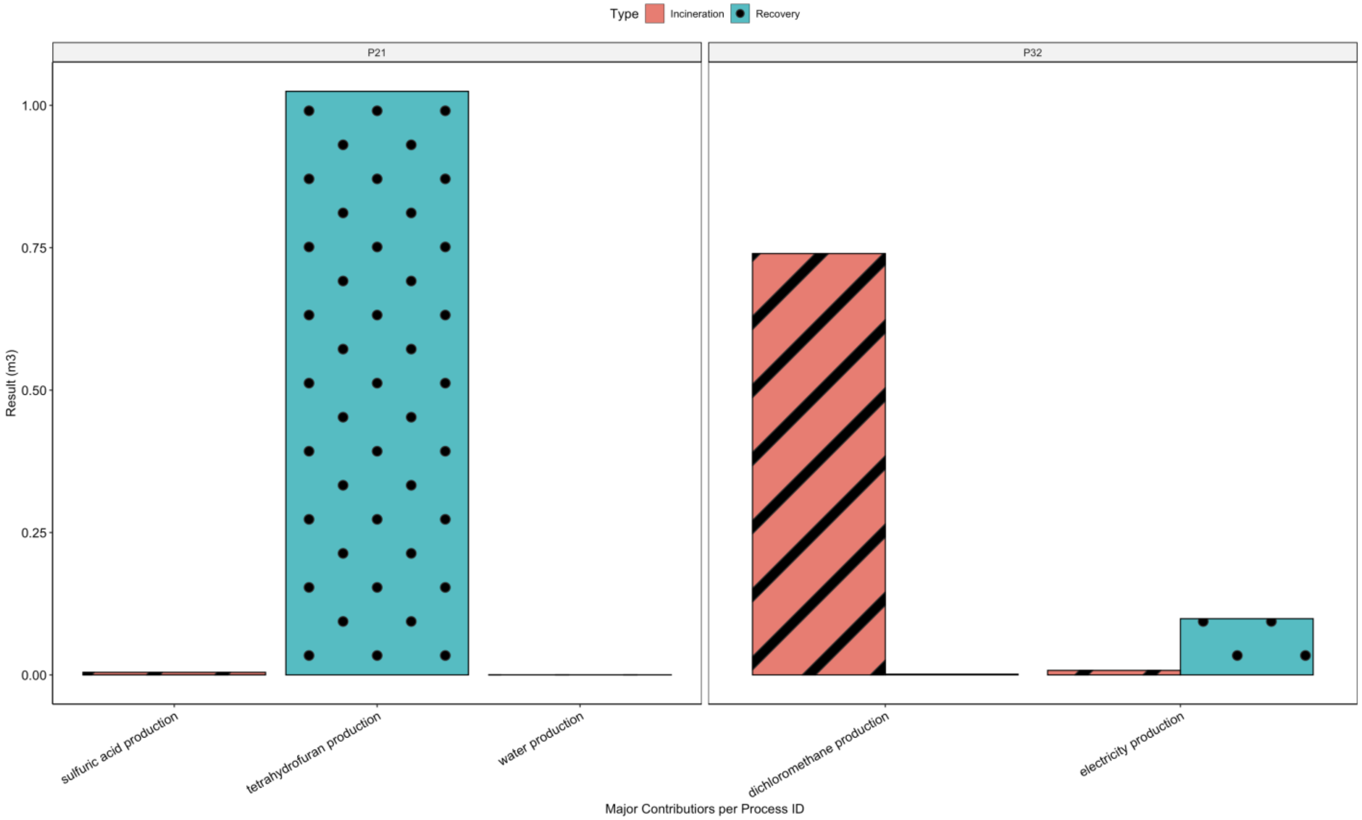

Figure 5-148. Major contributors for Process 21 and 32 for water consumption potential (WCP).

Overall, for the reactive processes, solvent production impacts was the largest contributor for all impact categories in the incineration option. The solvent production impacts significantly decreased during the recovery option due to the reuse of solvents. For some impact categories (e.g., LOP and WCP), 2-MeTHF had much larger impacts than other solvents due to the crop production required to produce the solvent. Treatment of spent solvent mixtures was the next largest contributor, then followed by electricity production. Treatment of spent solvent mixture impacts were eliminated in the recovery option since solvent was being reused. Electricity production increased in the recovery option due to the additional energy requirement from the implementation of the solvent recovery systems. Reactant production had minimal impacts when compared to the other contributors for all impact categories. For some impact categories, P32's ethyl acetate production produced a positive effect on the impacts for the recovery option.

In sum, for all crystallization types examined, solvent production was always the largest contributor for all processes in the incineration option. By implementing the solvent recovery systems, these impacts were able to be significantly reduced and allowed for lower impacts overall for the processes. Treatment of spent solvent mixtures was also a relatively large contributor to most processes for the incineration option. By implementing the solvent recovery systems, these impacts were eliminated, which helped decrease overall impacts for the processes. Electricity production was not usually the main contributor in the incineration option; however, it became more prominent in the recovery option due to the additional energy requirements needed for implementing the solvent recovery systems. However, these additional electricity production impacts usually did outweigh the decrease of impacts from solvent production and treatment of spent solvent mixtures. Results suggest that the recovery option is capable of significantly lowering overall impacts for all impact categories. The economic feasibility of implementing these systems will be examined in the next section.

5.6.5 LCIA Sensitivity Analysis

In conducting our LCIAs it is important to explore the sensitivity of our results to various assumptions and data sources. First, our LCI data collection focused primarily on crystallization processes at the laboratory scale. While we assumed linear scalability when extrapolating to larger industrial scales, it is essential to recognize that real-world industrial processes often involve efforts to optimize solvent usage during scaling up, a factor not explicitly considered in our analysis.

Additionally, we did not include the solvent required for equipment cleaning between batches in our LCIA. This omission may have underestimated the environmental impact by not accounting for the increased solvent waste associated with cleaning procedures.

Estimates of equipment energy usage, based on Parvatker et al. (2019), were validated through simple Aspen HYSYS simulations for select processes. However, conducting a more comprehensive simulation could provide deeper insights into specific energy requirements and further refine our LCIA results.

Moreover, the absence of API inventory data in our study means that the LCIA environmental impacts do not reflect any contributions from the API itself within the process.

Solvent inventory information was predominantly sourced from the Ecoinvent database, with solvents categorized as RoW (Rest of World) to denote data originating outside of Europe. While this approach allowed for broad comparability, it is important to acknowledge that region-specific variations may exist, which could influence LCIA outcomes. Further, some solvents in our inventory encompassed various synthesis routes, potentially impacting LCIA results. For consistency, we opted to use the most common synthesis method.

Last, the inventory data for 2-MeTHF, assumed to originate from agricultural crop production, lacked synthesis steps from agricultural crops to the final product. This gap may have affected the accuracy of LCIA results for processes involving 2-MeTHF.

5.7 Economic Analysis

Results from the previous sections have demonstrated that solvent recovery systems significantly reduce in total environmental impacts across all impact categories, however it is important to determine whether the implantation of such systems is economically feasible. The following section will examine the operating cost, capital cost, payback period, and return on investment of implementing these systems on three different production scales: 100, 1000, and 10,000 kg of API produced annually.

5.7.1 Operating Cost of Crystallization Processes

The operating cost associated with the processes were narrowed down to the cost associated with purchasing solvent, the cost of incinerating solvent waste, and the electricity cost associated with the energy requirement from all equipment. Figure 5-149 shows the breakdown of operating costs associated with each process and categorized by crystallization type. Although labour is an operational cost, it was not included in this figure since it requires the same number of operators for all three production scales. The cost of labour for the process, assuming operating 24 hours daily for 330 days annually is $237,600 annually, and the labour cost associated with the collection of waste to be sent for incineration (8 hours daily for 330 days annually) is $79,200. The purpose of this figure was to breakdown the remaining operating costs on the basis of kilogram of API produced.

It was found, that on average, 98.5% of the total operating cost was associated with solvent while only 1.3% and 0.2% were associated with incineration and electricity, respectively. Due to the large portion of operating cost being associated with solvent, incineration and electricity costs are near impossible to see in Figure 5-149. The cost breakdown of solvents can be found in Appendix C: Solvent Information. Overall, cooling crystallization had the lowest operating costs, excluding P33. This is mainly due to the lower amount of solvent being used in the process. P33 was elevated due to the large volume of methyl *tert*-butyl ether and its purchase price.

P16, P32, P43, and P49 had operating costs above $1000/kg API produced. P16's elevated operating cost was due to the high purchasing cost of isopropyl acetate and the large volume required. P32's high operating cost was due to the extremely large amount of dichloromethane used in the process. P43's high operating cost was associated with the large volumes of methyl *tert*-butyl ether and its purchase price. Finally, P49's high operating cost was associated with the high cost associated with purchasing dimethyl sulfoxide.

When comparing operating cost (Figure 5-149) with the total mass of solvent used per process (Figure 5-3), it can be seen that, in general, the purchase price of the solvent has a larger impact on operating cost than elevated volumes of solvent.

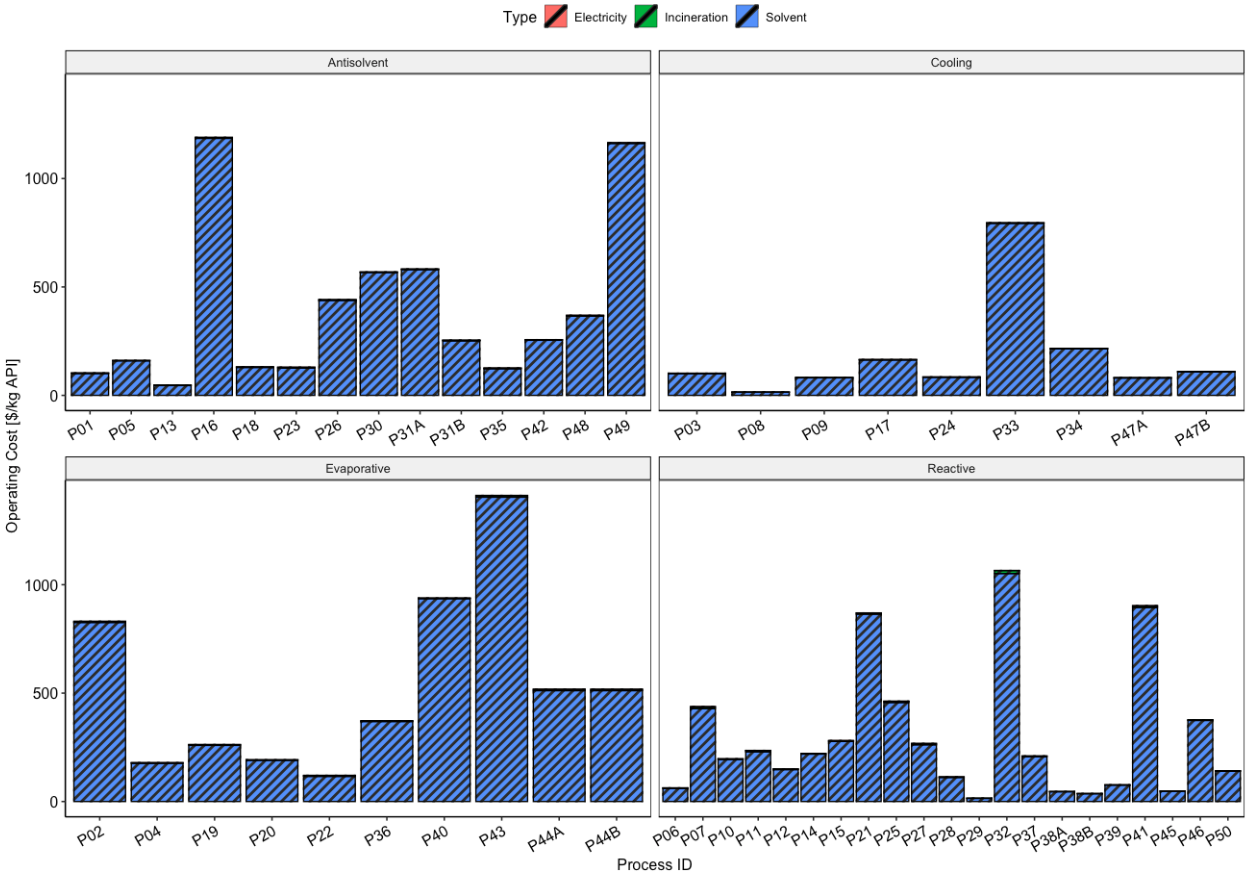

Figure 5-149. Operation cost associated to each crystallization process. Electricity and incineration components only comprised of 0.2 and 1.3%, respectively, and are extremely difficult to see in this figure. The bulk of the cost comes from purchase of solvent (98.5%).

5.7.2 Capital Cost of Solvent Recovery Systems

To determine the capital cost of the solvent recovery system, three different scales of API production were assessed (100, 1000, and 10,000 kg API produced on an annual basis). Figure 5-150 shows these capital costs for all three scales according to each process and categorized by crystallization type.

It is important to note that these three processes did not include any solvent recovery systems (P41, P46, P50) since they only used a single solvent, and its recovery post-filtration was at high enough purity levels to allow for reuse. Obviously, the capital cost increased with the larger quantities of API produced annually. However, this increase was not linear. By increasing the scale from 100 kg to 1000 capital cost of the solvent recovery system only doubled. When increasing the scale from 100 kg to 10,000 kg, the capital cost of was only four times the original cost.

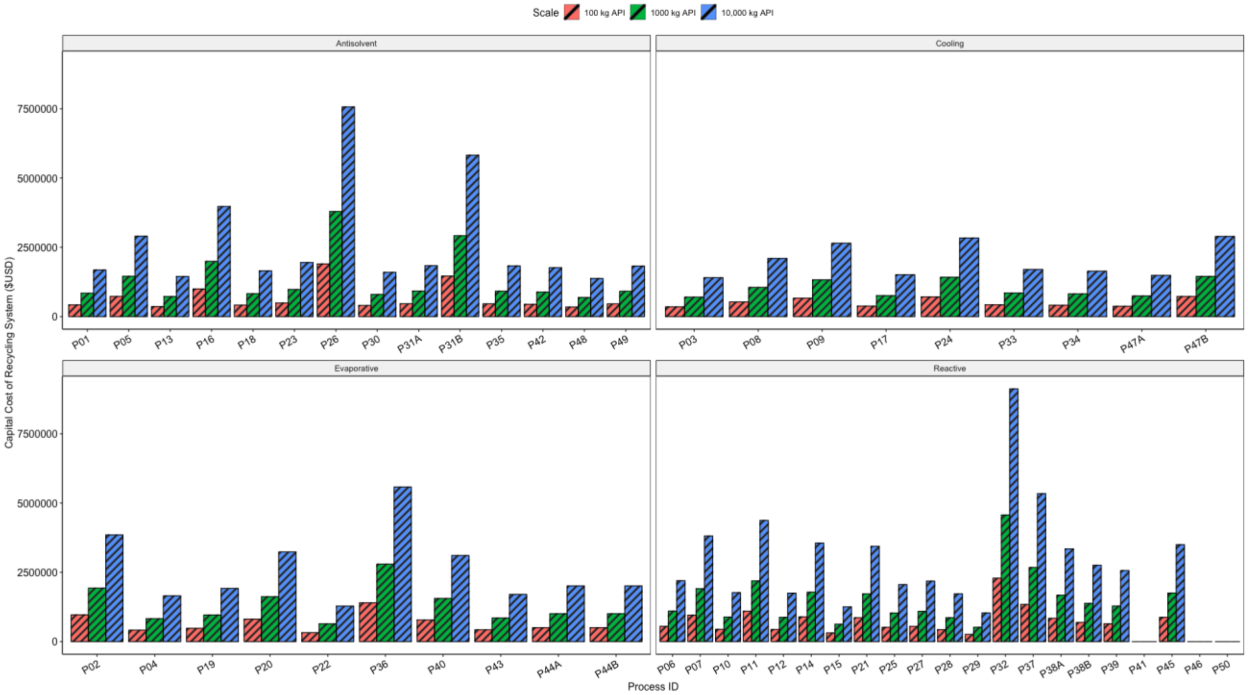

Figure 5-150. Capital cost associated to three scales of solvent recovery systems (100, 1000, and 10,000 kg of API produced annual).

5.7.3 Payback Period of Solvent Recovery Systems

The payback periods of the solvent recovery systems were determined by taking the capital cost of each system and using the cost savings of solvent reuse, savings from incineration, and cost savings associated with labour to the determine the payback period in years. The additional operating cost of electricity from the energy requirements of the solvent recovery equipment and additional labour requirement (24 hours daily for 330 days annually) were also considered. Three processes reached adequate solvent purity levels without the need of the implementation of solvent recovery systems (P41, P46, P50) and were not included in this analysis.

The 100 kg production scale was not profitable for any process and therefore not feasible. This was largely due to the labour cost of $237,600 associated with implementing the solvent recovery systems. Even with the large amount of solvent recovered, it could not make up for the large labour cost.

The 1000 kg production scale payback period results can be found in Figure 5-151. Twenty-five processes were not feasible due to the lack of annual profit. Like the 100 kg scale, these processes did not make enough profit to cover the additional labour cost due to implementing the solvent recovery systems. The remaining 26 processes showed a payback period range of 0.7 years (P42) to 23.7 years (P47B). The mean payback period for the 1000 kg scale was 8.7 ± 7.2 years. Since the life expectancy of the solvent recovery system was chosen to be 25 years, all 26 processes were feasible within this timeframe.

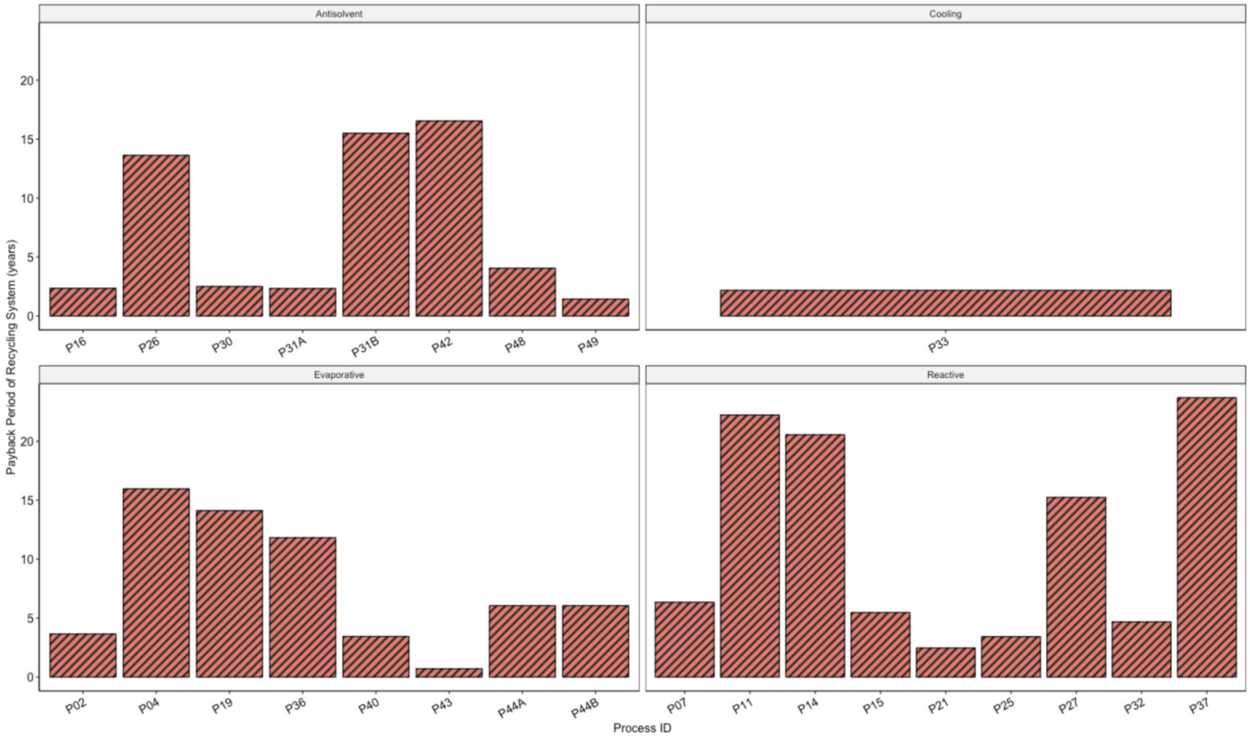

Figure 5-151. Payback periods for the 1000 kg API annual production scale. Only processes that were profitable in this figure.

The 10,000 kg production scale payback period results can be found in Figure 5-152. Only two processes were not feasible due to the lack of profit. These processes did not make enough profit to cover the additional labour cost of implementing the solvent recovery systems. The remaining 49 processes showed a payback period range of 0.13 years (P42) to 8.8 years (P47B). The mean payback period for the 10,000 kg scale was 2.2 ± 2.1 years. Since the life expectancy of the solvent recovery system was chosen to be 25 years, all 49 processes were feasible within this timeframe.

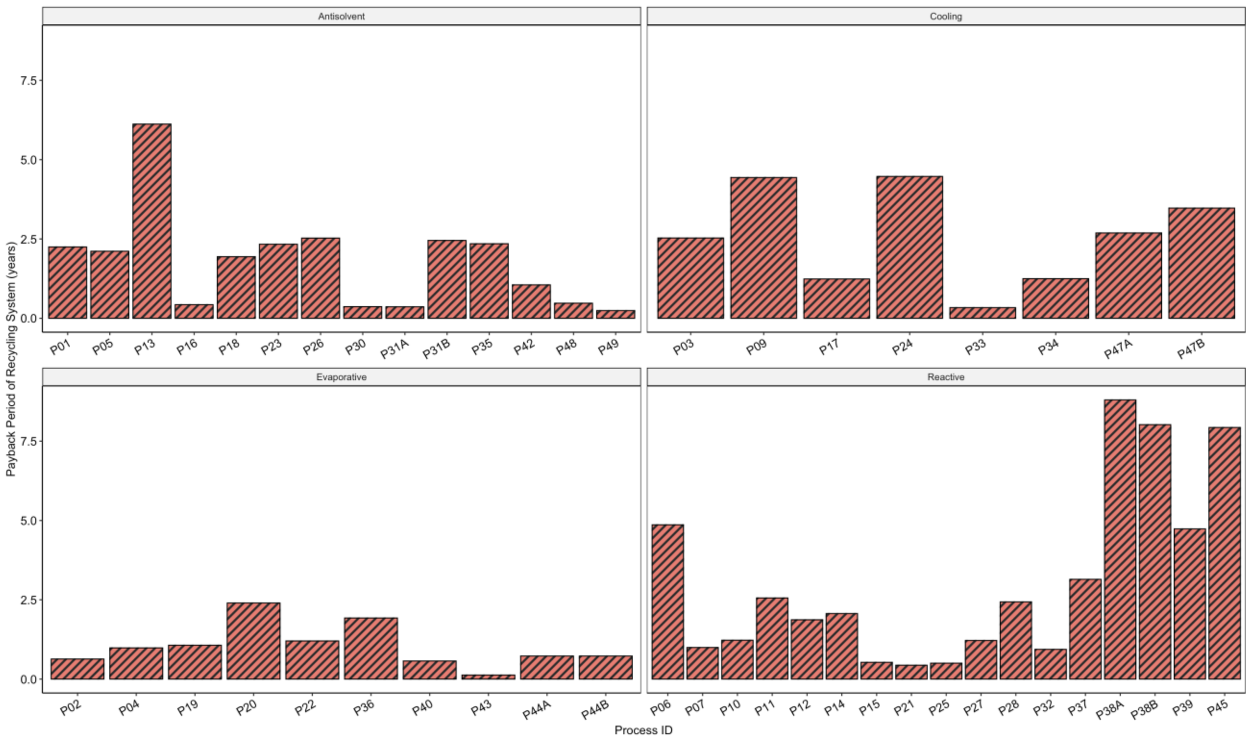

Figure 5-152. Payback periods for the 10,000 kg API annual production scale. Only processes that were profitable in this figure.

Overall, it was found that the payback period drastically decreased with increasing annual production scale of API. For a typical 25-year lifespan of the solvent recovery system, 96% of the 10,000 kg production scale processes were feasible while only 51% of the 1000 kg production scale processes were feasible. None of the 100 kg production scale processes were feasible due to the high labour cost associated with implementing a solvent recovery system.

For brand name pharmaceutical companies, drug patents typically last 20 years. The first 10 years of the patents are usually associated to the research and clinical trials stage (i.e., smaller production scales) while the last 10 years cover the fully scaled up process. Assuming the fully scaled up processes produced at least 10,000 kg of API annually, results show that these brand name pharmaceutical companies would be able to implement solvent recovery systems and payback the cost within less than 10 years for any of the processes.

5.7.4 Return on Investment of Solvent Recovery Systems

As mentioned in the previous section, none of the 100 kg production scale processes were profitable with the implementation of solvent recovery systems. Therefore, there was no return on investments.

The return on investment of solvent recovery systems for the 1000 kg production scale can be found in Figure 5-153. As mentioned in the previous section, only 26 processes were profitable. The range of ROIs were 0.22% (P05) to 140% (P43). The mean ROI for the 1000 kg production scale was 22.4 ± 29.3%.

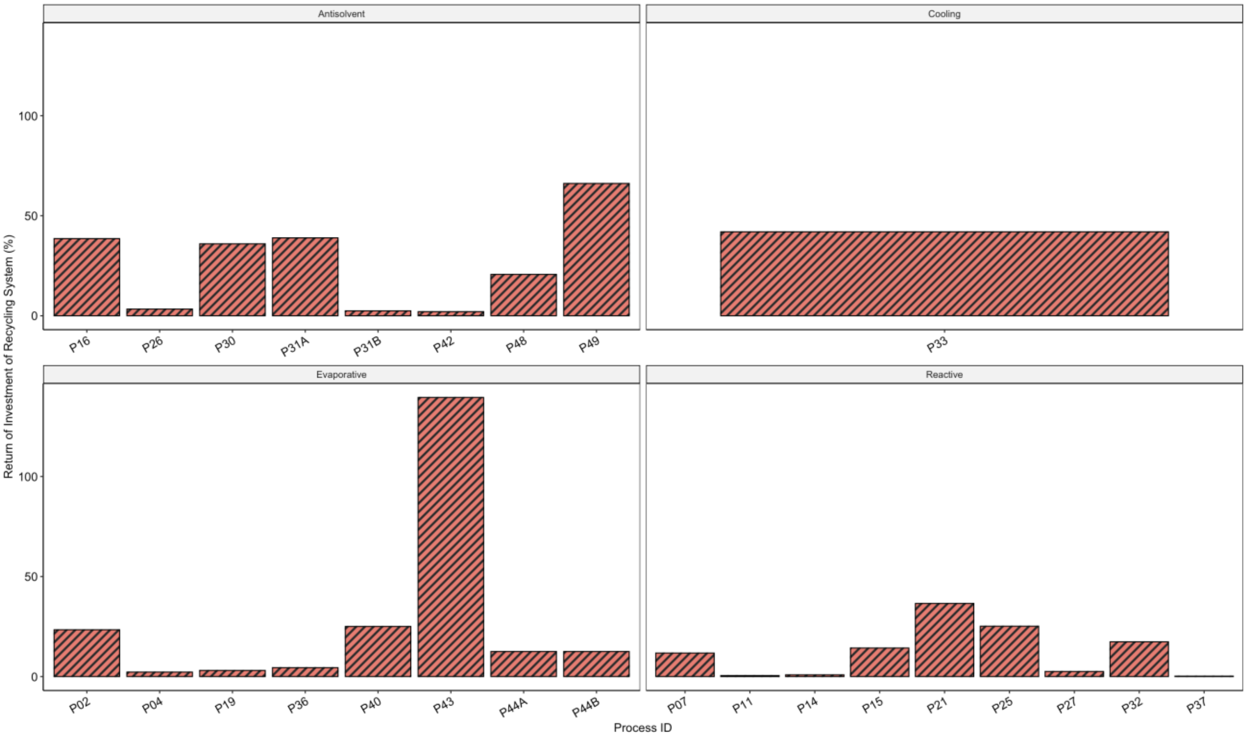

Figure 5-153. Return on investment for the 1000 kg API annual production scale. Only processes that were profitable in this figure.

The return of investment of solvent recovery systems for the 10,000 kg production scale can be found in Figure 5-153. As mentioned in the previous section, 49 processes were profitable. The range of ROIs were 7.4% (P38B) to 783% (P43). The mean ROI for the 10,000 kg production scale was 108 ± 133%.

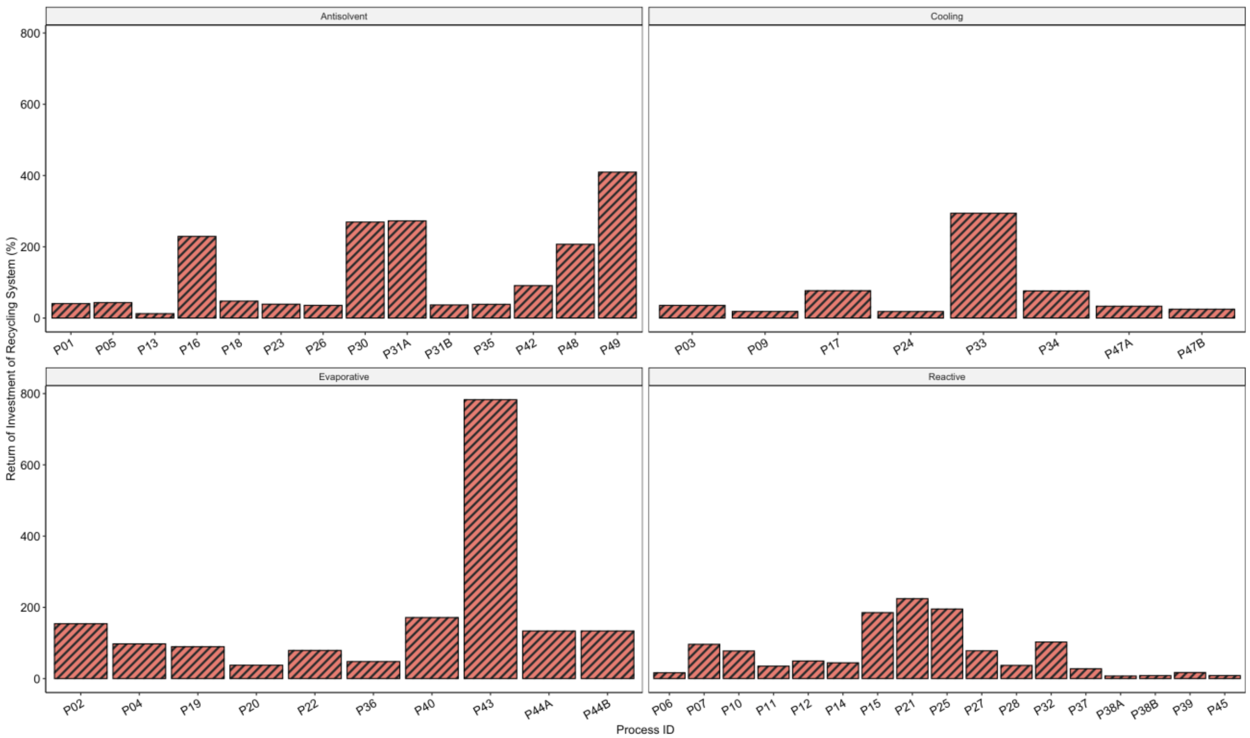

Figure 5-154. Return on investment for the 10,000 kg API annual production scale. Only processes that were profitable in this figure.

Overall, both the 1000 kg and 10,000 kg production scales showed high returns on investments for the solvent recovery systems. This strongly suggest that pharmaceutical companies should invest in solvent recovery systems because this would save them a lot of money.

5.7.5 Cost Savings

Most of the savings associated with solvent recovery systems come from solvent reuse and the reduction of cost associated with purchasing new solvent. Figure 5-155 shows the cost savings for each process by reusing solvent for the 1000 kg API annual production scale. On average, a cost savings of 76.4 ± 11.7% of operating costs comes from reuse of solvent.

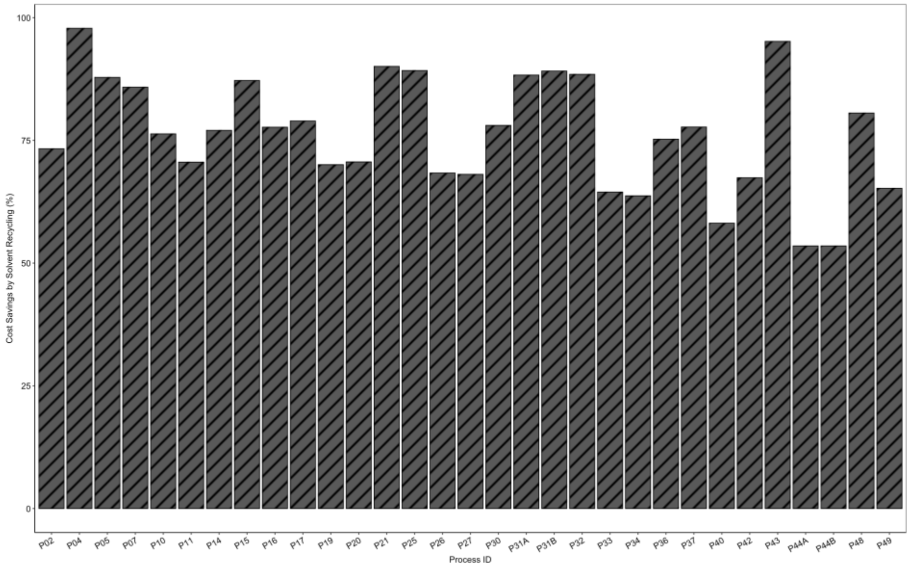

Figure 5-155. Cost savings by reuse of solvent when implementing solvent recovery systems for the 1000 kg API annual production scale. Only processes that had positive annual profit were considered.

Figure 5-156 shows the cost savings for each process by reusing solvent for the 10,000 kg API annual production scale. On average, a cost savings of 77.2 ± 11.8% of operating costs comes from reuse of solvent.

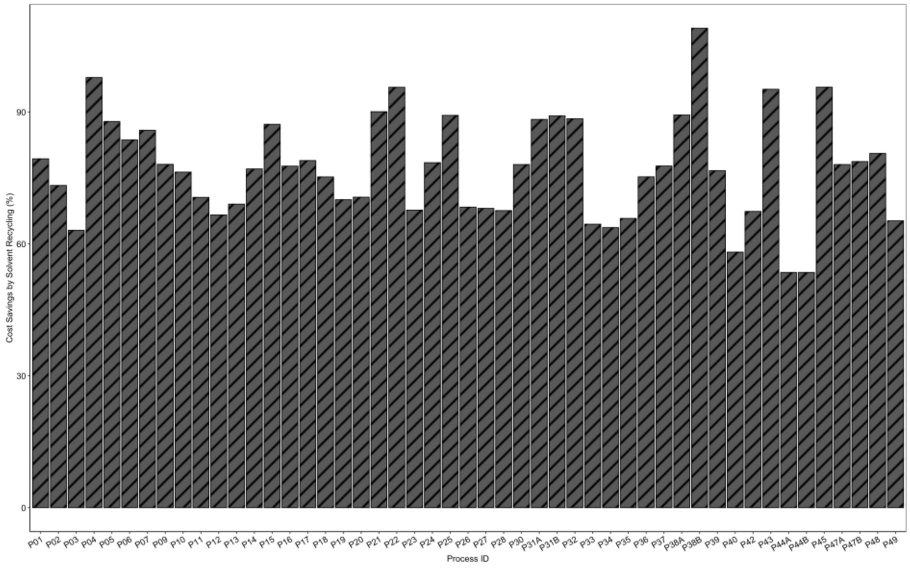

Figure 5-156. Cost savings by reuse of solvent when implementing solvent recovery systems for the 10,000 kg API annual production scale. Only processes that had positive annual profit were considered.

Overall, for all profitable processes at all scales, there was a 76.9 ± 11.7% cost savings by implementing solvent recovery systems instead of sending the spent solvent waste to incineration.

5.7.6 Economic Analysis Uncertainties

It is important to acknowledge the uncertainties inherent in this economic analysis. First, the capital cost estimates for the solvent recovery systems were intended as rough approximations. To refine our understanding, a more thorough capital cost estimation could be conducted for processes demonstrating viability. Moreover, the equations utilized to gauge capital costs were derived from data as far back as 2010, suggesting that capital expenses are likely to have escalated by 2024.

Additionally, the labour costs were estimated at a flat rate of $30 per hour, assuming 330 working days annually. However, these figures may fluctuate depending on the intricacies of the solvent recovery systems, thus warranting a deeper assessment.

Chapter 6: Conclusion

This project examined 54 crystallization processes for a total of 50 APIs for purification. Reactive crystallization processes were most common (21 processes – 38.9%) and then followed by antisolvent processes (14 processes – 25.9%). Evaporative and cooling processes had a similar number of processes, 10 (18.5%) and 9 (16.7%), respectively.

When examining the total mass of solvent used in the 54 processes, a total of 1250 kg of solvent was used. Water was the most prevalent solvent most commonly used in the API crystallization processes (used 22.6% of the time), accounting for 279 kg of the total mass. Dichloromethane, a class 2 solvent, accounted for 140 kg (11.3%) of the total mass. Heptane, a common antisolvent, accounted for 99 kg (8%) of the total mass. Other commonly used solvents included acetone (110 kg), ethyl acetate (92 kg), methanol (88 kg), ethanol (83 kg), isopropyl alcohol (76 kg), and tetrahydrofuran (59 kg).

It was found that class 3 solvents were used 74.1% of the time, while class 2 solvents were only used 25.9% of the time. Additionally, class 2 solvents were most used in reactive crystallization processes.

Reactive and evaporative crystallization processes tended to contain elevated amounts of solvents when compared to the other two crystallization types. However, some reactive processes (e.g., P06, P29, P38A, P38B, P38, and P45) used smaller amounts of solvents, similar to the amounts in cooling processes. Cooling had the lowest solvent usage over the other three crystallization types. Antisolvent processes had slightly higher usage of solvents from cooling processes, but lower than those for evaporative processes. Reactive process P32 used the largest amount of solvent (105 kg). This process also used larger amounts of class 2 solvent (dichloromethane). Therefore, P32 accounts for 75% of the total amount of dichloromethane used in all processes.

E-factors were determined to be highest in evaporative and reactive processes. As mentioned, P32 used very large amounts of dichloromethane, resulting in it the largest E-factor of all 54 processes. It is important to note that several reactive processes had very low E-factors. This is because these processes tended to use water as one of their main solvents. Evaporative processes had higher E-factors overall because organic solvents tended to be used, since they usually have lower boiling points than water. Antisolvent process E-Factors were higher than those of cooling processes because of the addition of an antisolvent (typically heptane) to the process.

The LCIAs of all processes showed that the incineration option produced greater results than the recovery option for all processes except P26. P26 had higher recovery option impacts due to poor separation caused by the close boiling points of the solvents. P16, P18, and P26 all used solvents that had relatively close boiling points (<2ºC) and showed a smaller decrease of impacts when implementing solvent recovery systems. Therefore, it is suggested that for these processes, alternative separation methods from distillation should be considered, such as pervaporation or membrane technologies. Cooling and antisolvent processes had smaller impacts across the impact categories. Evaporative and reactive processes produced more elevated results on average; however, reactive processes had a larger variance between processes when compared to evaporative processes.

When examining the LCIA solvent specific results, there were no significant differences between class 2 and class 3 solvents across the impact categories. Water always had the lowest impacts across all impact categories. Methanol and toluene also had relatively low impacts when compared to the remaining solvents. 2-MeTHF had high impacts throughout all categories, and this is likely associated with the amount of agricultural crops (corn, rice, and sugarcane) required to produce the solvent. Tetrahydrofuran had elevated impacts for most impact categories.

For all four crystallization types, solvent production was always showed to be the largest contributor in the incineration option. By implementing the solvent recovery systems, these impacts were able to be significantly reduced and allowed for lower impacts overall for the processes. Treatment of spent solvent mixtures also was shown to be a relatively large contributor to most processes for the incineration option. By implementing the solvent recovery systems, these impacts were eliminated, which helped decrease in lowering the overall impacts for the processes. Electricity production was not usually the main contributor in the incineration option; however, it became more prominent in the recovery option due to the additional energy requirements needed to operate the solvent recovery systems. However, these additional electricity production impacts usually outweighed the decrease in the impacts from solvent production and treatment of spent solvent mixtures. Results suggest that the recovery option is capable of significantly lowering overall impacts for all impact categories.

It was found, that on average, 98.5% of the total operating cost was associated with solvent while only 1.3% and 0.2% were associated to incineration and electricity, respectively. Overall, cooling crystallization had the lowest operating costs, excluding P33. This is mainly due to the smaller amount of solvent being used in the process. Elevated operating cost was usually due to the high purchasing cost of solvent and a large volume of it being used in the process. When comparing the operating cost with the total mass of solvent used per process, it was found that, in general, purchase price of the solvent has a larger impact on operating cost than the amount of solvent used.

The capital cost of the solvent recovery systems was significantly reduced (per kg API produced basis) at larger scales. Only a 4-fold capital cost increase was observed between the 100 kg to 10,000 kg production scale.

The payback period drastically decreased with increasing annual production scale of API. For a typical 25-year lifespan of the solvent recovery system, 96% of the 10,000 kg production scale processes were feasible while only 61% of the 1000 kg production scale processes were feasible. None of the 100 kg production scale processes were feasible due to the high labour cost associated with implementing a solvent recovery system.

Both the 1000 kg and 10,000 kg API production scales produced high returns on investments for the solvent recovery systems. This strongly suggest that pharmaceutical companies should invest in solvent recovery systems because they would save a lot of money. For all profitable processes at all scales, there was a 76.9 ± 11.7% cost savings by implementing solvent recovery systems instead of sending the spent solvent waste to incineration.

From the results, it can be determined that the most important variables effecting LCIAs and economics come from solvent choice and total volume of solvent used. Therefore, going forward, researchers should take into consideration which solvents they are using and try to limit the number of volumes required for the process. Ideally, researchers should avoid solvents like tetrahydrofuran and try to use more water, when possible.

Moving forward, it is recommended to continue the investigation of LCIAs for crystallization processes with a larger sample size. Expanding the sample size is crucial as it enhances the statistical robustness of the findings, thereby allowing for more reliable conclusions to be drawn from the data. Particularly, a larger sample size is suggested for all processes, with special emphasis on cooling and evaporative processes, which had relatively low numbers of processes, 9 and 10, respectively. Ideally, an equal number of samples should be chosen for all four crystallization types to facilitate better comparison between different methods.

Further, it is essential to explore alternative variables to enhance our understanding of environmental impacts associated with crystallization processes. Variables such as categorizing solvents based on their types (e.g., protic, aprotic) or by ranges in solvent viscosities could offer valuable insights into environmental implications beyond the scope of the current study.

Additionally, obtaining inventory data for all APIs would significantly contribute to a comprehensive cradle-to-gate/grave analysis. This approach will enable a deeper assessment of environmental impacts, leading to more thorough LCIA results and better-informed decision-making processes.

Future work could also involve examining ongoing research to assess the feasibility of modifying solvent choices to reduce environmental impacts while maintaining desired purities and yields. This aligns with the project's objectives and could provide valuable insights for optimizing environmental performance in crystallization processes.

Further, alternative solvent recovery technologies such as pervaporation or membrane units should be explored to address the limitations of traditional distillation methods. Several solvent recovery systems were found to have elevated impacts due to inefficient distillation separations, particularly with close-boiling solvents. Adopting alternative technologies could lead to more sustainable solvent recovery practices and mitigate associated environmental impacts.

Additionally, conducting a more detailed economic analysis to determine better capital cost estimates for each solvent recovery process is recommended. The economic analysis could also be expanded to include the capital cost required for the original crystallization process. Cost of labor could be better estimated once a more in-depth capital cost analysis is conducted to determine the cost associated with labor. An analysis on whether it is more feasible for the API facility to send its waste to an incineration plant or develop its own incineration plant should also be conducted.

Finally, once the important variables have been identified and validated, a comparative assessment method could be created to help researchers choose between various options. This could take the form of a tool where a researcher inputs criteria (e.g., solvents used, volumes of each solvent, type of crystallization method) for two or more options, and the tool evaluates these options using results from this project. By pursuing these avenues of research, we can further advance our understanding of environmental implications associated with crystallization processes and contribute to the development of more sustainable manufacturing practices in the pharmaceutical industry.

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Appendix A: Crystallization Process Details

The following appendix contains all process flow diagrams, equipment lists, mass flows, and energy requirements for all 54 processes analyzed.

A.1.1 Process 01 – Antisolvent Crystallization

The process flow diagram of Process 01 can be found in Figure A-1. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-1 and Table A-2, respectively. The mass of solvent recovered from Process 01 using solvent recovery techniques are reported in Table A-3.

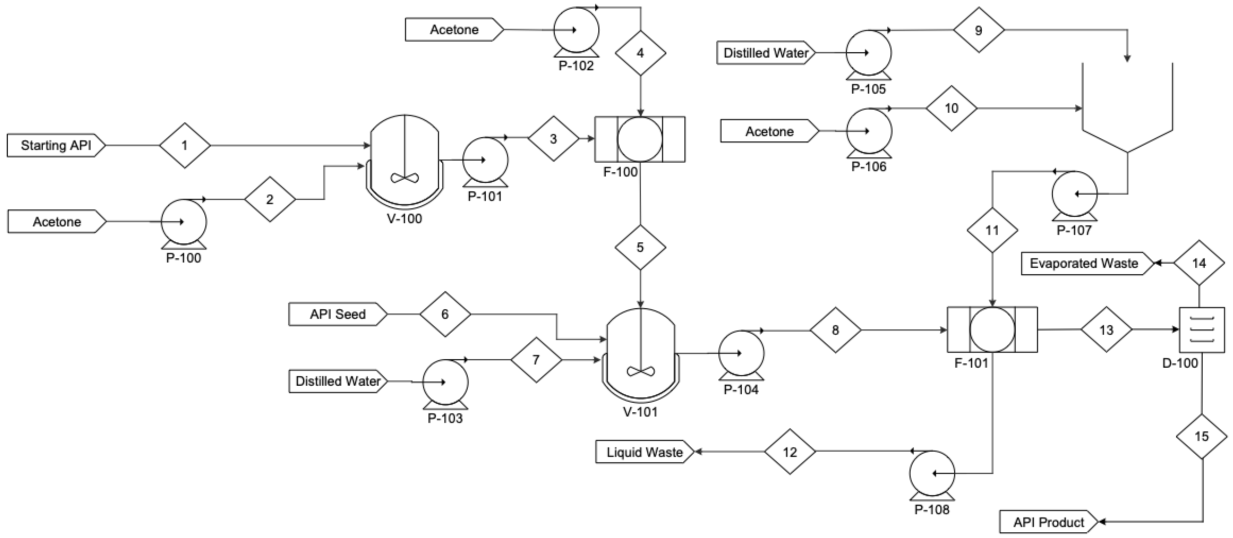


Figure A-1. Process flow diagram of Process 01 – Antisolvent Crystallization.

Table A-1. Mass of Each Component in Each Stream of Process 01 (According to Figure A-1). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API (g)	Acetone (g)	Distilled Water (g)
1	1100.11	0.00	0.00
2	0.00	6037.41	0.00
3	1100.11	6037.41	0.00
4	0.00	431.24	0.00
5	1100.11	6468.65	0.00

6	11.00	0.00	0.00
7	0.00	0.00	8226.08
8	1111.11	6468.65	8226.08
9	0.00	0.00	1645.22
10	0.00	1293.73	0.00
11	0.00	1293.73	1645.22
12	111.11	6209.91	7897.04
13	1000.00	1552.48	1974.26
14	0.00	1552.48	1974.26
15	1000.00	0.00	0.00
Solvent Recovery System	---	---	---
16	0.00	6147.81	30.89
17	111.11	62.10	7866.14
20	11.11	49.68	6292.91
21	100.00	12.42	1573.23
22	0.00	12.42	1573.23
23	100.00	0.00	0.00

Table A-2. Equipment Description for Process 01 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-100	Centrifugal Pump	9.24E-05	
P-101	Centrifugal Pump	1.09E-04	
P-102	Centrifugal Pump	6.60E-06	
P-103	Centrifugal Pump	1.26E-04	
P-104	Centrifugal Pump	2.42E-04	
P-105	Centrifugal Pump	2.52E-05	
P-106	Centrifugal Pump	1.98E-05	
P-107	Centrifugal Pump	4.50E-05	
P-108	Centrifugal Pump	2.18E-04	
V-100	Heating Vessel with Mixing	1.00E-01	Heating requirement

		3.18E-04	Mixing requirement
V-101	Cooling Vessel with Mixing	-6.34E-02	Cooling requirement
		8.13E-03	Mixing requirement
F-100	Polish Filtration Unit	7.57E-02	
F-101	Filtration Unit	1.87E-01	
D-100	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		1.79E+00	Heating requirement
Solvent Recovery System	---	---	---
SR-P-100	Centrifugal Pump	9.45E-05	
SR-P-101	Centrifugal Pump	1.23E-04	
SR-P-104	Centrifugal Pump	9.72E-05	
SR-C-100	Distillation Column	0.99978275	
SR-F-100	Filter	8.04E-02	
SR-D-100	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		1.37E+00	Heating requirement

Table A-3. Recovered Solvent from the Solvent Recovery System Implemented to Process 01 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Acetone	6178.70	99.50%
Water	6353.71	99.04%

A.1.2 Process 02 – Evaporative Crystallization

The process flow diagram of Process 02 can be found in Figure A-2. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-4 and Table A-5, respectively. The mass of solvent recovered from Process 02 using solvent recovery techniques are reported in Table A-6.

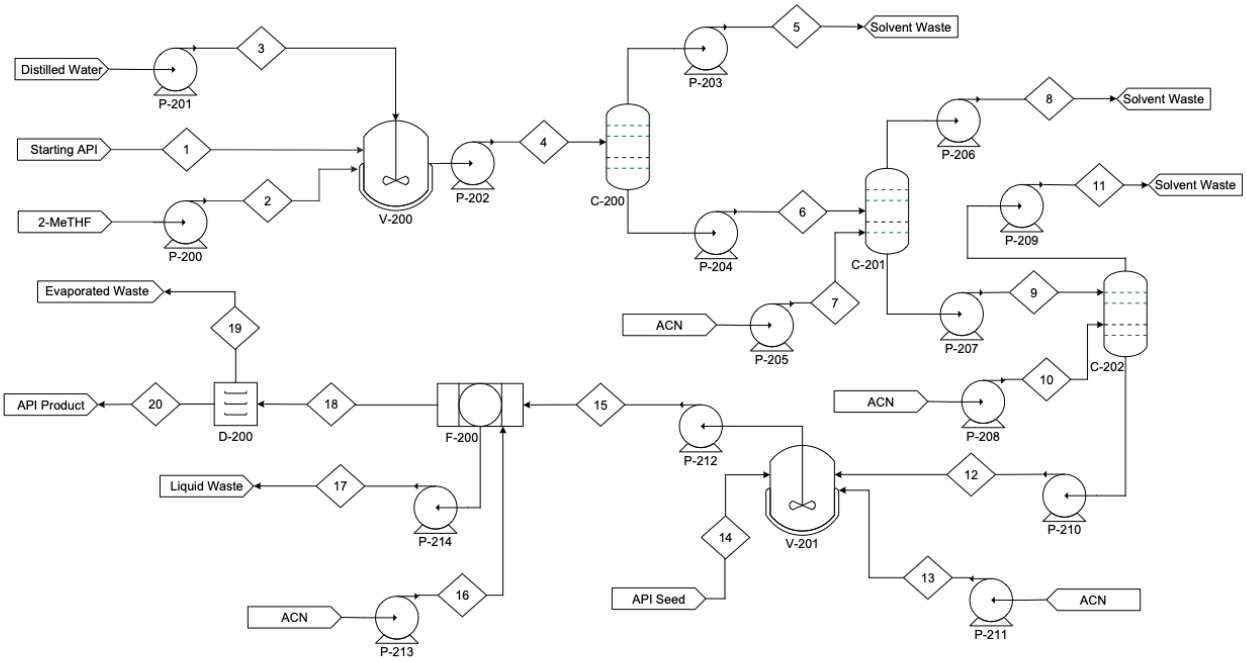


Figure A-2. Process flow diagram of Process 02 – Evaporative Crystallization.

Table A-4. Mass of Each Component in Each Stream of Process 02 (According to Figure A-2). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API (g)	2-MeTHF (g)	Distilled Water (g)	Acetonitrile (g)
1	1042.21	0.00	0.00	0.00
2	0.00	10324.55	0.00	0.00
3	0.00	0.00	415.63	0.00
4	1042.21	10324.55	415.63	0.00
5	0.00	3382.18	0.00	0.00
6	1042.21	6942.37	415.63	0.00
7	0.00	0.00	0.00	7864.10
8	0.00	559.53	0.00	3591.67
9	1042.21	6382.84	415.63	4272.44
10	0.00	0.00	0.00	7864.10
11	0.00	48.48	0.00	3212.44
12	1042.21	6334.36	415.63	8924.10
13	0.00	0.00	0.00	1474.52
14	10.42	0.00	0.00	0.00
15	1052.63	6334.36	415.63	10398.62

16	0.00	0.00	0.00	1310.68
17	52.63	5067.49	332.51	9367.44
18	1000.00	1266.87	83.13	2341.86
19	0.00	1266.87	83.13	2341.86
20	1000.00	0.00	0.00	0.00
Solvent Recovery System	---	---	---	---
21	0.00	5618.74	14.12	14.12
22	52.63	8.28	318.39	16157.43
23	0.00	8.28	72.10	15995.86
24	52.63	0.00	246.29	161.57
23	0.00	0.00	0.80	159.96
24	52.63	0.00	245.48	1.62
25	5.26	0.00	196.39	1.29
26	47.37	0.00	49.10	0.32
27	0.00	0.00	49.10	0.32
28	47.37	0.00	0.00	0.00

Table A-5. Equipment Description for Process 02 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment**	**Energy Requirement (kWh)**	**Note**
P-200	Centrifugal Pump	1.58E-04	
P-201	Centrifugal Pump	6.36E-06	
P-202	Centrifugal Pump	1.80E-04	
P-203	Centrifugal Pump	5.17E-05	
P-204	Centrifugal Pump	1.29E-04	
P-205	Centrifugal Pump	1.20E-04	
P-206	Centrifugal Pump	6.35E-05	
P-207	Centrifugal Pump	1.85E-04	
P-208	Centrifugal Pump	1.20E-04	
P-209	Centrifugal Pump	4.99E-05	
P-210	Centrifugal Pump	2.56E-04	
P-211	Centrifugal Pump	2.26E-05	
P-212	Centrifugal Pump	2.78E-04	

P-213	Centrifugal Pump	2.01E-05	
P-214	Centrifugal Pump	2.27E-04	
V-200	Mixing Vessel with Heating	3.31E-01	Heating requirement
		7.74E-04	Mixing Requirement
V-201	Mixing Vessel with Cooling	-9.84E-01	Cooling Requirement
		2.33E-02	Mixing Requirement
C-200	Distillation Column	6.84E-01	
C-201	Distillation Column	7.81E+00	
C-202	Distillation Column	7.01E+00	
F-200	Filtration Unit	1.95E-04	
D-200	Vacuum Dryer	2.32E+00	Vacuum pump requirement
		1.02E+00	Heating requirement
Solvent Recovery System	---	---	---
SR-P-200	Pump	8.64E-05	
SR-P-201	Pump	2.53E-04	
SR-P-202	Pump	2.46E-04	
SR-P-203	Pump	7.05E-06	
SR-P-204	Pump	2.46E-06	
SR-P-205	Pump	4.59E-06	
SR-P-206	Pump	3.11E-06	
SR-C-200	Distillation Column	1.99E+01	
SR-C-201	Distillation Column	6.66E+00	
SR-C-202	Distillation Column	1.41E+00	
F-200	Filter	3.00E-06	
D-200	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		4.25E-02	Heating requirement

Table A-6. Recovered Solvent from the Solvent Recovery System Implemented to Process 02 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
2-Methyl tetrahydrofuran	5646.98	99.50%
Water	202.94	99.35%
Acetonitrile	16237.00	99.50%

A.1.3 Process 03 – Cooling Crystallization

The process flow diagram of Process 03 can be found in Figure A-3. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-7 and Table A-8, respectively. The mass of solvent recovered from Process 03 using solvent recovery techniques are reported in Table A-9.

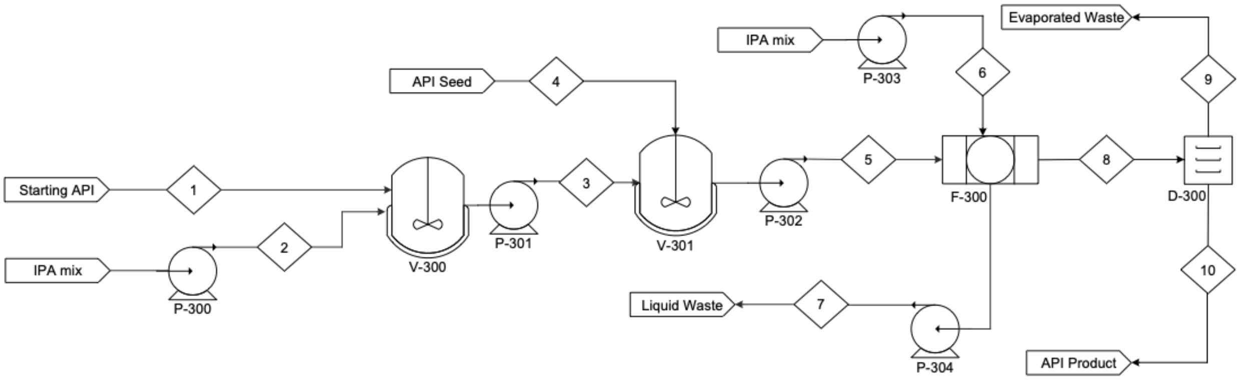


Figure A-3. Process flow diagram of Process 03 – Cooling Crystallization.

Table A-7. Mass of Each Component in Each Stream of Process 03 (According to Figure A-3). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**API (g)**	**IPA (g)**	**THF (g)**	**Distilled Water (g)**
1	1100.11	0.00	0.00	0.00
2	0.00	6886.37	39.08	4.39
3	1100.11	6886.37	39.08	4.39
4	11.00	0.00	0.00	0.00
5	1111.11	6886.37	39.08	4.39

6	0.00	2582.39	14.65	1.65
7	111.11	7575.01	42.98	4.83
8	1000.00	1893.75	10.75	1.21
9	0.00	1893.75	10.75	1.21
10	1000.00	0.00	0.00	0.00
Solvent Recovery System	**---**	**---**	**---**	**---**
16	0.00	0.11	42.55	0.11
17	111.11	7574.90	0.43	4.72
20	11.11	6059.92	0.34	3.78
21	100.00	1514.98	0.09	0.94
22	0.00	1514.98	0.09	0.94
23	100.00	0.00	0.00	0.00

Table A-8. Equipment Description for Process 03 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment**	**Energy Requirement (kWh)**	Note
P-300	Centrifugal Pump	1.06E-04	
P-301	Centrifugal Pump	1.23E-04	
P-302	Centrifugal Pump	1.23E-04	
P-303	Centrifugal Pump	3.98E-05	
P-304	Centrifugal Pump	1.18E-04	
V-300	Heating Vessel with Mixing	1.19E+00	Heating requirement
		6.49E-04	Mixing requirement
V-301	Cooling Vessel with Mixing	-1.51E+00	Cooling requirement
		2.76E-02	Mixing requirement
F-300	Filter	1.06E-01	
D-300	Vacuum dryer	5.79E-01	Vacuum pump requirement
		7.54E-01	Heating requirement
Solvent Recovery System	**---**	**---**	**---**

SR-P-300	Centrifugal Pump	6.54E-07	
SR-P-301	Centrifugal Pump	1.18E-04	
SR-P-302	Centrifugal Pump	9.29E-05	
SR-C-300	Distillation Column	1.67E+00	
SR-F-100	Filtration Unit	7.69E-02	
SR-D-100	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		2.47E-01	Heating requirement

Table A-9. Recovered Solvent from the Solvent Recovery System Implemented to Process 03 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Tetrahydrofuran	42.77	99.50%
Isopropyl Alcohol	6075.15	99.75%

A.1.4 Process 04 – Evaporative Crystallization

The process flow diagram of Process 04 can be found in Figure A-4. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-10 and Table A-11, respectively. The mass of solvent recovered from Process 04 using solvent recovery techniques are reported in Table A-12.

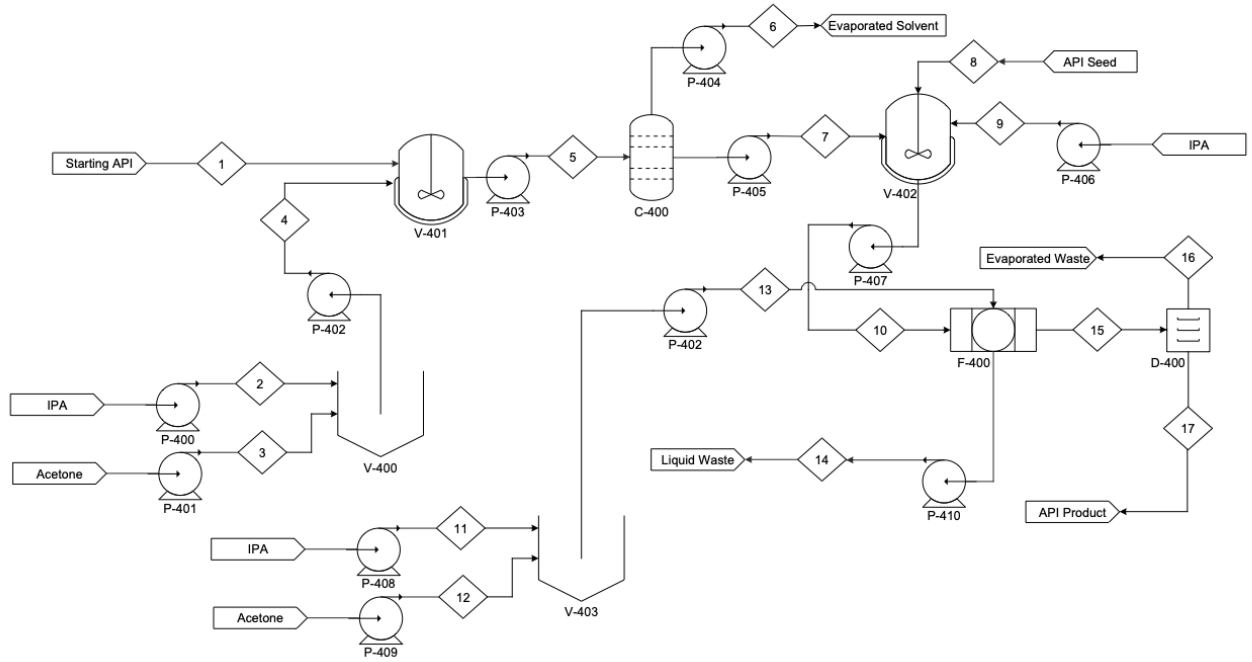


Figure A-4. Process flow diagram of Process 04 – Evaporative Crystallization.

Table A-10. Mass of Each Component in Each Stream of Process 04 (According to Figure A-4). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**API (g)**	**IPA (g)**	**Acetone (g)**
1	1047.39	0.00	0.00
2	0.00	1646.50	0.00
3	0.00	0.00	6569.26
4	0.00	1646.50	6569.26
5	1047.39	1646.50	6569.26
6	0.00	0.00	3284.63
7	1047.39	1646.50	3284.63
8	5.24	0.00	0.00
9	0.00	6586.02	0.00
10	1052.63	8232.52	3284.63
11	0.00	2956.17	0.00
12	0.00	0.00	328.46
13	0.00	2956.17	328.46
14	52.63	10069.82	3251.78
15	1000.00	1118.87	361.31

16	0.00	1118.87	361.31
17	1000.00	0.00	0.00
Solvent Recovery System	---	---	---
21	0.00	32.52	6471.05
22	52.63	10037.30	65.36
25	5.26	8029.84	52.29
26	47.37	2007.46	13.07
27	0.00	2007.46	13.07
28	47.37	0.00	0.00

Table A-11. Equipment Description for Process 04 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment**	**Energy Requirement (kWh)**	**Note**
P-400	Centrifugal Pump	2.48E-05	
P-401	Centrifugal Pump	9.90E-05	
P-402	Centrifugal Pump	1.24E-04	
P-403	Centrifugal Pump	1.40E-04	
P-404	Centrifugal Pump	4.95E-05	
P-405	Centrifugal Pump	9.01E-05	
P-406	Centrifugal Pump	9.93E-05	
P-407	Centrifugal Pump	1.90E-04	
P-408	Centrifugal Pump	4.46E-05	
P-409	Centrifugal Pump	4.95E-06	
P-410	Centrifugal Pump	4.95E-05	
P-411	Centrifugal Pump	2.02E-04	
C-400	Distillation Column	8.39E-02	
V-400	Solvent mixture vessel	0.00E+00	
V-401	Heating Vessel with Mixing	2.15E-01	Heating requirement
		2.94E-04	Mixing requirement
V-402	Cooling Vessel with Mixing	-1.08E+00	Cooling requirement

		2.23E-02	Mixing requirement
V-403	Solvent Mixture Vessel	0.00E+00	
F-400	Filtration Unit	3.28E-02	
D-400	Vacuum Dryer	2.32E+00	Vacuum pump requirement
		4.51E-01	Heating requirement
Solvent Recovery System	---	---	---
SR-P-400	Centrifugal Pump	9.95E-05	
SR-P-401	Centrifugal Pump	1.55E-04	
SR-P-402	Centrifugal Pump	1.24E-04	
SR-C-200	Distillation Column	3.51E-01	
F-200	Filtration Unit	1.02E-04	
D-200	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		6.82E-01	Heating requirement

Table A-12. Recovered Solvent from the Solvent Recovery System Implemented to Process 04 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Acetone	6503.57	99.50%
Isopropanol	11372.03	99.29%

A.1.5 Process 05 – Antisolvent Crystallization

The process flow diagram of Process 05 can be found in Figure A-5. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-13 and Table A-14, respectively. The mass of solvent recovered from Process 05 using solvent recovery techniques are reported in Table A-15.

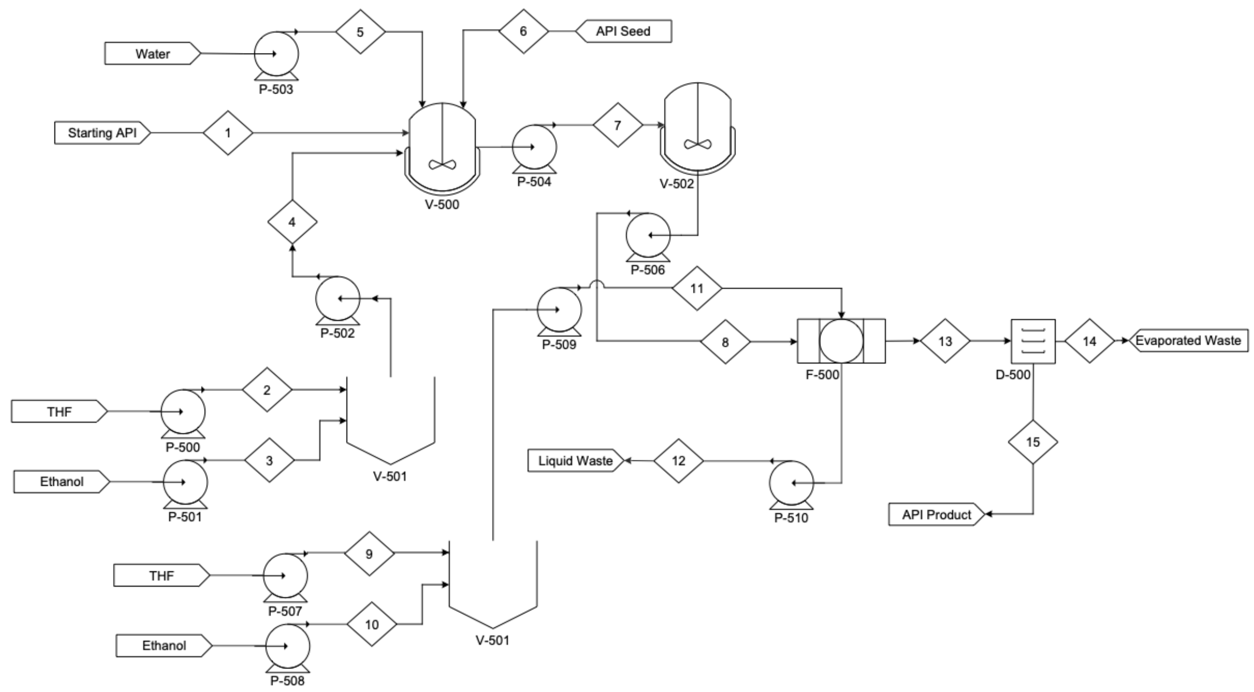


Figure A-5. Process flow diagram of Process 05 – Antisolvent Crystallization.

Table A-13. Mass of Each Component in Each Stream of Process 05 (According to Figure A-5). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API (g)	THF (g)	Ethanol (g)	Water (g)
1	1047.39	0.00	0.00	0.00
2	0.00	5208.48	0.00	0.00
3	0.00	0.00	1156.95	0.00
4	0.00	5208.48	1156.95	0.00
5	0.00	0.00	0.00	1461.95
6	5.24	0.00	0.00	0.00
7	1052.63	5208.48	1156.95	1461.95
8	1052.63	5208.48	1156.95	1461.95
9	0.00	0.00	0.00	417.70
10	0.00	0.00	1322.23	0.00
11	0.00	0.00	1322.23	417.70
12	52.63	4687.64	2231.26	1691.69
13	1000.00	520.85	247.92	187.97
14	0.00	520.85	247.92	187.97

15	1000.00	0.00	0.00	0.00
Solvent Recovery System	**---**	**---**	**---**	**---**
16	0.00	5.55	2208.95	5.55
17	52.63	4682.09	22.31	1686.14
16	0.00	4635.26	22.31	0.98
17	52.63	46.82	0.00	1685.16
20	5.26	37.46	0.00	1348.13
21	47.37	9.36	0.00	337.03
22	0.00	9.36	0.00	337.03
23	47.37	0.00	0.00	0.00

Table A-14. Equipment Description for Process 05 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Description**	**Energy Requirement (kWh)**	**Note**
P-505	Centrifugal Pump	1.36E-04	
P-506	Centrifugal Pump	6.39E-06	
P-507	Centrifugal Pump	2.02E-05	
P-508	Centrifugal Pump	2.66E-05	
P-509	Centrifugal Pump	1.33E-04	
V-500	Heating Vessel with Mixing	4.48E-02	Heating requirement
		5.75E-03	Mixing requirement
V-501	Solvent Mixture Tank	0.00E+00	
V-502	Cooling Vessel with Mixing	-4.52E-01	Cooling requirement
		2.76E-03	Mixing requirement
V-503	Solvent mixture tank	0.00E+00	
F-500	Filtration Unit	1.06E-01	
D-500	Vacuum Dryer	3.32E-01	Heating requirement
		5.79E-01	Vacuum pump requirement
Solvent Recovery System	**---**	**---**	**---**

SR-P-500	Centrifugal Pump	3.40E-05	
SR-P-501	Centrifugal Pump	9.86E-05	
SR-P-502	Centrifugal Pump	7.13E-05	
SR-C-500	Distillation Column	3.97E+00	
SR-C-501	Distillation Column	3.61E+00	
SR-F-500	Filtration Unit	1.78E-02	
SR-D-500	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		2.92E-01	Heating requirement

Table A-15. Recovered Solvent from the Solvent Recovery System Implemented to Process 04 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Ethanol	2220.05	99.50%
Tetrahydrofuran	4658.56	99.50%
Water	1390.85	96.93%

A.1.6 Process 06 – Reactive Crystallization

The process flow diagram of Process 06 can be found in Figure A-6. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-16 and Table A-17, respectively. The mass of solvent recovered from Process 06 using solvent recovery techniques are reported in Table A-18.

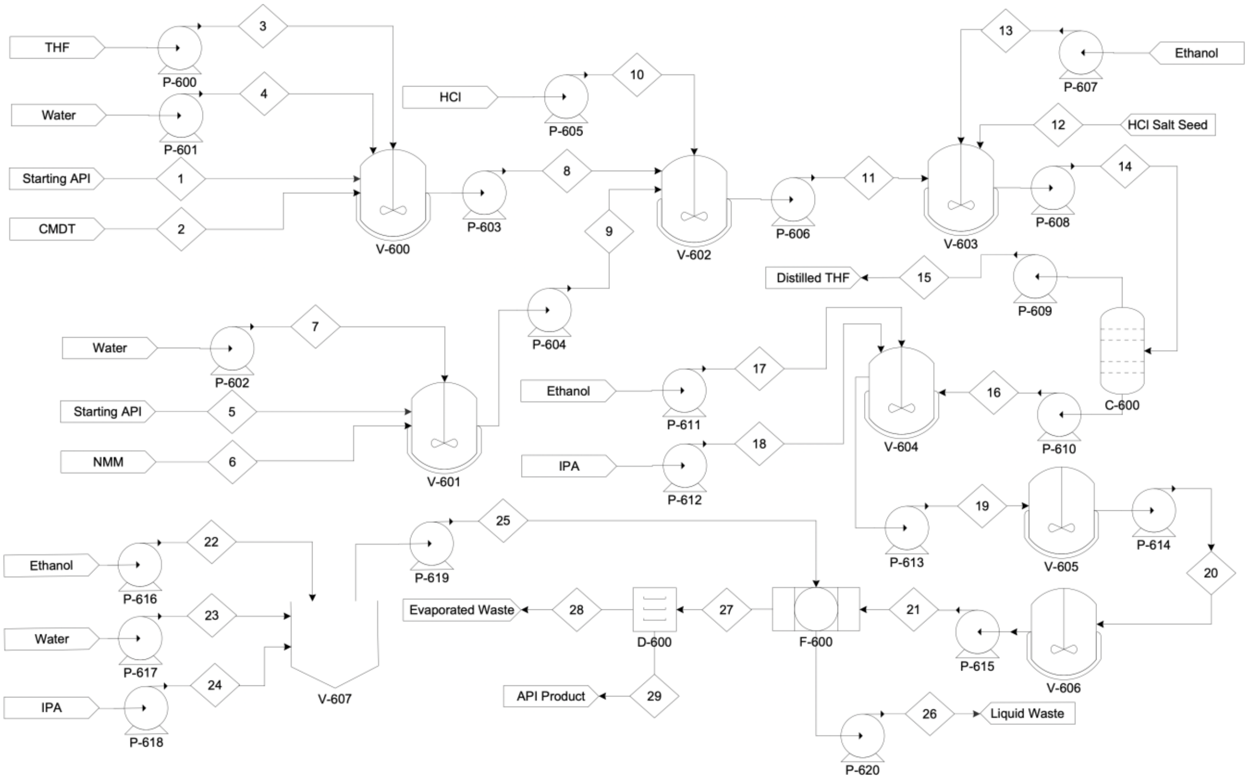


Figure A-6. Process flow diagram of Process 06 – Reactive Crystallization.

Table A-16. Mass of Each Component in Each Stream of Process 06 (According to Figure A-6). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**Starting API (g)**	**CMDT (g)**	**Tetrahydrofuran (g)**	**Water (g)**	**NMM (g)**	**Hydrochloric Acid (g)**	**Ethanol (g)**	**Isopropyl Alcohol (g)**	**API Product (g)**
1	194.04	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	0.00	174.30	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3	0.00	0.00	861.54	0.00	0.00	0.00	0.00	0.00	0.00
4	0.00	0.00	0.00	193.46	0.00	0.00	0.00	0.00	0.00
5	213.45	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
6	0.00	0.00	0.00	0.00	386.21	0.00	0.00	0.00	0.00
7	0.00	0.00	0.00	870.57	0.00	0.00	0.00	0.00	0.00
8	213.45	0.00	0.00	870.57	386.21	0.00	0.00	0.00	0.00
9	194.04	174.30	861.54	193.46	0.00	0.00	0.00	0.00	0.00
10	0.00	0.00	0.00	0.00	0.00	143.11	0.00	0.00	0.00
11	0.00	0.00	861.54	1064.02	0.00	0.00	0.00	0.00	1111.11

12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.11
13	0.00	0.00	0.00	0.00	0.00	0.00	918.59	0.00	0.00
14	0.00	0.00	861.54	1064.02	0.00	0.00	918.59	0.00	1111.11
15	0.00	0.00	861.54	0.00	0.00	0.00	0.00	0.00	0.00
16	0.00	0.00	0.00	1064.02	0.00	0.00	918.59	0.00	1111.11
17	0.00	0.00	0.00	0.00	0.00	0.00	765.49	0.00	0.00
18	0.00	0.00	0.00	0.00	0.00	0.00	0.00	915.10	0.00
19	0.00	0.00	0.00	1064.02	0.00	0.00	1684.08	915.10	1111.11
20	0.00	0.00	0.00	1064.02	0.00	0.00	1684.08	915.10	1111.11
21	0.00	0.00	0.00	1064.02	0.00	0.00	1684.08	915.10	1111.11
22	0.00	0.00	0.00	0.00	0.00	0.00	153.10	0.00	0.00
23	0.00	0.00	0.00	193.46	0.00	0.00	0.00	0.00	0.00
24	0.00	0.00	0.00	0.00	0.00	0.00	0.00	152.52	0.00
25	0.00	0.00	0.00	193.46	0.00	0.00	153.10	152.52	0.00
26	0.00	0.00	0.00	1005.99	0.00	0.00	1469.75	854.09	111.11
27	0.00	0.00	0.00	251.50	0.00	0.00	367.44	213.52	1000.00
28	0.00	0.00	0.00	251.50	0.00	0.00	367.44	213.52	0.00
29	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1000.00
Solvent Recovery System	---	---	---	---	---	---	---	---	---
30	0.00	0.00	0.00	3.66	0.00	0.00	1455.05	3.66	0.00
31	0.00	0.00	0.00	1002.33	0.00	0.00	14.70	850.44	111.11
32	0.00	0.00	0.00	2.12	0.00	0.00	2.12	841.93	0.00
33	0.00	0.00	0.00	1000.22	0.00	0.00	12.58	8.50	111.11
34	0.00	0.00	0.00	800.17	0.00	0.00	10.07	6.80	11.11
35	0.00	0.00	0.00	200.04	0.00	0.00	2.52	1.70	100.00
36	0.00	0.00	0.00	200.04	0.00	0.00	2.52	1.70	0.00
37	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	100.00

Table A-17. Equipment Description for Process 06 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Description**	**Energy Requirement (kWh)**	**Note**
P-600	Centrifugal Pump	1.32E-05	
P-601	Centrifugal Pump	2.96E-06	
P-602	Centrifugal Pump	1.33E-05	
P-603	Centrifugal Pump	2.25E-05	
P-604	Centrifugal Pump	2.18E-05	
P-605	Centrifugal Pump	2.19E-06	
P-606	Centrifugal Pump	4.65E-05	
P-607	Centrifugal Pump	1.41E-05	
P-608	Centrifugal Pump	6.05E-05	
P-609	Centrifugal Pump	1.32E-05	
P-610	Centrifugal Pump	4.73E-05	
P-611	Centrifugal Pump	1.17E-05	
P-612	Centrifugal Pump	1.40E-05	
P-613	Centrifugal Pump	7.30E-05	
P-614	Centrifugal Pump	7.30E-05	
P-615	Centrifugal Pump	7.30E-05	
P-616	Centrifugal Pump	2.34E-06	
P-617	Centrifugal Pump	2.96E-06	
P-618	Centrifugal Pump	2.33E-06	
P-619	Centrifugal Pump	7.64E-06	
P-620	Centrifugal Pump	5.26E-05	
V-600	Cooling Vessel with Mixing	-4.42E-03	Cooling requirement
		1.21E-03	Mixing requirement
V-601	Heating Vessel with Mixing	3.03E-03	Heating requirement
		2.36E-04	Mixing requirement
V-602	Cooling Vessel with Mixing	-1.31E-02	Cooling requirement
		6.49E-03	Mixing requirement

V-603	Heating Vessel with Mixing	1.78E-01	Heating requirement
		5.80E-03	Mixing requirement
V-604	Cooling Vessel with Mixing	1.09E-01	Cooling requirement
		1.76E-03	Mixing requirement
V-605	Heating Vessel with Mixing	1.24E-01	Heating requirement
		4.10E-03	Mixing requirement
V-605	Cooling Vessel with Mixing	-3.12E-01	Cooling requirement
		1.99E-02	Mixing requirement
V-607	Solvent Vessel	0.00E+00	
C-600	Distillation Column	1.36E+01	
F-600	Filtration Unit	5.27E-02	
D-600	Vacuum Dryer	3.98E-01	Heating requirement
		4.83E-01	Vacuum pump requirement
Solvent Recovery System	---	---	---
SR-P-600	Centrifugal Pump	2.24E-05	
SR-P-601	Centrifugal Pump	3.03E-05	
SR-P-602	Centrifugal Pump	1.29E-05	
SR-P-601	Centrifugal Pump	1.73E-05	
SR-P-602	Centrifugal Pump	1.27E-05	
SR-C-600	Distillation Column	5.69E-02	
SR-C-601	Distillation Column	9.35E-03	
SR-F-600	Filtration Unit	1.13E-02	
SR-D-600	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		1.74E-01	Heating requirement

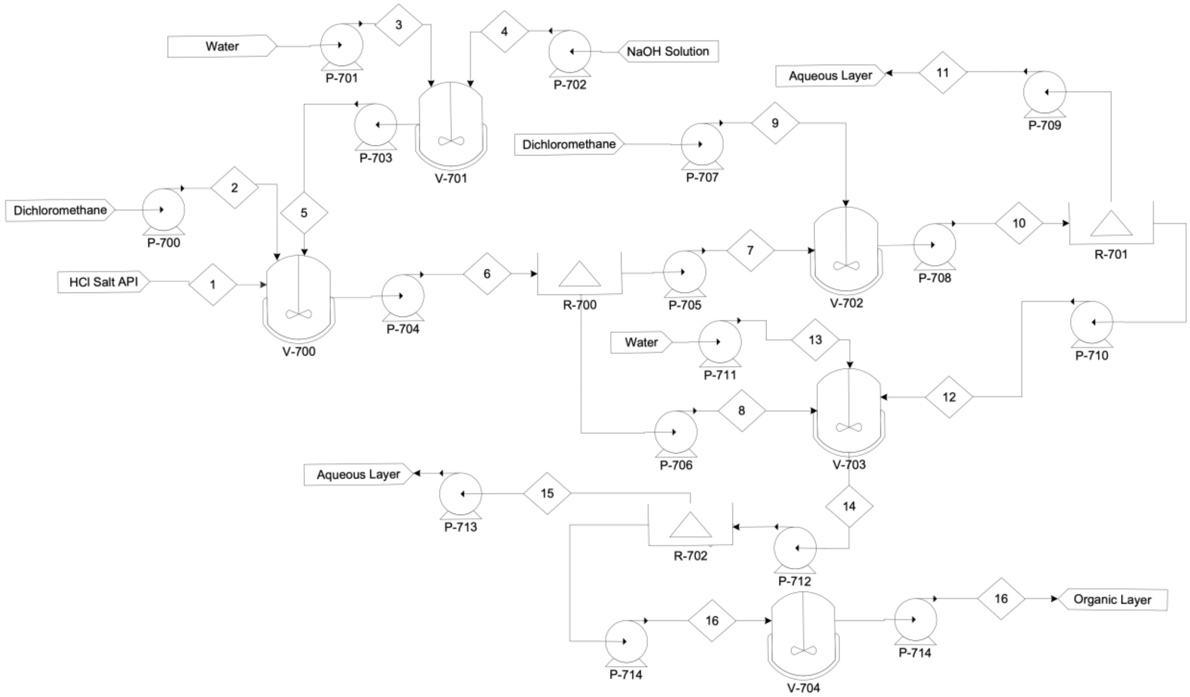
Table A-18. Recovered Solvent from the Solvent Recovery System Implemented to Process 06 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Ethanol	1462.36	99.50%

Isopropyl Alcohol	846.16	99.50%
Water	828.15	96.62%
Tetrahydrofuran	861.54	100.00%

A.1.7 Process 07 – Reactive Crystallization

The process flow diagram of Process 07 can be found in Figure A-7. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-19 and Table A-20, respectively. The mass of solvent recovered from Process 06 using solvent recovery techniques are reported in Table A-21.



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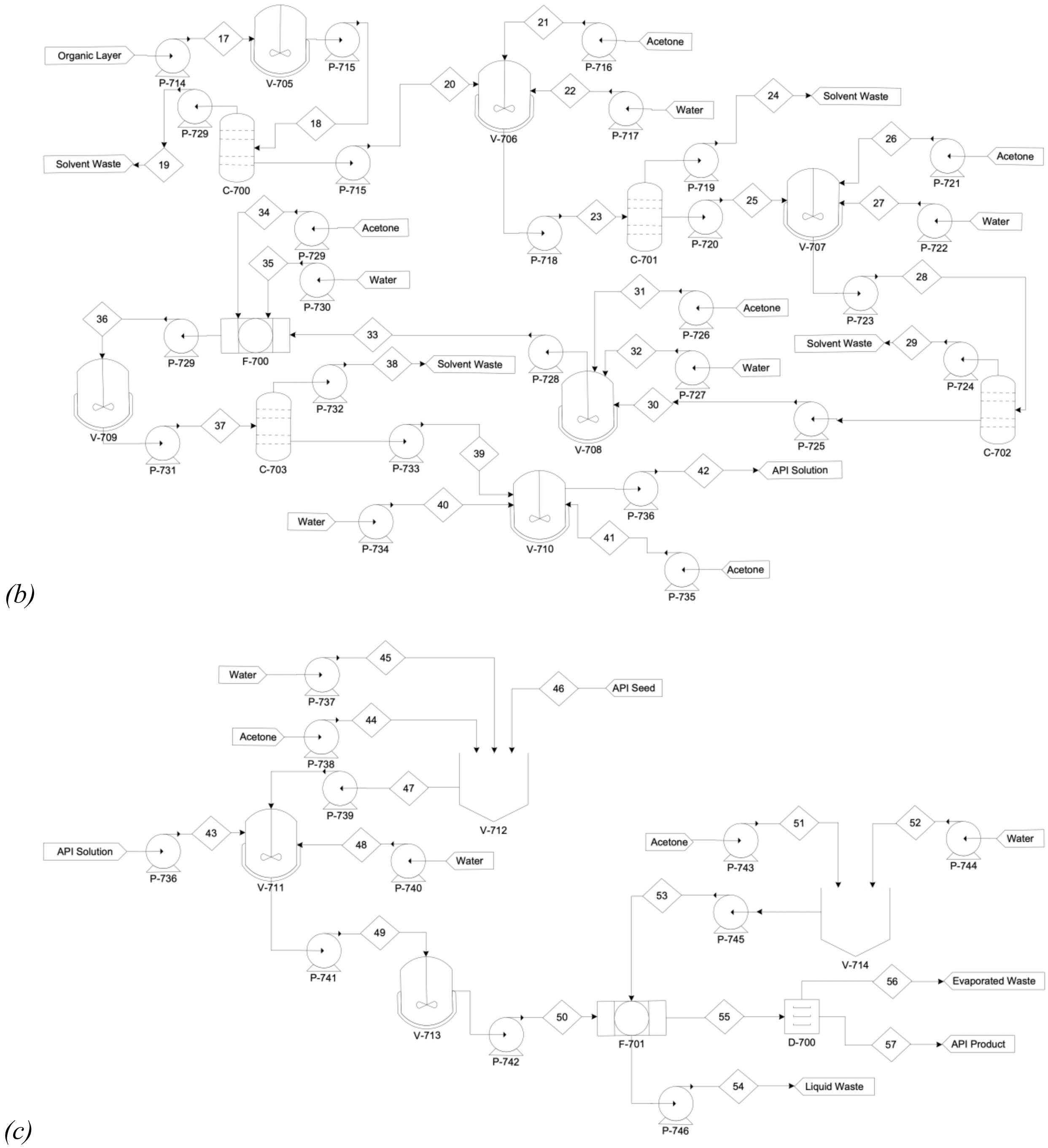

Figure A-7. Process flow diagrams divided into three major steps (a, b, and c) of Process 07 – Reactive Crystallization

Table A-19. Mass of Each Component in Each Stream of Process 07 (According to Figure A-7). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**Starting API (g)**	**Dichloromethane (g)**	**Water (g)**	**Sodium Hydroxide (g)**	**API Product (g)**	**Acetone (g)**

1	714.54	0.00	0.00	0.00	0.00	0.00
2	0.00	11404.07	0.00	0.00	0.00	0.00
3	0.00	0.00	3561.99	0.00	0.00	0.00
4	0.00	0.00	391.82	391.82	0.00	0.00
5	0.00	0.00	3953.80	391.82	0.00	0.00
6	0.00	11404.07	3953.80	0.00	1107.54	0.00
7	0.00	0.00	3953.80	0.00	0.00	0.00
8	0.00	11404.07	0.00	0.00	1107.54	0.00
9	0.00	4751.70	0.00	0.00	0.00	0.00
10	0.00	16155.77	3953.80	0.00	0.00	0.00
11	0.00	0.00	3953.80	0.00	0.00	0.00
12	0.00	16155.77	0.00	0.00	0.00	0.00
13	0.00	0.00	4274.38	0.00	0.00	0.00
14	0.00	16155.77	4274.38	0.00	1107.54	0.00
15	0.00	0.00	4274.38	0.00	0.00	0.00
16	0.00	16155.77	0.00	0.00	1107.54	0.00
17	0.00	16155.77	0.00	0.00	1107.54	0.00
18	0.00	16155.77	0.00	0.00	1107.54	0.00
19	0.00	12354.41	0.00	0.00	0.00	0.00
20	0.00	3801.36	0.00	0.00	1107.54	0.00
21	0.00	0.00	0.00	0.00	0.00	5041.80
22	0.00	0.00	712.40	0.00	0.00	0.00
23	0.00	3801.36	712.40	0.00	1107.54	5041.80
24	0.00	3801.36	0.00	0.00	0.00	1120.40
25	0.00	0.00	712.40	0.00	1107.54	3921.40
26	0.00	0.00	0.00	0.00	0.00	5041.80
27	0.00	0.00	712.40	0.00	0.00	0.00
28	0.00	0.00	1424.79	0.00	1107.54	8963.20
29	0.00	0.00	0.00	0.00	0.00	5602.00
30	0.00	0.00	1424.79	0.00	1107.54	3361.20
31	0.00	0.00	0.00	0.00	0.00	5041.80
32	0.00	0.00	712.40	0.00	0.00	0.00
33	0.00	0.00	2137.19	0.00	1107.54	8403.00

34	0.00	0.00	0.00	0.00	0.00	1680.60
35	0.00	0.00	142.48	0.00	0.00	0.00
36	0.00	0.00	2279.67	0.00	1107.54	10083.60
37	0.00	0.00	0.00	0.00	0.00	7394.64
38	0.00	0.00	2279.67	0.00	1107.54	2688.96
39	0.00	0.00	2279.67	0.00	1107.54	2688.96
40	0.00	0.00	1094.73	0.00	0.00	0.00
41	0.00	0.00	0.00	0.00	0.00	5475.64
42	0.00	0.00	3374.40	0.00	1107.54	8164.60
43	0.00	0.00	50.08	0.00	0.00	0.00
44	0.00	0.00	0.00	0.00	0.00	167.89
45	0.00	0.00	0.00	0.00	3.57	0.00
46	0.00	0.00	50.08	0.00	3.57	167.89
47	0.00	0.00	7480.17	0.00	0.00	0.00
48	0.00	0.00	10904.65	0.00	1111.11	8332.49
49	0.00	0.00	10904.65	0.00	1111.11	8332.49
50	0.00	0.00	0.00	0.00	0.00	373.47
51	0.00	0.00	949.86	0.00	0.00	0.00
52	0.00	0.00	949.86	0.00	0.00	373.47
53	0.00	0.00	9483.61	0.00	111.11	6964.77
54	0.00	0.00	2370.90	0.00	1000.00	1741.19
55	0.00	0.00	2370.90	0.00	0.00	1741.19
56	0.00	0.00	0.00	0.00	1000.00	0.00
Solvent Recovery System	---	---	---	---	---	---
57	0.00	3763.34	9.46	0.00	0.00	9.46
58	0.00	38.01	9474.16	0.00	111.11	8085.17
59	0.00	20.11	20.11	0.00	0.00	8004.32
60	0.00	17.90	9454.04	0.00	111.11	80.85
61	0.00	14.32	7563.24	0.00	11.11	64.68
62	0.00	23.69	1910.92	0.00	100.00	8020.49
63	0.00	23.69	1910.92	0.00	0.00	8020.49
64	0.00	0.00	0.00	0.00	100.00	0.00

57	0.00	3763.34	9.46	0.00	0.00	9.46
58	0.00	38.01	9474.16	0.00	111.11	8085.17
59	0.00	20.11	20.11	0.00	0.00	8004.32
60	0.00	17.90	9454.04	0.00	111.11	80.85

Table A-20. Equipment Description for Process 07 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Description**	**Energy Requirement (kWh)**	**Note**
P-700	Centrifugal Pump	1.74E-04	
P-701	Centrifugal Pump	5.45E-05	
P-702	Centrifugal Pump	1.20E-05	
P-703	Centrifugal Pump	6.65E-05	
P-704	Centrifugal Pump	2.52E-04	
P-705	Centrifugal Pump	6.05E-05	
P-706	Centrifugal Pump	1.91E-04	
P-707	Centrifugal Pump	7.27E-05	
P-708	Centrifugal Pump	3.08E-04	
P-709	Centrifugal Pump	6.05E-05	
P-710	Centrifugal Pump	2.47E-04	
P-711	Centrifugal Pump	6.54E-05	
P-712	Centrifugal Pump	3.30E-04	
P-713	Centrifugal Pump	6.54E-05	
P-714	Centrifugal Pump	2.64E-04	
P-715	Centrifugal Pump	2.64E-04	
P-716	Centrifugal Pump	1.89E-04	
P-717	Centrifugal Pump	7.51E-05	
P-718	Centrifugal Pump	7.71E-05	
P-719	Centrifugal Pump	1.09E-05	
P-720	Centrifugal Pump	1.63E-04	
P-721	Centrifugal Pump	7.53E-05	
P-722	Centrifugal Pump	8.78E-05	
P-723	Centrifugal Pump	7.71E-05	

P-724	Centrifugal Pump	1.09E-05	
P-725	Centrifugal Pump	1.76E-04	
P-726	Centrifugal Pump	8.57E-05	
P-727	Centrifugal Pump	9.02E-05	
P-728	Centrifugal Pump	7.71E-05	
P-729	Centrifugal Pump	1.09E-05	
P-730	Centrifugal Pump	1.78E-04	
P-731	Centrifugal Pump	2.57E-05	
P-732	Centrifugal Pump	2.18E-06	
P-733	Centrifugal Pump	2.06E-04	
P-734	Centrifugal Pump	1.13E-04	
P-735	Centrifugal Pump	9.30E-05	
P-736	Centrifugal Pump	1.67E-05	
P-737	Centrifugal Pump	8.38E-05	
P-738	Centrifugal Pump	1.93E-04	
P-739	Centrifugal Pump	7.66E-07	
P-740	Centrifugal Pump	2.57E-06	
P-741	Centrifugal Pump	3.39E-06	
P-742	Centrifugal Pump	1.14E-04	
P-743	Centrifugal Pump	3.11E-04	
P-744	Centrifugal Pump	3.11E-04	
P-745	Centrifugal Pump	5.71E-06	
P-746	Centrifugal Pump	1.45E-05	
P-747	Centrifugal Pump	2.02E-05	
P-748	Centrifugal Pump	2.53E-04	
V-700	Heating Vessel with Mixing	1.26E-01	Heating requirement
		5.22E-03	Mixing requirement
V-701	Mixing Vessel	4.70E-04	Mixing requirement
V-702	Mixing Vessel	1.14E-03	Mixing requirement
V-703	Mixing Vessel	1.08E-03	Mixing requirement
V-704	Cooling Vessel with Mixing	-1.86E-01	Cooling requirement
		8.89E-04	Mixing requirement
V-705	Heating Vessel with Mixing	1.02E-01	Heating requirement

		2.43E-04	Mixing requirement
V-706	Heating Vessel	1.67E-01	Heating requirement
		1.65E-04	Mixing requirement
V-707	Heating Vessel	1.34E-01	Heating requirement
		2.20E-05	Mixing requirement
V-708	Cooling Vessel	-4.35E-02	Cooling requirement
		2.25E-05	Mixing requirement
V-709	Heating Vessel	1.17E-01	Heating requirement
		2.16E-05	Mixing requirement
V-710	Cooling Vessel	-3.36E-01	Cooling requirement
		2.32E-05	Mixing requirement
V-711	Heating Vessel	9.44E-01	Heating requirement
		7.72E-03	Mixing requirement
V-710	Solvent Vessel	0.00E+00	
V-711	Cooling Vessel	-8.57E-01	Cooling requirement
		1.54E-02	Mixing requirement
V-712	Solvent Vessel	0.00E+00	
R-700	Centrifuge	0.00E+00	
R-701	Centrifuge	0.00E+00	
R-702	Centrifuge	0.00E+00	
C-700	Distillation Column	1.64E+00	
C-701	Distillation Column	1.63E+00	
C-702	Distillation Column	1.28E+00	
C-703	Distillation Column	2.01E+00	
F-700	Filtration Unit	1.35E-01	
F-701	Filtration Unit	2.17E-01	
D-700	Vacuum Dryer	2.16E+00	Heating requirement
		1.16E+00	Vacuum pump requirement
Solvent Recovery System	---	---	---
SR-P-700	Centrifugal Pump	5.79E-05	
SR-P-701	Centrifugal Pump	2.71E-04	

SR-P-702	Centrifugal Pump	1.23E-04	
SR-P-701	Centrifugal Pump	1.48E-04	
SR-P-702	Centrifugal Pump	1.17E-04	
SR-C-700	Distillation Column	2.95E+00	
SR-C-701	Distillation Column	2.55E+00	
SR-F-700	Filtration Unit	9.66E-02	
SR-D-700	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		6.81E-01	Heating requirement

Table A-21. Recovered Solvent from the Solvent Recovery System Implemented to Process 07 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Acetone	21041.18	99.81%
Water	11927.73	99.24%
Dichloromethane	16136.67	99.88%

A.1.8 Process 08 – Cooling Crystallization

The process flow diagram of Process 08 can be found in Figure A-8. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-22 and Table A-23, respectively. The mass of solvent recovered from Process 08 using solvent recovery techniques are reported in Table A-24.

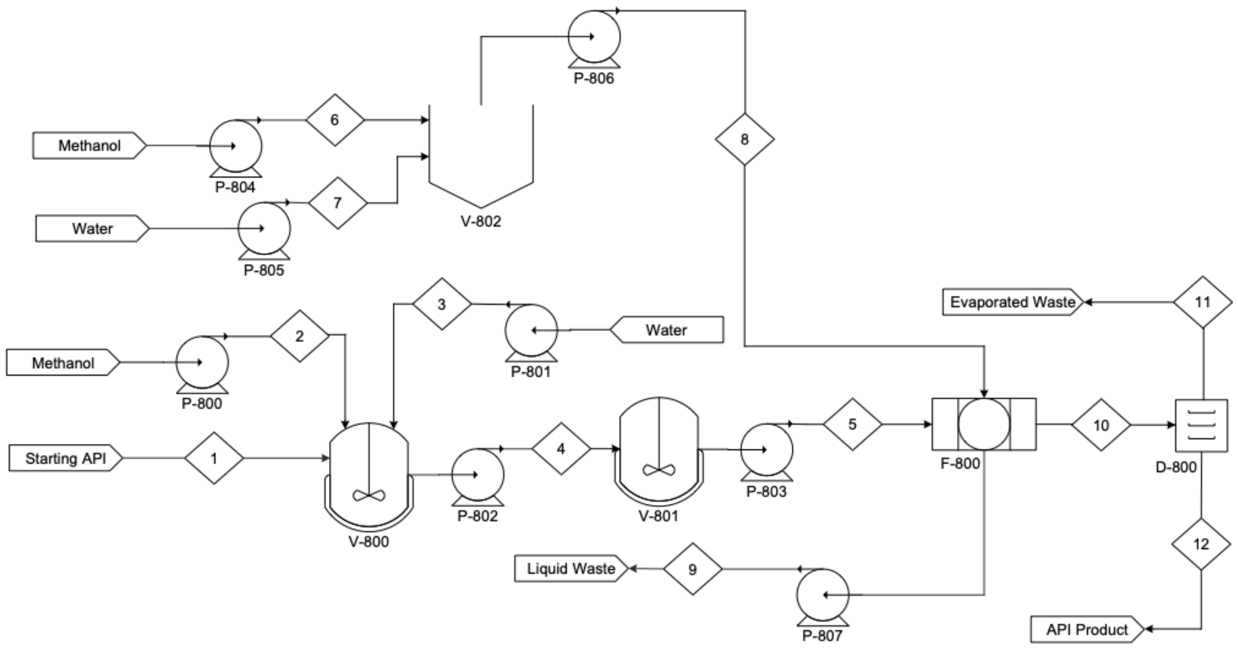

Figure A-8. Process flow diagram of Process 08 – Cooling Crystallization.

Table A-22. Mass of Each Component in Each Stream of Process 08 (According to Figure A-8). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**API (g)**	**Methanol (g)**	**Water (g)**
1	1111.11	0.00	0.00
2	0.00	2200.00	0.00
3	0.00	0.00	443.11
4	1111.11	2200.00	443.11
5	1111.11	2200.00	443.11
6	0.00	792.00	0.00
7	0.00	0.00	110.78
8	0.00	792.00	110.78
9	111.11	2393.60	443.11
10	1000.00	598.40	110.78
11	0.00	598.40	110.78
12	1000.00	0.00	0.00
Solvent Recovery System	---	---	---
13	0.00	2369.67	11.91
14	111.11	23.94	431.20

15	0.00	23.70	0.12
16	111.11	0.24	431.08
17	11.11	0.19	344.87
18	100.00	0.05	86.22
19	0.00	0.05	86.22
20	100.00	0.00	0.00

Table A-23. Equipment Description for Process 08 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-800	Centrifugal Pump	3.37E-05	
P-801	Centrifugal Pump	6.78E-06	
P-802	Centrifugal Pump	5.74E-05	
P-803	Centrifugal Pump	5.74E-05	
P-804	Centrifugal Pump	1.21E-05	
P-805	Centrifugal Pump	1.69E-06	
P-806	Centrifugal Pump	1.38E-05	
P-807	Centrifugal Pump	4.51E-05	
V-800	Heating Vessel with Mixing	4.35E-02	Heating requirement
		1.68E-03	Mixing requirement
V-801	Cooling Vessel with Mixing	-6.87E-02	Cooling requirement
		2.97E-02	Mixing requirement
V-802	Solvent Vessel	0.00E+00	
F-800	Filtration Unit	4.66E-02	
D-800	Vacuum Dryer	3.43E-01	Heating requirement
		2.32E+00	Vacuum pump requirement
Solvent Recovery System	---	---	---
SR-P-800	Centrifugal Pump	3.64E-05	
SR-P-801	Centrifugal Pump	8.66E-06	
SR-P-802	Centrifugal Pump	3.64E-07	

SR-P-803	Centrifugal Pump	8.30E-06	
SR-P-804	Centrifugal Pump	5.45E-06	
SR-C-800	Distillation Column	1.06E+00	
SR-C-801	Distillation Column	5.84E-02	
SR-F-800	Filtration Unit	5.42E-03	
SR-D-800	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		7.44E-02	Heating requirement

Table A-24. Recovered Solvent from the Solvent Recovery System Implemented to Process 08 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Methanol	2381.57	99.50%
Water	356.17	96.83%

A.1.9 Process 09 – Cooling Crystallization

The process flow diagram of Process 09 can be found in Figure A-9. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-25 and Table A-26, respectively. The mass of solvent recovered from Process 09 using solvent recovery techniques are reported in Table A-27.

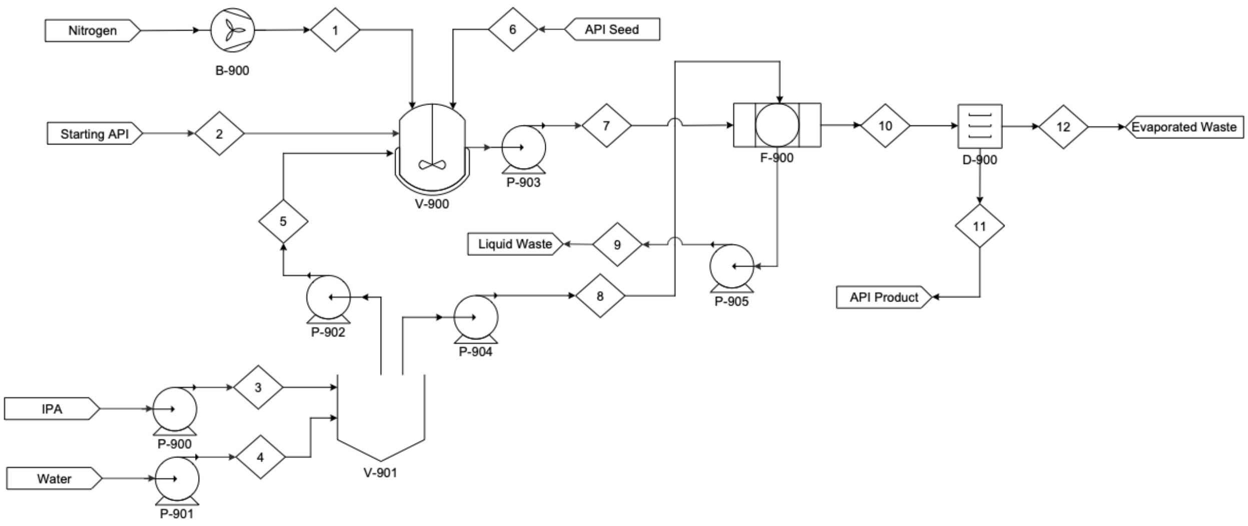

Figure A-9. Process flow diagram of Process 09 – Cooling Crystallization.

Table A-25. Mass of Each Component in Each Stream of Process 09 (According to Figure A-9). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**API (g)**	**IPA (g)**	**Water (g)**
1	0.00	0.00	0.00
2	1100.11	0.00	0.00
3	0.00	7626.54	0.00
4	0.00	0.00	197.43
5	0.00	5084.36	131.62
6	11.00	0.00	0.00
7	1111.11	5084.36	131.62
8	0.00	2542.18	65.81
9	111.11	6101.23	157.94
10	1000.00	1525.31	39.49
11	1000.00	0.00	0.00
12	0.00	1525.31	39.49
Solvent Recovery System	---	---	---
13	0.00	6040.22	30.35
14	111.11	61.01	127.59
15	0.00	60.71	0.00
16	111.11	0.31	127.59
17	11.11	0.25	102.07
18	100.00	0.06	25.52
19	0.00	0.06	25.52
20	100.00	0.00	0.00

Table A-26. Equipment Description for Process 09 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-900	Centrifugal Pump	1.17E-04	
P-901	Centrifugal Pump	3.02E-06	

P-902	Centrifugal Pump	7.98E-05	
P-903	Centrifugal Pump	9.68E-05	
P-904	Centrifugal Pump	3.99E-05	
P-905	Centrifugal Pump	9.75E-05	
V-900	Mixing Vessel	8.55E-03	Mixing requirement
V-901	Solvent Vessel	0.00E+00	
F-900	Filter	8.94E-02	
D-900	Vacuum dryer	6.40E-01	Heating requirement
		1.74E+00	Vacuum pump requirement
Solvent Recovery System	---	---	---
SR-P-900	Centrifugal Pump	9.29E-05	
SR-P-901	Centrifugal Pump	4.59E-06	
SR-P-902	Centrifugal Pump	9.29E-07	
SR-P-903	Centrifugal Pump	3.66E-06	
SR-P-904	Centrifugal Pump	1.74E-06	
SR-C-900	Distillation Column	2.22E+00	
SR-C-901	Distillation Column	1.22E-01	
SR-F-900	Filtration Unit	2.39E-03	
SR-D-900	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		2.20E-02	Heating requirement

Table A-27. Recovered Solvent from the Solvent Recovery System Implemented to Process 09 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Isopropyl Alcohol	6070.57	99.50%
Water	113.43	89.99%

A.1.10 Process 10 – Reactive Crystallization

The process flow diagram of Process 10 can be found in Figure A-10. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-28 and Table A-29, respectively. The mass of solvent recovered from Process 10 using solvent recovery techniques are reported in Table A-30.

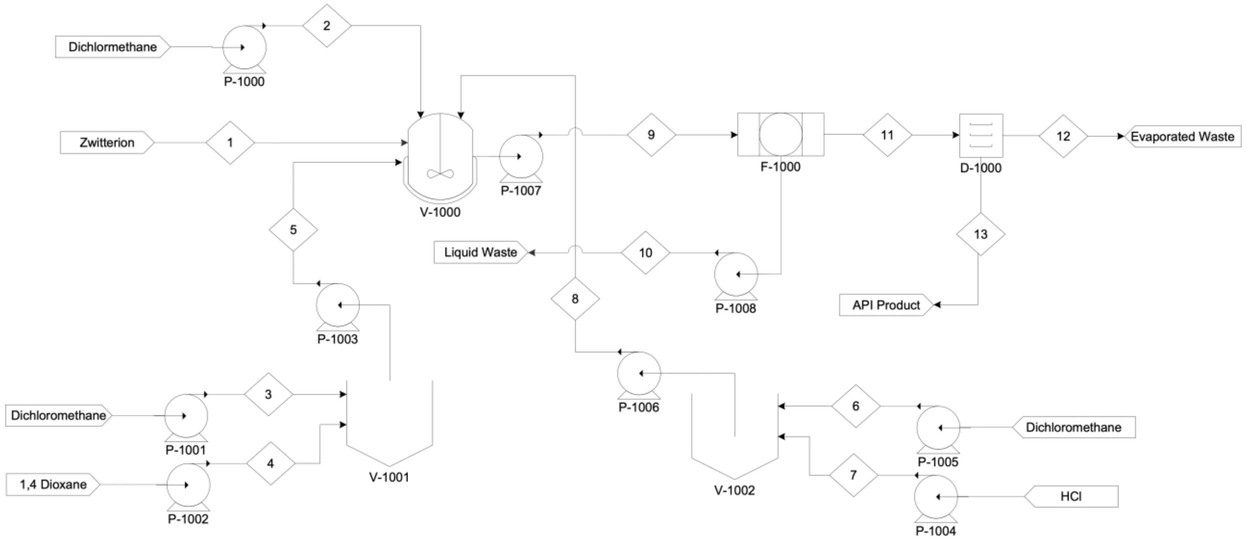

Figure A-10. Process flow diagram of Process 10 – Reactive Crystallization.

Table A-28. Mass of Each Component in Each Stream of Process 10 (According to Figure A-10). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**Starting API (g)**	**Dichloromethane (g)**	**1,4-Dioxane (g)**	**HCl (g)**	**API Product (g)**
1	802.24	0.00	0.00	0.00	0.00
2	0.00	18778.74	0.00	0.00	0.00
3	0.00	0.00	1404.72	0.00	0.00
4	0.00	0.00	0.00	198.90	0.00
5	802.24	0.00	1404.72	0.00	0.00
6	0.00	0.00	641.79	0.00	0.00
7	0.00	0.00	0.00	109.98	0.00
8	0.00	0.00	641.79	109.98	1111.11
9	0.00	18778.74	2046.50	0.00	1111.11
10	0.00	15022.99	1637.20	0.00	111.11
11	0.00	3755.75	409.30	0.00	1000.00
12	0.00	3755.75	409.30	0.00	0.00
13	0.00	0.00	0.00	0.00	1000.00

Solvent Recovery System	---	---	---	---	---
14	0.00	14872.76	74.74	0.00	0.00
15	0.00	150.23	1562.47	0.00	111.11
16	0.00	120.18	1249.97	0.00	11.11
17	0.00	30.05	312.49	0.00	100.00
18	0.00	30.05	312.49	0.00	0.00
19	0.00	0.00	0.00	0.00	100.00

Table A-29. Equipment Description for Process 10 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-1000	Centrifugal Pump	2.87E-04	
P-1001	Centrifugal Pump	2.15E-05	
P-1002	Centrifugal Pump	3.04E-06	
P-1003	Centrifugal Pump	3.38E-05	
P-1004	Centrifugal Pump	9.82E-06	
P-1005	Centrifugal Pump	1.68E-06	
P-1006	Centrifugal Pump	2.85E-05	
P-1007	Centrifugal Pump	3.36E-04	
P-1008	Centrifugal Pump	2.55E-04	
V-1000	Mixing Vessel	1.64E-02	Mixing requirement
V-1001	Solvent Vessel	0	
V-1002	Solvent Vessel	0	
F-1000	Filtration Unit	0.219363579	
D-1000	Vacuum dryer	5.75E-01	Heating requirement
		1.15865841	Vacuum pump requirement
Solvent Recovery System	---	---	---
SR-P-1000	Centrifugal Pump	2.29E-04	
SR-P-1001	Centrifugal Pump	2.79E-05	

SR-P-1002	Centrifugal Pump	2.11E-05	
SR-C-1000	Distillation Column	1.78E+00	
SR-F-1000	Filtration Unit	1.82E-02	
SR-D-1000	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		5.49E-02	Heating requirement

Table A-30. Recovered Solvent from the Solvent Recovery System Implemented to Process 10 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Dichloromethane	14947.50	99.50%
1,4-Dioxane	1381.27	90.49%

A.1.11 Process 11 – Reactive Crystallization

The process flow diagram of Process 11 can be found in Figure A-11. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-31 and Table A-32, respectively. The mass of solvent recovered from Process 11 using solvent recovery techniques are reported in Table A-33.

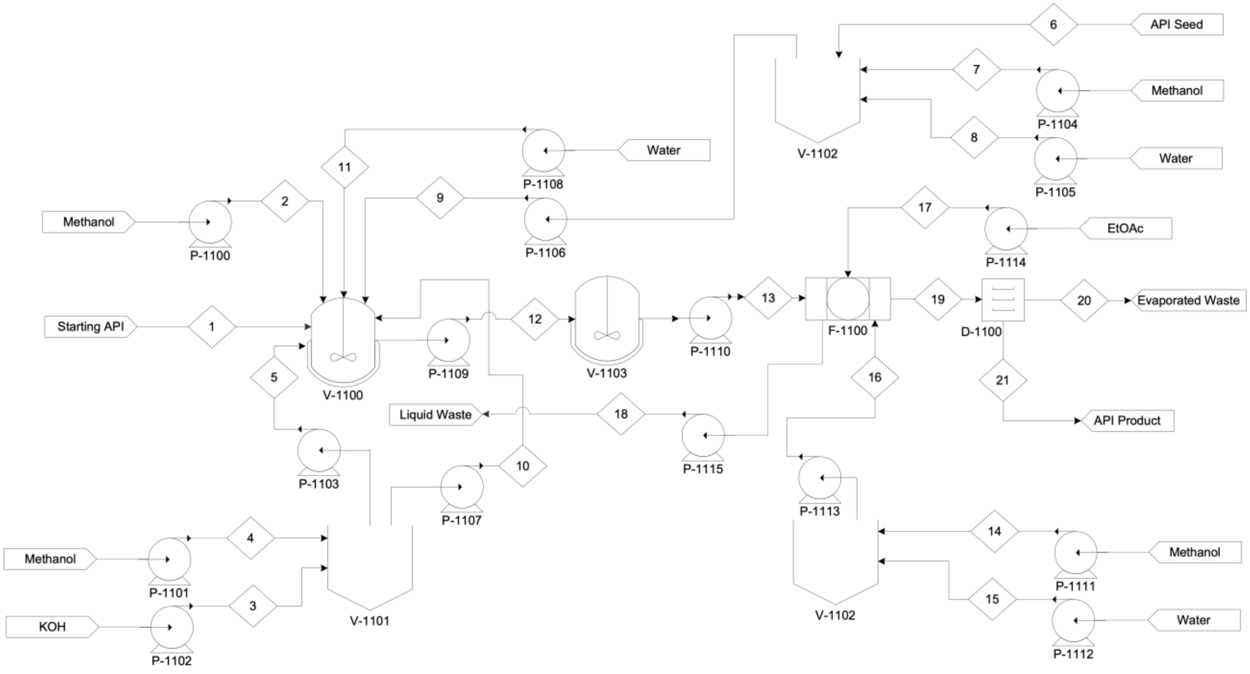

Figure A-11. Process flow diagram of Process 11 – Reactive Crystallization.

Table A-31. Mass of Each Component in Each Stream of Process 11 (According to Figure A-11). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**Starting API (g)**	**Methanol (g)**	**Potassium Hydroxide (g)**	**Water (g)**	**EtOAc (g)**	**API Product (g)**
1	1020.15	0.00	0.00	0.00	0.00	0.00
2	0.00	8079.58	0.00	0.00	0.00	0.00
3	0.00	0.00	85.86	0.00	0.00	0.00
4	0.00	1525.63	0.00	0.00	0.00	0.00
5	0.00	1525.63	85.86	0.00	0.00	0.00
6	0.00	0.00	0.00	0.00	0.00	5.10
7	0.00	1346.60	0.00	0.00	0.00	0.00
8	0.00	0.00	0.00	2373.21	0.00	0.00
9	0.00	1346.60	0.00	2373.21	0.00	5.10
10	0.00	0.00	0.00	14239.25	0.00	0.00
11	0.00	10951.81	85.86	16612.45	0.00	1111.11
12	0.00	10951.81	0.00	16612.45	0.00	1111.11
13	0.00	2693.19	0.00	0.00	0.00	0.00
14	0.00	0.00	0.00	4746.42	0.00	0.00
15	0.00	2693.19	0.00	4746.42	0.00	0.00
16	0.00	0.00	0.00	0.00	7361.40	0.00
17	0.00	10916.01	0.00	17087.10	5889.12	111.11
18	0.00	2729.00	0.00	4271.77	1472.28	1000.00
19	0.00	2729.00	0.00	4271.77	1472.28	0.00
20	0.00	0.00	0.00	0.00	0.00	1000.00
Solvent Recovery System	---	---	---	---	---	---
21	0.00	10806.85	0.00	27.15	27.15	0.00
22	0.00	109.16	0.00	17059.94	5861.97	111.11
23	0.00	14.58	0.00	14.58	5803.35	0.00
24	0.00	94.58	0.00	17045.36	58.62	111.11
25	0.00	75.66	0.00	13636.29	46.90	11.11
26	0.00	18.92	0.00	3409.07	11.72	100.00

27	0.00	18.92	0.00	3409.07	11.72	0.00
28	0.00	0.00	0.00	0.00	0.00	100.00

Table A-32. Equipment Description for Process 11 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-1100	Centrifugal Pump	1.24E-04	
P-1101	Centrifugal Pump	1.31E-06	
P-1102	Centrifugal Pump	2.33E-05	
P-1103	Centrifugal Pump	2.47E-05	
P-1104	Centrifugal Pump	2.06E-05	
P-1105	Centrifugal Pump	3.63E-05	
P-1106	Centrifugal Pump	5.69E-05	
P-1107	Centrifugal Pump	2.18E-04	
P-1108	Centrifugal Pump	4.23E-04	
P-1109	Centrifugal Pump	4.22E-04	
P-1110	Centrifugal Pump	4.12E-05	
P-1111	Centrifugal Pump	7.26E-05	
P-1112	Centrifugal Pump	1.14E-04	
P-1113	Centrifugal Pump	1.13E-04	
P-1114	Centrifugal Pump	5.19E-04	
V-1100	Reactor Vessel with Heating and Mixing	6.87E-01	Heating requirement
		1.28E-02	Mixing requirement
V-1101	Solvent Vessel	0.00E+00	
V-1102	Solvent Vessel	0.00E+00	
V-1103	Cooling Vessel with Mixing	-6.87E-01	Cooling requirement
		5.77E-03	Mixing requirement
V-1104	Solvent Vessel	0.00E+00	
F-1100	Filtration Unit	4.24E-01	
D-1100	Vacuum Dryer	5.01E+00	Heating requirement

		1.16E+00	Vacuum pump requirement
Solvent Recovery System	---	---	---
SR-P-1100	Centrifugal Pump	1.66E-04	
SR-P-1101	Centrifugal Pump	3.54E-04	
SR-P-1102	Centrifugal Pump	8.92E-05	
SR-P-1101	Centrifugal Pump	2.65E-04	
SR-P-1102	Centrifugal Pump	2.11E-04	
SR-C-1100	Distillation Column	2.26E+01	
SR-C-1101	Distillation Column	6.96E+00	
SR-F-1100	Filtration Unit	1.73E-01	
SR-D-1100	Vacuum Dryer	5.79E-01	
		2.95E+00	

Table A-33. Recovered Solvent from the Solvent Recovery System Implemented to Process 11 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Methanol	10861.15	99.50%
Water	13769.96	99.03%
Ethyl Acetate	5832.51	99.50%

A.1.12 Process 12 – Reactive Crystallization

The process flow diagram of Process 12 can be found in Figure A-12. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-34 and Table A-35, respectively. The mass of solvent recovered from Process 12 using solvent recovery techniques are reported in Table A-36.

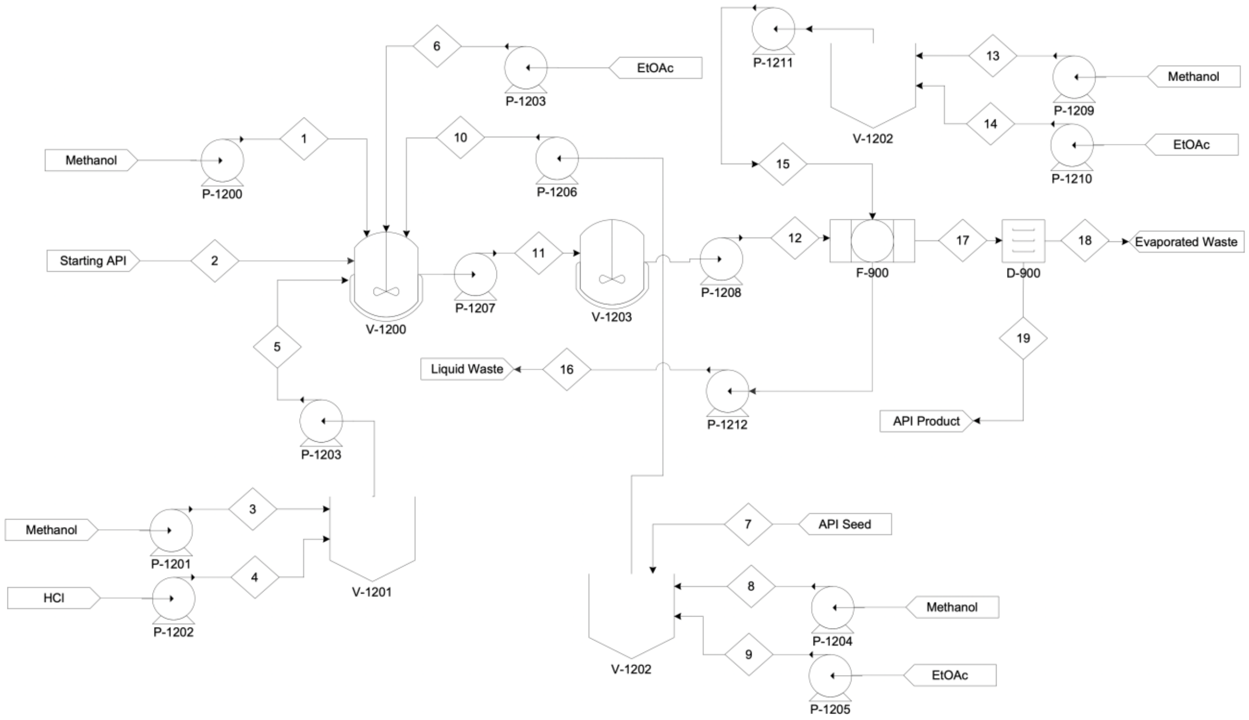

Figure A-12. Process flow diagram of Process 12 – Reactive Crystallization.

Table A-34. Mass of Each Component in Each Stream of Process 12 (According to Figure A-12). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**API (g)**	**Methanol (g)**	**Hydrochloric Acid (g)**	**EtOAc (g)**	**API Product (g)**
1	625.75	0.00	0.00	0.00	0.00
2	0.00	4955.90	0.00	0.00	0.00
3	0.00	3469.13	0.00	0.00	0.00
4	0.00	0.00	479.11	0.00	0.00
5	0.00	3469.13	479.11	0.00	1104.85
6	0.00	0.00	0.00	8466.34	0.00
7	0.00	0.00	0.00	0.00	6.26
8	0.00	594.71	0.00	0.00	0.00
9	0.00	0.00	0.00	1015.96	0.00
10	0.00	594.71	0.00	1015.96	6.26
11	0.00	9019.74	0.00	9482.30	1111.11
12	0.00	9019.74	0.00	9482.30	1111.11
13	0.00	594.71	0.00	0.00	0.00

14	0.00	0.00	0.00	1015.96	0.00
15	0.00	594.71	0.00	10498.26	0.00
16	0.00	7691.56	0.00	8398.60	111.11
17	0.00	1922.89	0.00	2099.65	1000.00
18	0.00	1922.89	0.00	2099.65	0.00
19	0.00	0.00	0.00	0.00	1000.00
Solvent Recovery System	---	---	---	---	---
20	0.00	7614.65	0.00	38.26	0.00
21	0.00	76.92	0.00	8360.34	111.11
22	0.00	61.53	0.00	6688.27	11.11
23	0.00	15.38	0.00	1672.07	100.00
24	0.00	15.38	0.00	1672.07	0.00
25	0.00	0.00	0.00	0.00	100.00

Table A-35. Equipment Description for Process 12 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-1200	Centrifugal Pump	7.58E-05	
P-1201	Centrifugal Pump	5.31E-05	
P-1202	Centrifugal Pump	7.33E-06	
P-1203	Centrifugal Pump	7.73E-05	
P-1204	Centrifugal Pump	1.30E-04	
P-1205	Centrifugal Pump	9.10E-06	
P-1206	Centrifugal Pump	1.55E-05	
P-1207	Centrifugal Pump	2.47E-05	
P-1208	Centrifugal Pump	3.00E-04	
P-1209	Centrifugal Pump	3.00E-04	
P-1210	Centrifugal Pump	9.10E-06	
P-1211	Centrifugal Pump	1.55E-05	
P-1212	Pump	1.70E-04	

P-1213	Pump	2.48E-04	
V-1200	Reactor Vessel with Heating and Mixing	1.23E-01	Heating requirement
		8.49E-03	Mixing requirement
V-1201	Reactant Vessel	0.00E+00	
V-1202	Solvent Vessel	0.00E+00	
V-1203	Cooling Vessel	-1.23E-01	Cooling requirement
		8.49E-03	Mixing requirement
V-1204	Solvent Vessel	0.00E+00	
F-1200	Filtration Unit	3.07E-01	
D-1200	Vacuum Dryer	1.08E+00	Heating requirement
		1.16E+00	Vacuum pump requirement
Solvent Recovery System	---	---	---
SR-P-1200	Centrifugal Pump	1.17E-04	
SR-P-1201	Centrifugal Pump	1.31E-04	
SR-P-1202	Centrifugal Pump	1.03E-04	
SR-C-1200	Distillation Column	7.43E+00	
SR-F-1200	Filtration Unit	8.55E-02	
SR-D-1200	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		7.91E-03	Heating requirement

Table A-36. Recovered Solvent from the Solvent Recovery System Implemented to Process 12 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Methanol	7652.91	99.50%
EtOAc	6760.92	98.93%

A.1.13 Process 13 – Antisolvent Crystallization

The process flow diagram of Process 13 can be found in Figure A-13. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-37 and Table A-38, respectively. The mass of solvent recovered from Process 13 using solvent recovery techniques are reported in Table A-39.

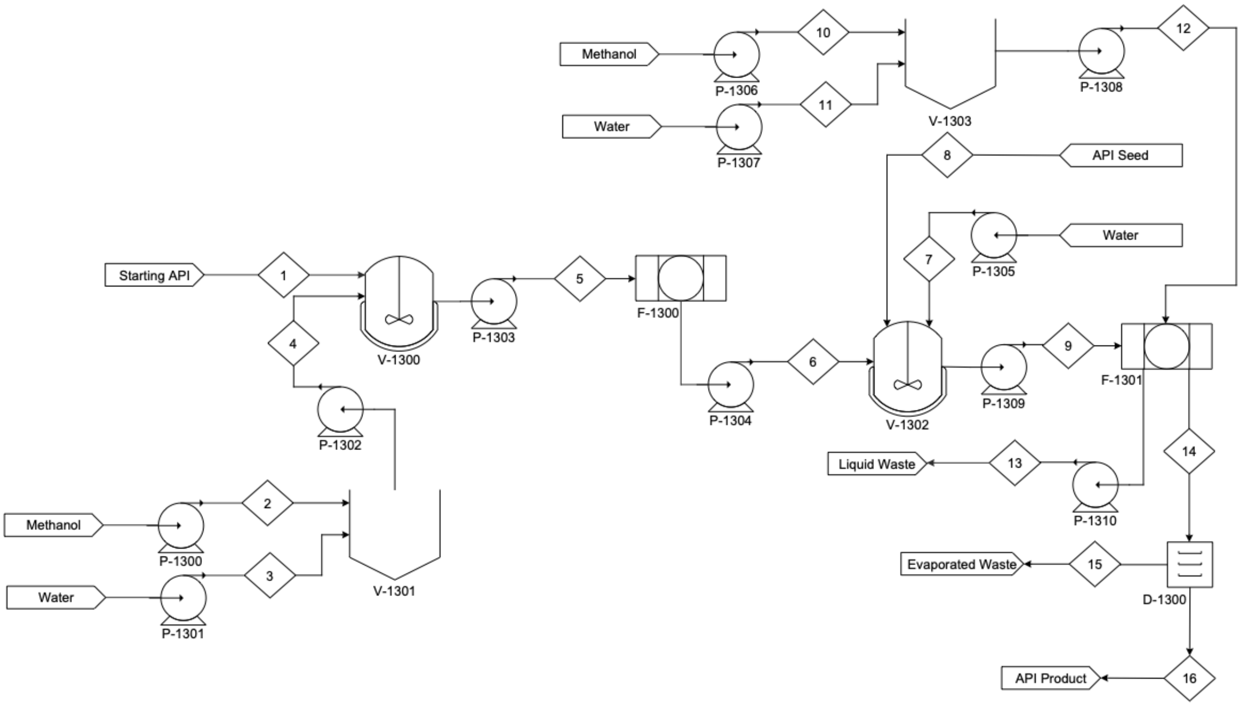

Figure A-13. Process flow diagram of Process 13 – Antisolvent Crystallization.

Table A-37. Mass of Each Component in Each Stream of Process 13 (According to Figure A-13). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**API (g)**	**Methanol (g)**	**Water (g)**
1	1100.11	0.00	0.00
2	0.00	4879.21	0.00
3	0.00	0.00	1535.535008
4	0.00	4879.21	1535.54
5	1100.11	4879.21	1535.54
6	1100.11	4879.21	1535.54
7	0.00	0.00	1096.81
8	11.00	0.00	0.00
9	1111.11	4879.21	2632.35
10	0.00	784.16	0.00
11	0.00	0.00	2303.30
12	0.00	784.16	2303.30
17	111.11	4530.70	3948.52

18	1000.00	1132.67	987.13
19	0.00	1132.67	987.13
16	1000.00	0.00	0.00
Solvent Recovery System	---	---	---
17	0.00	4485.39	22.54
18	111.11	45.31	3925.98
19	11.11	36.25	3140.78
20	100.00	9.06	785.20
21	0.00	9.06	785.20
22	100.00	0.00	0.00

Table A-38. Equipment Description for Process 13 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-1300	Centrifugal Pump	7.47E-05	
P-1301	Centrifugal Pump	2.35E-05	
P-1302	Centrifugal Pump	9.81E-05	
P-1303	Centrifugal Pump	1.15E-04	
P-1304	Centrifugal Pump	1.15E-04	
P-1305	Centrifugal Pump	1.68E-05	
P-1306	Centrifugal Pump	1.32E-04	
P-1307	Centrifugal Pump	1.20E-05	
P-1308	Centrifugal Pump	3.52E-05	
P-1309	Centrifugal Pump	4.72E-05	
P-1310	Centrifugal Pump	1.31E-04	
V-1300	Heating Vessel with Mixing	1.36E-01	Heating requirement
		7.57E-04	Mixing requirement
V-1301	Solvent Mixture Vessel	0.00E+00	
V-1302	Cooling Vessel with Mixing	-1.87E-01	Cooling requirement
		2.72E-02	Mixing requirement
V-1303	Solvent Mixture Vessel	0.00E+00	
F-1300	Polish Filtration Unit	7.51E-02	

F-1301	Filtration	1.17E-01	
D-1300	Vacuum Dryer	1.32E+00	Heating requirement
		5.79E-01	Vacuum pump requirement
Solvent Recovery System	---	---	---
SR-P-1300	Centrifugal Pump	6.90E-05	
SR-P-1301	Centrifugal Pump	6.25E-05	
SR-P-1302	Centrifugal Pump	4.88E-05	
SR-C-1300	Distillation Column	2.41E+00	
SR-F-1300	Filtration Unit	4.08E-02	
SR-D-1300	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		6.81E-01	Heating requirement

Table A-39. Recovered Solvent from the Solvent Recovery System Implemented to Process 13 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Methanol	4507.93	99.50%
Water	3188.14	98.51%

A.1.14 Process 14 – Reactive Crystallization

The process flow diagram of Process 14 can be found in Figure A-14. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-40 and Table A-41, respectively. The mass of solvent recovered from Process 14 using solvent recovery techniques are reported in Table A-42.

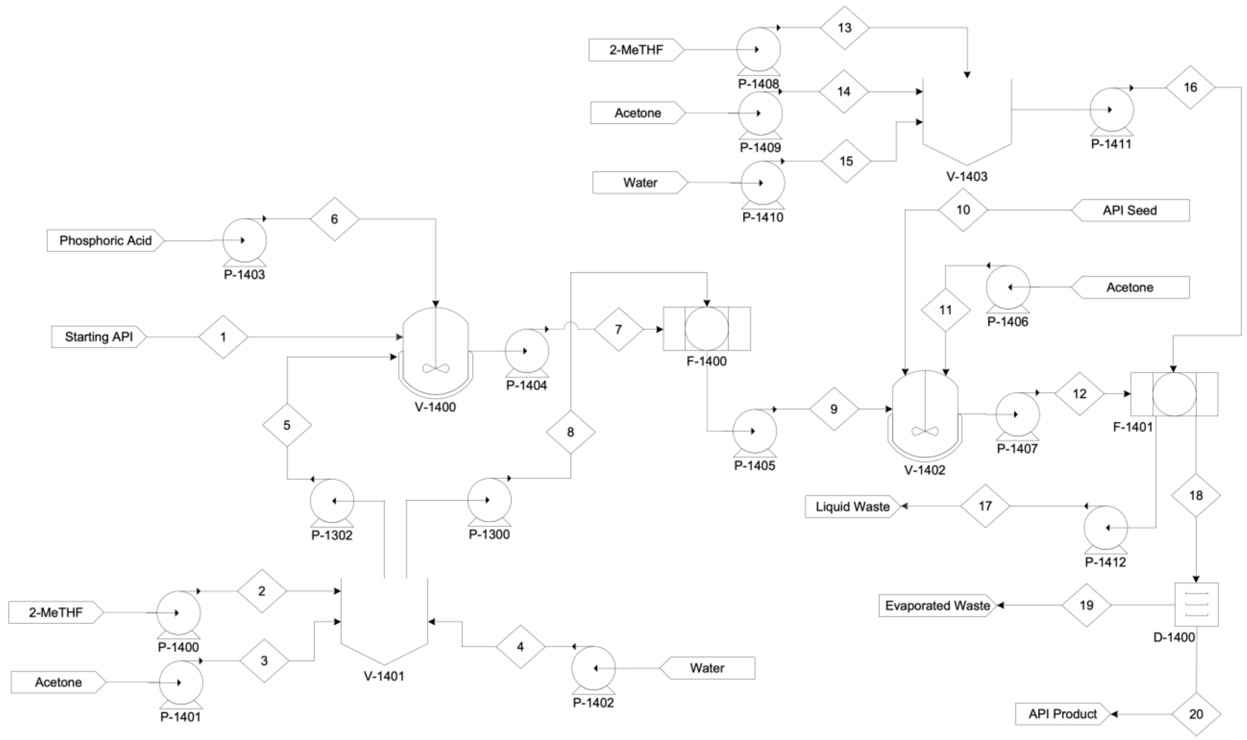

Figure A-14. Process flow diagram of Process 14 – Reactive Crystallization.

Table A-40. Mass of Each Component in Each Stream of Process 14 (According to Figure A-14). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**API Freebase (g)**	**2-MeTHF (g)**	**Acetone (g)**	**Water (g)**	**Phosphoric Acid (g)**	**API Product (g)**
1	913.68	0.00	0.00	0.00	0.00	0.00
2	0.00	1755.63	0.00	0.00	0.00	0.00
3	0.00	0.00	1611.727563	0.00	0.00	0.00
4	0.00	0.00	0.00	2732.81	0.00	0.00
5	0.00	1638.59	1504.28	2550.62	0.00	0.00
6	0.00	0.00	0.00	0.00	186.43	0.00
7	0.00	1638.59	1504.28	2550.62	0.00	1100.11
8	0.00	117.04	107.45	182.19	0.00	0.00
9	0.00	1755.63	1611.73	2732.81	0.00	1100.11
10	0.00	0.00	0.00	0.00	0.00	11.00
11	0.00	0.00	12893.82	0.00	0.00	0.00
12	0.00	1755.63	14505.55	2732.81	0.00	1111.11

13	0.00	210.68	0	0	0.00	0.00
14	0.00	0.00	1719.18	0.00	0.00	0.00
15	0.00	0.00	0.00	300.61	0.00	0.00
16	0.00	210.68	1719.18	300.61	0.00	0.00
17	0.00	1573.05	12979.78	2426.74	0.00	111.11
18	0.00	393.26	3244.94	606.68	0.00	1000.00
19	0.00	393.26	3244.94	606.68	0.00	0.00
20	0.00	0.00	0.00	0.00	0.00	1000.00
Solvent Recovery System	---	---	---	---	---	---
21	0.00	32.29	12849.98	32.29	0.00	0.00
22	0.00	1540.76	129.80	2394.45	0.00	111.11
23	0.00	1525.35	3.83	3.83	0.00	0.00
24	0.00	15.41	125.97	2390.62	0.00	111.11
25	0.00	12.33	100.77	1912.49	0.00	11.11
26	0.00	3.08	25.19	478.12	0.00	100.00
27	0.00	3.08	25.19	478.12	0.00	0.00
28	0.00	0.00	0.00	0.00	0.00	100.00

Table A-41. Equipment Description for Process 14 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-1400	Centrifugal Pump	2.69E-05	
P-1401	Centrifugal Pump	2.47E-05	
P-1402	Centrifugal Pump	4.18E-05	
P-1403	Centrifugal Pump	8.71E-05	
P-1404	Centrifugal Pump	2.85E-06	
P-1405	Centrifugal Pump	1.04E-04	
P-1406	Centrifugal Pump	6.22E-06	
P-1407	Centrifugal Pump	1.10E-04	
P-1408	Centrifugal Pump	1.97E-04	

P-1409	Centrifugal Pump	3.08E-04	
P-1410	Centrifugal Pump	3.22E-06	
P-1411	Centrifugal Pump	2.63E-05	
P-1412	Centrifugal Pump	4.60E-06	
P-1413	Centrifugal Pump	3.41E-05	
P-1414	Centrifugal Pump	2.61E-04	
V-1400	Reactor Vessel with Heating and Mixing	1.17E-01	Heating requirement
		1.62E-03	Mixing requirement
V-1401	Solvent Vessel	0.00E+00	
V-1402	Cooling Vessel with Mixing	-3.24E-01	Cooling requirement
		3.12E-02	Mixing requirement
V-1403	Solvent Vessel	0.00E+00	
F-1300	Polish Filtration Unit	6.79E-02	
F-1401	Filtration Unit	2.23E-01	
D-1400	Vacuum Dryer	7.50E-01	Heating requirement
		7.72E-01	Vacuum pump requirement
Solvent Recovery System	---	---	---
SR-P-1400	Centrifugal Pump	1.98E-04	
SR-P-1401	Centrifugal Pump	6.39E-05	
SR-P-1402	Centrifugal Pump	2.35E-05	
SR-P-1403	Centrifugal Pump	4.04E-05	
SR-P-1404	Centrifugal Pump	3.12E-05	
SR-C-1400	Distillation Column	5.80E-01	
SR-C-1401	Distillation Column	1.30E+00	
SR-F-1400	Filtration Unit	2.64E-02	
SR-D-1400	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		4.14E-01	Heating requirement

Table A-42. Recovered Solvent from the Solvent Recovery System Implemented to Process 14 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
2-Methyl tetrahydrofuran	1533.02	99.50%
Acetone	12914.55	99.50%
Water	2036.70	93.90%

A.1.15 Process 15 – Reactive Crystallization

The process flow diagram of Process 15 can be found in Figure A-15. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-43 and Table A-44, respectively. The mass of solvent recovered from Process 15 using solvent recovery techniques are reported in Table A-45.

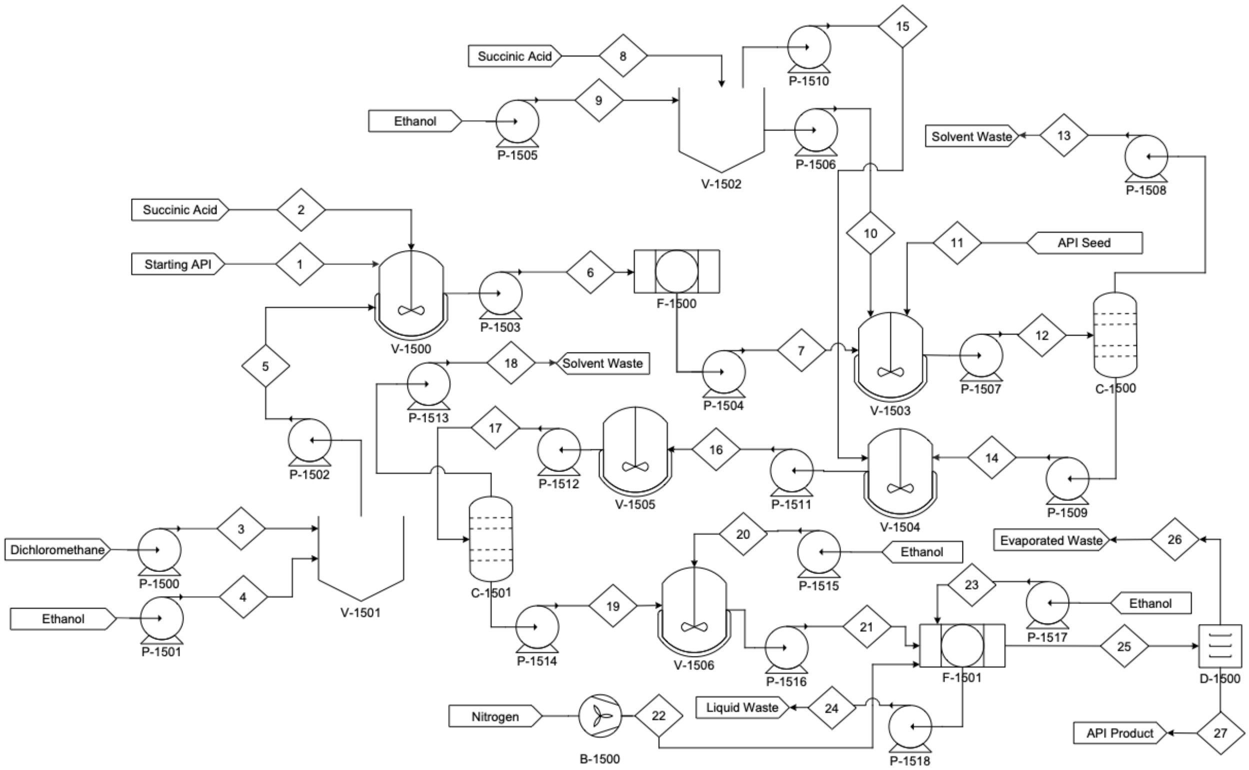

Figure A-15. Process flow diagram of Process 15 – Reactive Crystallization.

Table A-43. Mass of Each Component in Each Stream of Process 15 (According to Figure A-15). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	Starting API (g)	Succinic Acid (g)	Dichloromethane (g)	Ethanol (g)	API Product (g)
1	472.61	0.00	0.00	0.00	0.00
2	0.00	173.53	0.00	0.00	0.00
3	0.00	0.00	10214.30672	0.00	0.00
4	0.00	0.00	0.00	3262.79	0.00
5	0.00	0.00	10214.31	3262.79	0.00
6	472.61	173.53	10214.31	3262.79	0.00
7	472.61	173.53	10214.31	3262.79	0.00
8	0.00	455.52	0.00	0.00	0.00
9	0.00	0.00	0.00	5593.35	0.00
10	0.00	0.33	0.00	1864.45	0.00
11	0.00	0.00	0.00	0.00	9.45
12	0.00	0.00	10214.31	5127.24	1111.11
13	0.00	0.00	6285.73	0.00	0.00
14	0.00	0.00	3928.58	5127.24	1111.11
15	0.00	455.19	0.00	3728.90	0.00
16	0.00	0.00	3928.58	8856.14	1111.11
17	0.00	0.00	3928.58	8856.14	1111.11
18	0.00	0.00	3928.58	1398.34	0.00
19	0.00	0.00	0.00	7457.80	1111.11
20	0.00	0.00	0.00	3728.90	0.00
21	0.00	0.00	0.00	11186.70	1111.11
22	0.00	0.00	0.00	0.00	0.00
23	0.00	0.00	0.00	1491.56	0.00
24	0.00	0.00	0.00	10142.61	111.11
25	0.00	0.00	0.00	2535.65	1000.00
26	0.00	0.00	0.00	2535.65	0.00
27	0.00	0.00	0.00	0.00	1000.00

Solvent Recovery System	**---**	**---**	**---**	**---**	**---**
28	0.00	0.00	3889.29	19.54	0.00
29	0.00	0.00	39.29	1378.79	0.00

Table A-44. Equipment Description for Process 15 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-1500	Centrifugal Pump	1.56E-04	
P-1501	Centrifugal Pump	4.99E-05	
P-1502	Centrifugal Pump	2.06E-04	
P-1503	Centrifugal Pump	2.16E-04	
P-1504	Centrifugal Pump	2.16E-04	
P-1505	Centrifugal Pump	8.56E-05	
P-1506	Centrifugal Pump	2.85E-05	
P-1507	Centrifugal Pump	2.52E-04	
P-1508	Centrifugal Pump	9.62E-05	
P-1509	Centrifugal Pump	1.56E-04	
P-1510	Centrifugal Pump	6.40E-05	
P-1511	Centrifugal Pump	2.13E-04	
P-1512	Centrifugal Pump	2.13E-04	
P-1513	Centrifugal Pump	8.15E-05	
P-1514	Centrifugal Pump	1.31E-04	
P-1515	Centrifugal Pump	5.71E-05	
P-1516	Centrifugal Pump	1.88E-04	
P-1517	Centrifugal Pump	2.28E-05	
P-1518	Centrifugal Pump	1.57E-04	
V-1500	Heating Vessel	1.72E-04	Mixing requirement
		5.63E-02	Heating requirement
V-1501	Solvent Vessel	0.00E+00	
V-1502	Solvent Vessel	0.00E+00	

V-1503	Heating Vessel	8.20E-03	Mixing requirement
		2.19E-01	Heating requirement
V-1504	Cooling Vessel	5.06E-03	Mixing requirement
		-2.98E-02	Cooling requirement
V-1505	Heating Vessel	3.62E-03	Mixing requirement
		4.04E-01	Heating requirement
V-1506	Cooling Vessel	7.75E-03	Mixing requirement
		-3.40E-01	Cooling requirement
C-1500	Distillation Column	6.82E-01	
C-1501	Distillation Column	8.39E-01	
B-1500	Blower	0.00E+00	
F-1500	Polish Filtration Unit	1.41E-01	
F-1501	Filtration Unit	1.38E-01	
D-1500	Dryer	8.42E-01	Heating requirement
		7.72E-01	Vacuum pump requirement
Solvent Recovery System	---	---	---
SR-P-1500	Centrifugal Pump	5.98E-05	
SR-P-1501	Centrifugal Pump	2.17E-05	
SR-C-1500	Distillation Column	5.08E-01	

Table A-45. Recovered Solvent from the Solvent Recovery System Implemented to Process 15 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
Dichloromethane	10194.57	99.81%
Ethanol	11671.80	98.71%

A.1.16 Process 16 – Antisolvent Crystallization

The process flow diagram of Process 16 can be found in Figure A-16. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-46 and Table A-47, respectively. The mass of solvent recovered from Process 16 using solvent recovery techniques are reported in Table A-48.

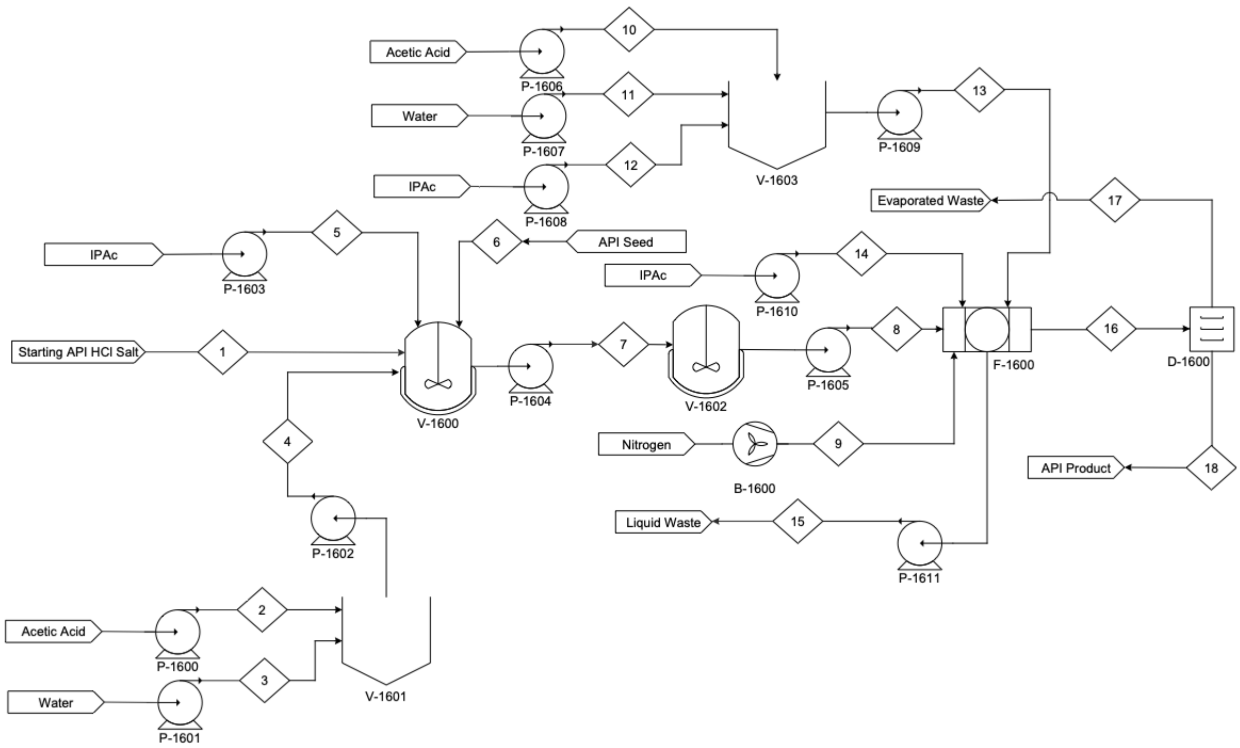

Figure A-16. Process flow diagram of Process 16 – Reactive Crystallization.

Table A-46. Mass of Each Component in Each Stream of Process 16 (According to Figure A-16). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API (g)	Acetic Acid (g)	Water (g)	IPAc (g)
1	1105.58	0.00	0.00	0.00
2	0.00	9925.37	0.00	0.00
3	0.00	0.00	496.02	0.00
4	0.00	9925.37	496.02	0.00
5	0.00	0.00	0.00	17313.43
6	5.53	0.00	0.00	0.00
7	1111.11	9925.37	496.02	17313.43
8	1111.11	9925.37	496.02	17313.43
9	-	-	-	-
10	0.00	551.41	0.00	0.00
11	0.00	0.00	27.56	0.00
12	0.00	0.00	0.00	961.86

13	0.00	551.41	27.56	961.86
14	0.00	0.00	0.00	1442.79
15	111.11	8381.43	418.86	15774.46
16	1000.00	2095.36	104.72	3943.62
17	0.00	2095.36	104.72	3943.62
18	1000.00	0.00	0.00	0.00
Solvent Recovery System	**---**	**---**	**---**	**---**
19	0.00	39.24	39.24	15616.72
20	111.11	8342.19	379.62	157.74
21	0.00	0.94	375.83	0.94
22	111.11	8341.24	3.80	156.80
23	11.11	6673.00	3.04	125.44
24	100.00	1668.25	0.76	31.36
25	0.00	1668.25	0.76	31.36
26	100.00	0.00	0.00	0.00

Table A-47. Equipment Description for Process 16 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-1600	Centrifugal Pump	1.52E-04	
P-1601	Centrifugal Pump	7.59E-06	
P-1602	Centrifugal Pump	1.59E-04	
P-1603	Centrifugal Pump	2.65E-04	
P-1604	Centrifugal Pump	4.41E-04	
P-1605	Centrifugal Pump	4.41E-04	
P-1606	Centrifugal Pump	8.44E-06	
P-1607	Centrifugal Pump	4.22E-07	
P-1608	Centrifugal Pump	1.47E-05	
P-1609	Centrifugal Pump	2.36E-05	
P-1610	Centrifugal Pump	2.21E-05	
P-1611	Centrifugal Pump	3.78E-04	

V-1600	Heating Vessel with Mixing	1.12E+00	Heating requirement
		2.01E-02	Mixing requirement
V-1601	Solvent Vessel	0.00E+00	
V-1602	Cooling Vessel with Mixing	-9.88E-01	Cooling requirement
		1.10E-02	Mixing requirement
V-1603	Solvent Vessel	0.00E+00	
F-1600	Filtration Unit	3.18E-01	
D-1600	Vacuum Dryer	1.05E+00	
		7.72E-01	
Solvent Recovery System	---	---	---
SR-P-1600	Centrifugal Pump	2.40E-04	
SR-P-1601	Centrifugal Pump	1.38E-04	
SR-P-1602	Centrifugal Pump	5.78E-06	
SR-P-1603	Centrifugal Pump	1.32E-04	
SR-P-1604	Centrifugal Pump	1.04E-04	
SR-C-1600	Distillation Column	9.21E+00	
SR-C-1601	Distillation Column	1.46E+01	
SR-F-1600	Filtration Unit	8.61E-02	
SR-D-1600	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		2.66E-01	Heating requirement

Table A-48. Recovered Solvent from the Solvent Recovery System Implemented to Process 16 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Acetic Acid	6812.58	97.95%
Water	377.72	99.50%
Isopropyl Acetate	15695.19	99.50%

A.1.17 Process 17 – Cooling Crystallization

The process flow diagram of Process 17 can be found in Figure A-17. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-49 and Table A-50, respectively. The mass of solvent recovered from Process 17 using solvent recovery techniques are reported in Table A-51.

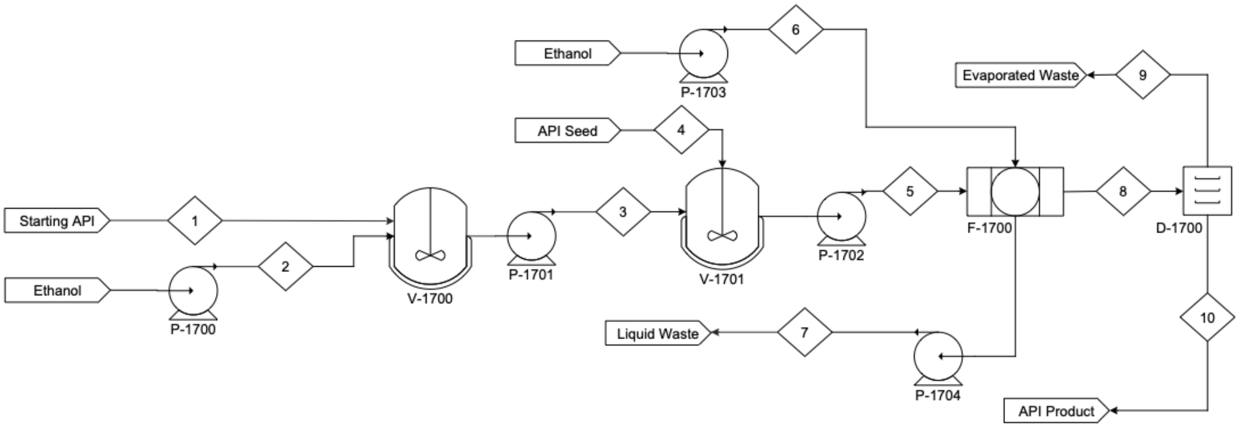

Figure A-17. Process flow diagram of Process 17 – Cooling Crystallization.

Table A-49. Mass of Each Component in Each Stream of Process 17 (According to Figure A-17). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**API (g)**	**Ethanol (g)**
1	1105.58	0.00
2	0.00	10467.66
3	1105.58	10467.66
4	5.53	0.00
5	1111.11	10467.66
6	0.00	1744.61
7	111.11	9769.82
8	1000.00	2442.45
9	0.00	2442.45
10	1000.00	0.00
Solvent Recovery System	---	---
11	0.00	9672.12
12	111.11	97.70
13	11.11	78.16
14	100.00	19.54
15	0.00	19.54

16	100.00	0.00

Table A-50. Equipment Description for Process 17 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-1700	Centrifugal Pump	1.60E-04	
P-1701	Centrifugal Pump	1.77E-04	
P-1702	Centrifugal Pump	1.77E-04	
P-1703	Centrifugal Pump	2.67E-05	
P-1704	Centrifugal Pump	1.51E-04	
V-1700	Heating Vessel with Mixing	3.22E-01	Heating requirement
		4.97E-04	Mixing requirement
V-1701	Cooling Vessel with Mixing	-4.59E-01	Cooling requirement
		2.73E-02	Mixing requirement
F-1700	Filtration Unit	1.33E-01	
D-1700	Vacuum Dryer	1.22E+00	Heating requirement
		5.79E-01	Vacuum pump requirement
Solvent Recovery System	---	---	---
SR-P-1700	Centrifugal Pump	1.48E-04	
SR-P-1701	Centrifugal Pump	3.19E-06	
SR-P-1702	Centrifugal Pump	1.37E-06	
SR-C-1300	Distillation Column	2.84E+00	
SR-F-1300	Filtration Unit	2.09E-03	
SR-D-1300	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		6.49E-03	Heating requirement

Table A-51. Recovered Solvent from the Solvent Recovery System Implemented to Process 17 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
Ethanol	9761.39	99.89%

A.1.18 Process 18 – Antisolvent Crystallization

The process flow diagram of Process 18 can be found in Figure A-18. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-52 and Table A-53, respectively. The mass of solvent recovered from Process 18 using solvent recovery techniques are reported in Table A-54.

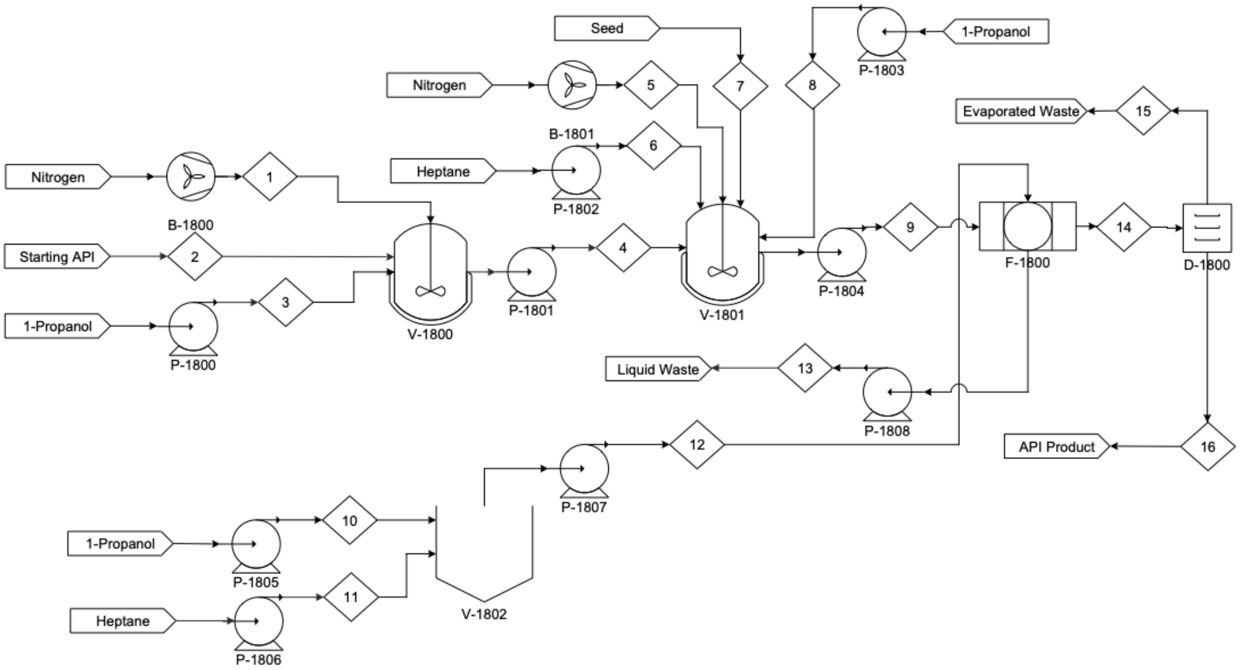

Figure A-18. Process flow diagram of Process 18 – Antisolvent Crystallization.

Table A-52. Mass of Each Component in Each Stream of Process 18 (According to Figure A-18). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API (g)	1-Propanol (g)	Heptane (g)
1	-	-	-
2	1105.58	0.00	0.00
3	0.00	3551.14	0
4	1105.58	3551.14	0.00
5	-	-	-
6	0.00	0.00	189.05

7	5.53	0.00	0.00
8	0.00	10431.46	0.00
9	1111.11	13982.60	189.05
10	0.00	665.84	0
11	0.00	0.00	1701.49
12	0.00	665.84	1701.49
13	111.11	11718.75	1512.44
14	1000.00	2929.69	378.11
15	0.00	2929.69	378.11
16	1000.00	0.00	0.00
Solvent Recovery System	---	---	---
17	0.00	11601.56	58.30
18	111.11	117.19	1454.14
19	11.11	93.75	1163.31
20	100.00	23.44	290.83
21	0.00	23.44	290.83
22	100.00	0.00	1.00

Table A-53. Equipment Description for Process 18 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-1800	Centrifugal Pump	5.43E-05	
P-1801	Centrifugal Pump	7.12E-05	
P-1802	Centrifugal Pump	2.89E-06	
P-1803	Centrifugal Pump	1.60E-04	
P-1804	Centrifugal Pump	2.34E-04	
P-1805	Centrifugal Pump	1.02E-05	
P-1806	Centrifugal Pump	2.60E-05	
P-1807	Centrifugal Pump	3.62E-05	
P-1808	Centrifugal Pump	2.04E-04	
V-1800	Heating Vessel with Mixing	4.13E-01	Heating requirement

		4.81E-04	Mixing requirement
V-1801	Cooling Vessel with Mixing	-5.24E-02	Cooling requirement
		2.61E-02	Mixing requirement
V-1301	Solvent Mixture Vessel	0	
F-1800	Filtration Unit	4.90E-05	
D-1800	Vacuum Dryer	7.24E-01	Heating requirement
		4.01E+00	Vacuum pump requirement
Solvent Recovery System	---	---	---
SR-P-1800	Centrifugal Pump	1.78E-04	
SR-P-1801	Centrifugal Pump	2.57E-05	
SR-P-1802	Centrifugal Pump	1.94E-05	
SR-C-1800	Distillation Column	6.33E+01	
SR-F-1800	Filtration Unit	1.68E-02	
SR-D-1800	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		4.75E-02	Heating requirement

Table A-54. Recovered Solvent from the Solvent Recovery System Implemented to Process 18 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
1-Propanol	11659.86	99.50%
Heptane	1268.17	91.73%

A.1.19 Process 19 – Evaporative Crystallization

The process flow diagram of Process 19 can be found in Figure A-19. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-55 and Table A-56, respectively. The mass of solvent recovered from Process 19 using solvent recovery techniques are reported in Table A-57.

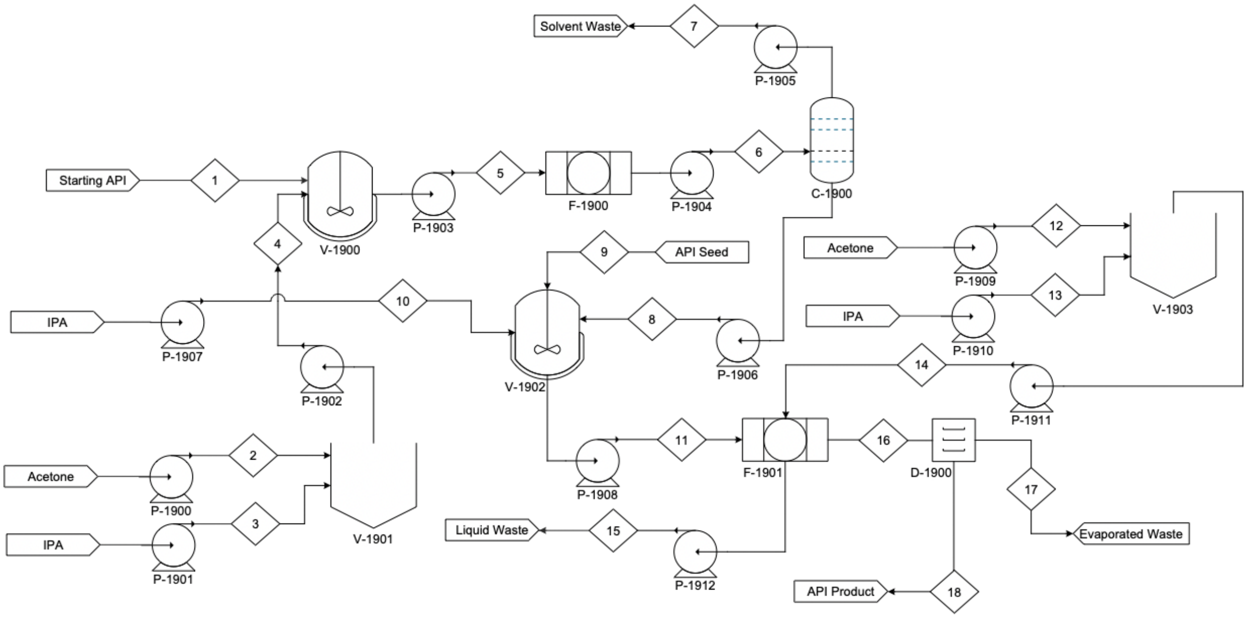

Figure A-19. Process flow diagram of Process 19 – Evaporative Crystallization.

Table A-55. Mass of Each Component in Each Stream of Process 19 (According to Figure A-19). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API (g)	Acetone (g)	IPA (g)
1	1105.584243	0	0.00
2	0.00	6934.22	0.00
3	0.00	0.00	1737.978429
4	0.00	6934.22	1737.98
5	1105.584243	6934.22	1737.98
6	1105.58	6934.22	1737.98
7	0.00	4853.96	347.60
8	1105.58	2080.27	1390.38
9	5.53	0.00	0.00
10	0.00	0.00	13903.82743
11	1111.11	2080.27	15294.21
12	0.00	434.49	0.00
	0.00	0.00	3041.46
13	111.11	2011.81	14668.54
14	1000.00	502.95	3667.13

15	0.00	502.95	3667.13
16	1000.00	0.00	0.00
Solvent Recovery System	**---**	**---**	**---**
17	0.00	6797.11	34.16
18	111.11	68.66	14981.98
19	11.11	54.93	11985.58
20	100.00	13.73	2996.40
21	0.00	13.73	2996.40
22	100.00	0.00	0.00

Table A-56. Equipment Description for Process 19 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-1900	Centrifugal Pump	1.06E-04	
P-1901	Centrifugal Pump	2.66E-05	
P-1902	Centrifugal Pump	1.33E-04	
P-1903	Centrifugal Pump	1.50E-04	
P-1904	Centrifugal Pump	1.50E-04	
P-1905	Centrifugal Pump	7.96E-05	
P-1906	Centrifugal Pump	7.00E-05	
P-1907	Centrifugal Pump	2.13E-04	
P-1908	Centrifugal Pump	2.83E-04	
P-1909	Centrifugal Pump	6.65E-06	
P-1910	Centrifugal Pump	4.65E-05	
P-1911	Centrifugal Pump	2.57E-04	
V-1900	Heating Vessel with Mixing	2.27E-01	Heating requirement
		2.94E-04	Mixing requirement
V-1901	Solvent Mixture Vessel	0.00E+00	
V-1902	Cooling Vessel with Mixing	-1.89E+00	Cooling requirement
		2.23E-02	Mixing requirement
V-1903	Solvent Mixture Vessel	0.00E+00	
C-1900	Distillation Column	1.31E-01	

F-1900	Polish Filtration Unit	2.41E-05	
F-1901	Filtration Unit	5.79E-05	
D-1900	Dryer	7.72E-01	Vacuum pump requirement
		1.44E+00	Heating requirement
Solvent Recovery System	---	---	---
SR-P-1900	Centrifugal Pump	1.05E-04	
SR-P-1901	Centrifugal Pump	2.32E-04	
SR-P-1902	Centrifugal Pump	1.84E-04	
SR-C-1900	Distillation Column	5.26E-01	
SR-F-1900	Filtration Unit	1.52E-01	
SR-D-1900	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		1.02E+00	Heating requirement

Table A-57. Recovered Solvent from the Solvent Recovery System Implemented to Process 19 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
Acetone	6831.27	99.50%
Isopropyl Alcohol	12051.62	99.45%

A.1.20 Process 20 – Antisolvent Crystallization

The process flow diagram of Process 20 can be found in Figure A-20. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-58 and Table A-59, respectively. The mass of solvent recovered from Process 20 using solvent recovery techniques are reported in Table A-60.

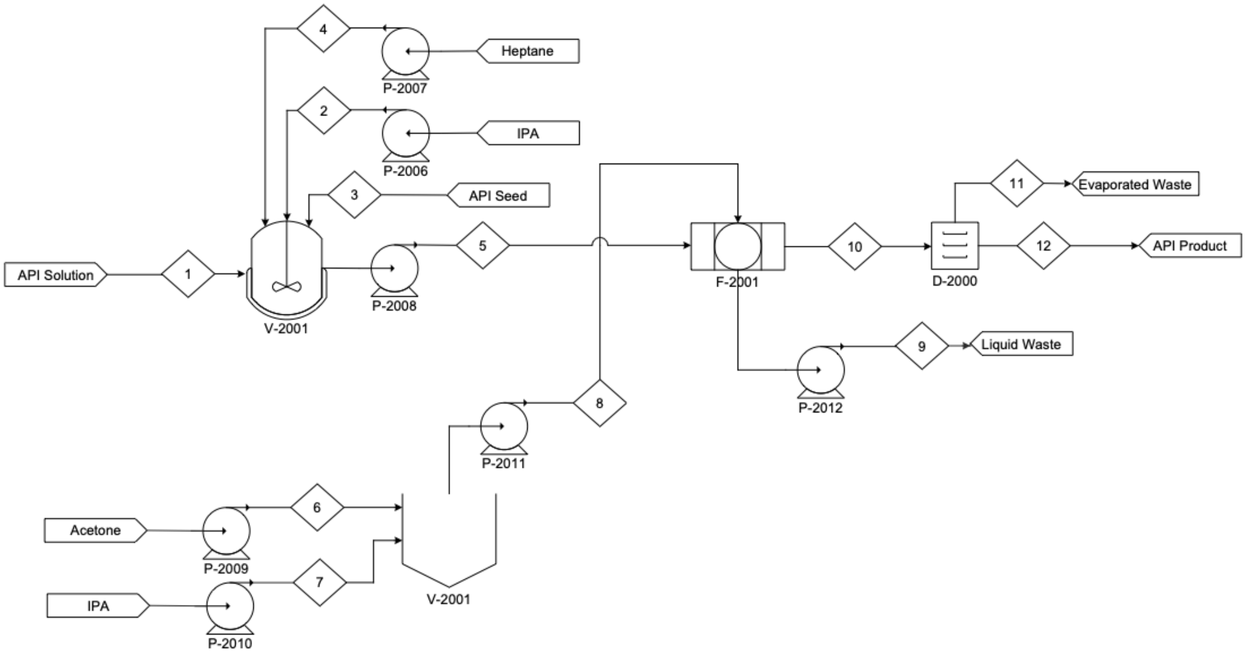

Figure A-20. Process flow diagram of Process 20 – Antisolvent Crystallization.

Table A-58. Mass of Each Component in Each Stream of Process 20 (According to Figure A-20). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API (g)	Heptane (g)	IPA (g)
1	1111.11	0.00	3333.33
2	0.00	0.00	3930.00
3	11.11	0.00	0.00
4	0.00	5700.00	0.00
5	1111.11	5700.00	7263.33
6	0.00	0.00	1310.00
7	0.00	1140.00	0.00
8	0.00	1140.00	1310.00
9	111.11	5472.00	6858.67
10	1000.00	1368.00	1714.67
11	0.00	1368.00	1714.67
12	1000.00	0.00	0.00
Solvent Recovery System	---	---	---
13	0.00	34.12	6790.08

14	111.11	5437.88	68.59
15	11.11	4350.30	54.87
16	100.00	1087.58	13.72
17	0.00	1087.58	13.72
18	100.00	0.00	0.00

Table A-59. Equipment Description for Process 20 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-2000	Centrifugal Pump	6.01E-05	
P-2001	Centrifugal Pump	8.72E-05	
P-2002	Centrifugal Pump	2.15E-04	
P-2003	Centrifugal Pump	2.00E-05	
P-2004	Centrifugal Pump	1.74E-05	
P-2005	Centrifugal Pump	3.75E-05	
V-2000	Cooing Vessel with Mixing	-9.62E-01	Cooling requirement
		2.89E-02	Mixing requirement
V-2001	Solvent Vessel	0.00E+00	
F-2000	Filtration Unit	1.65E-01	
D-2000	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		8.92E-01	Heating requirement
Solvent Recovery System	---	---	---
P-2000	Centrifugal Pump	6.01E-05	
SR-P-2000	Centrifugal Pump	1.04E-04	
SR-P-2001	Centrifugal Pump	8.59E-05	
SR-P-2004	Centrifugal Pump	6.76E-05	
SR-C-2000	Distillation Column	4.06E+00	
SR-F-2000	Filtration Unit	5.62E-02	
SR-D-2000	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		1.57E-01	Heating requirement

Table A-60. Recovered Solvent from the Solvent Recovery System Implemented to Process 20 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
Heptane	4416.28	98.51%
Isopropyl Alcohol	6824.20	99.50%

A.1.21 Process 21 – Reactive Crystallization

The process flow diagram of Process 21 can be found in Figure A-21. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-61 and Table A-62, respectively. The mass of solvent recovered from Process 21 using solvent recovery techniques are reported in Table A-63.

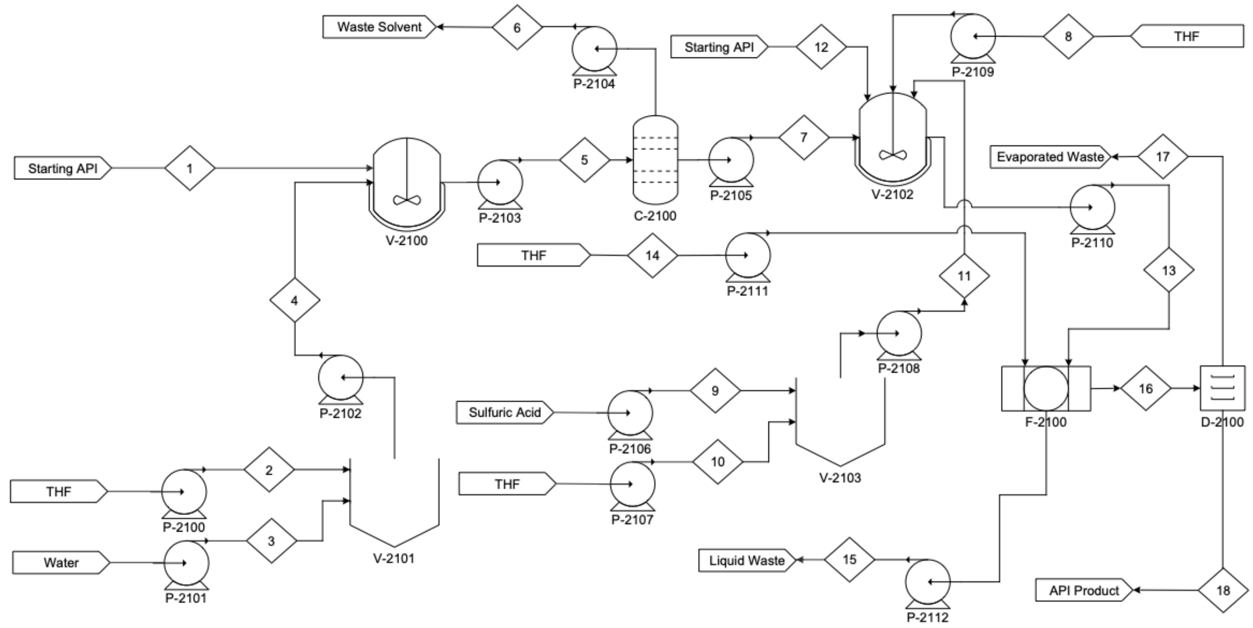

Figure A-21. Process flow diagram of Process 21 – Antisolvent Crystallization.

Table A-61. Mass of Each Component in Each Stream of Process 21 (According to Figure A-21). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	Starting API (g)	THF (g)	Water (g)	Sulfuric Acid (g)	API Product
1	846.35	0.00	0.00	0.00	0.00
2	0.00	25252.30	0.00	0.00	0.00

3	0.00	0.00	1181.33	0.00	0.00
4	0.00	25252.30	1181.33	0.00	0.00
5	846.35	25252.30	1181.33	0.00	0.00
6	0.00	20292.02	0.00	0.00	0.00
7	846.35	4960.27	1181.33	0.00	0.00
8	0.00	7515.56	0.00	0.00	0.00
9	0.00	0.00	0.00	222.45	0.00
10	0.00	3757.78	0.00	0.00	0.00
11	0.00	3757.78	0.00	222.45	0.00
12	0.00	0.00	0.00	0.00	42.32
13	0.00	16233.62	1181.33	0.00	1111.11
14	0.00	1503.11	0.00	0.00	0.00
15	0.00	14189.39	945.07	0.00	111.11
16	0.00	3547.35	236.27	0.00	1000.00
17	0.00	3547.35	236.27	0.00	0.00
18	0.00	0.00	0.00	0.00	1000.00
Solvent Recovery System	---	---	---	---	---
19	0.00	14047.49	70.59	0.00	0.00
20	0.00	141.89	874.47	0.00	111.11
21	0.00	140.47	0.71	0	0
22	0.00	1.42	873.77	0.00	111.11
23	0.00	1.14	699.02	0	11.11111112
24	0.00	0.28	174.75	0.00	100.00
25	0.00	0.28	174.75	0.00	0
26	0.00	0.00	0.00	0.00	100.00

Table A-62. Equipment Description for Process 21 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-2100	Pump	3.86E-04	
P-2101	Pump	1.81E-05	
P-2102	Pump	4.04E-04	

P-2103	Pump	4.17E-04	
P-2104	Pump	3.10E-04	
P-2105	Pump	1.07E-04	
P-2106	Pump	1.15E-04	
P-2107	Pump	3.40E-06	
P-2108	Pump	5.75E-05	
P-2109	Pump	6.09E-05	
P-2110	Pump	2.83E-04	
P-2111	Pump	2.30E-05	
P-2112	Pump	2.33E-04	
V-2100	Heating Vessel	1.58E-01	Heating requirement
		1.15E-02	Mixing requirement
V-2101	Solvent Vessel	0.00E+00	
V-2102	Cooling Vessel	-4.34E-01	Cooling requirement
		1.13E-02	Mixing requirement
V-2103	Solvent Vessel	0.00E+00	
C-2100	Distillation Column	4.44E+00	
F-2100	Filter	5.26E-05	
D-2100	Vacuum Dryer	1.16E+00	Vacuum pump requirement
		7.95E-01	Heating requirement
Solvent Recovery System	---	---	---
SR-P-2100	Pump	2.16E-04	
SR-P-2101	Pump	1.73E-05	
SR-P-2102	Pump	2.16E-06	
SR-P-2103	Pump	1.51E-05	
SR-P-2104	Pump	1.09E-05	
SR-C-2300	Distillation Column	2.26E+00	
SR-C-2300	Distillation Column	1.19E-01	
SR-F-2300	Filter	7.11E-03	
SR-D-2300	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		1.51E-01	Heating requirement

Table A-63. Recovered Solvent from the Solvent Recovery System Implemented to Process 21 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Tetrahydrofuran	34551.29	99.79%
Water	711.26	99.84%

A.1.22 Process 22 – Evaporative Crystallization

The process flow diagram of Process 22 can be found in Figure A-22. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-64 and Table A-65, respectively. The mass of solvent recovered from Process 22 using solvent recovery techniques are reported in Table A-66.

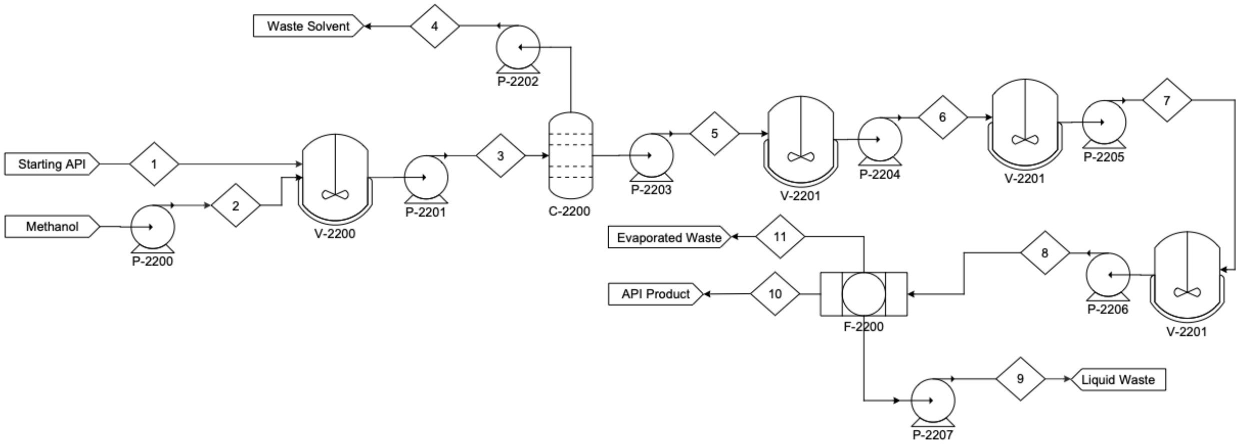

Figure A-22. Process flow diagram of Process 22 – Evaporative Crystallization.

Table A-64. Mass of Each Component in Each Stream of Process 22 (According to Figure A-22). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	Starting API (g)	MeOH (g)
1	1111.11	0.00
2	0.00	29040.00
3	1111.11	29040.00
4	0.00	22000.00
5	1111.11	7040.00
6	1111.11	7040.00

7	1111.11	7040.00
8	1111.11	7040.00
9	111.11	5632.00
10	1000.00	1408.00
11	0.00	1408.00
Solvent Recovery System	---	---
12	0.00	27355.68
13	111.11	1684.32
14	11.11	1347.46
15	100.00	336.86
16	0.00	336.86

Table A-65. Equipment Description for Process 22 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-2200	Centrifugal Pump	4.44E-04	
P-2201	Centrifugal Pump	4.61E-04	
P-2202	Centrifugal Pump	3.37E-04	
P-2203	Centrifugal Pump	1.25E-04	
P-2204	Centrifugal Pump	1.25E-04	
P-2205	Centrifugal Pump	1.25E-04	
P-2206	Centrifugal Pump	1.25E-04	
P-2207	Centrifugal Pump	8.79E-05	
V-2200	Heating Vessel	5.72E-04	Mixing requirement
		4.78E-01	Heating requirement
V-2201	Cooling Vessel	4.93E-03	Mixing requirement
		-1.68E-01	Cooling requirement
V-2202	Heating Vessel	1.48E-02	Mixing requirement
		5.24E-02	Heating requirement
V-2203	Cooling Vessel	2.46E-03	Mixing requirement
		-5.24E-02	Cooling requirement
C-2200	Distillation Column	8.71E+00	

F-2200	Filtration Unit	2.26E-05	
Solvent Recovery System	**---**	**---**	**---**
SR-P-2200	Centrifugal Pump	4.19E-04	
SR-P-2201	Centrifugal Pump	2.75E-05	
SR-C-2200	Distillation Column	1.04E+01	
SR-F-2200	Filtration Unit	1.80E-02	

Table A-66. Recovered Solvent from the Solvent Recovery System Implemented to Process 22 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Methanol	28714.25	99.96%

A.1.23 Process 23 – Antisolvent Crystallization

The process flow diagram of Process 23 can be found in Figure A-23. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-67 and Table A-68, respectively. The mass of solvent recovered from Process 23 using solvent recovery techniques are reported in Table A-69.

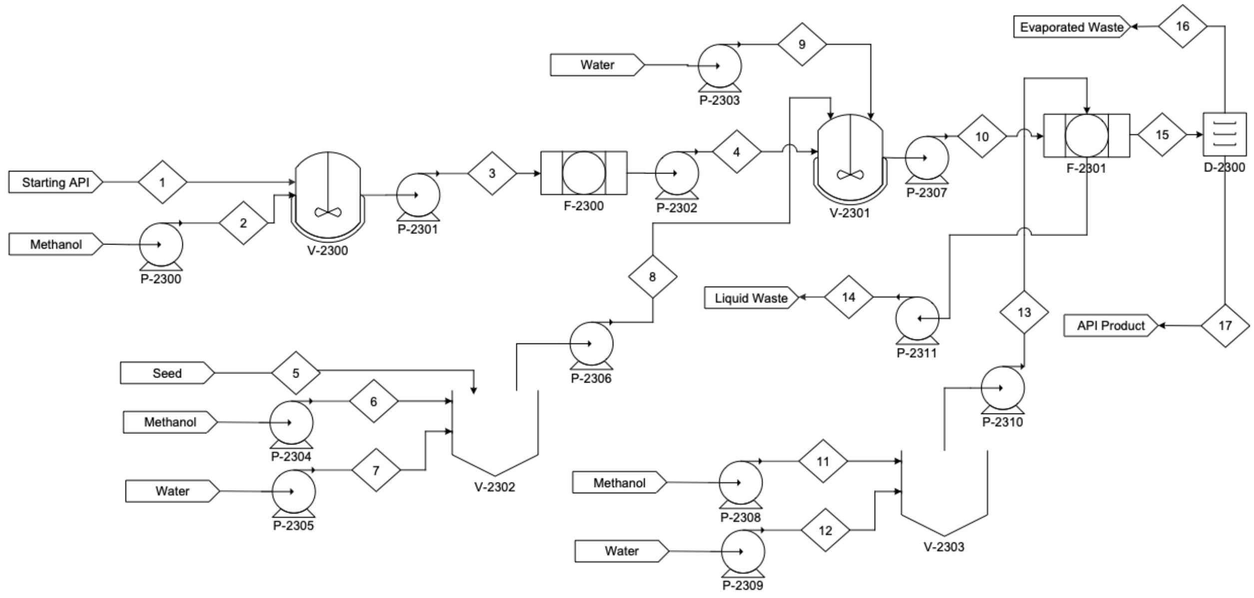

Figure A-23. Process flow diagram of Process 23 – Antisolvent Crystallization.

Table A-67. Mass of Each Component in Each Stream of Process 23 (According to Figure A-23). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**Starting API (g)**	**MeOH (g)**	**Water (g)**
1	1100.11	0.00	0.00
2	0.00	11326.74	0.00
3	1100.11	11326.74	0.00
4	1100.11	11326.74	0.00
5	11.00	0.00	0.00
6	0.00	435.64	0.00
7	0.00	0.00	548.41
8	11.00	435.64	548.41
9	0.00	0.00	13710.13
10	1111.11	11762.39	14258.54
11	0.00	1306.93	0.00
12	0.00	0.00	1645.22
13	0.00	1306.93	1645.22
14	111.11	10455.46	12723.00
15	1000.00	2613.86	3180.75
16	0.00	2613.86	3180.75
17	1000.00	0.00	0.00
Solvent Recovery System	---	---	---
18	0.00	10350.90	52.01
19	111.11	104.55	12670.99
20	11.11	83.64	10136.79
21	100.00	20.91	2534.20
22	0.00	20.91	2534.20
23	100.00	0.00	1.00

Table A-68. Equipment Description for Process 23 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-2300	Centrifugal Pump	1.73E-04	
P-2301	Centrifugal Pump	1.90E-04	
P-2302	Centrifugal Pump	1.90E-04	
P-2303	Centrifugal Pump	6.67E-06	
P-2304	Centrifugal Pump	8.39E-06	
P-2305	Centrifugal Pump	1.52E-05	
P-2306	Centrifugal Pump	2.10E-04	
P-2307	Centrifugal Pump	4.15E-04	
P-2308	Centrifugal Pump	2.00E-05	
P-2309	Centrifugal Pump	2.52E-05	
P-2310	Centrifugal Pump	4.52E-05	
P-2311	Centrifugal Pump	3.56E-04	
V-2300	Heating Vessel	3.24E-03	Mixing requirement
		1.46E-01	Heating requirement
V-2301	Cooling Vessel	2.69E-02	Mixing requirement
		-1.46E-01	Cooling requirement
V-2302	Solvent Mixture Vessel	0	
V-2303	Solvent Wash Vessel	0	
F-2300	Polish Filtration Unit	3.45E-05	
F-2301	Filtration Unit	8.36E-05	
D-2300	Vacuum Dryer	3.86E-01	
		3.80E+00	
Solvent Recovery System	---	---	---
SR-P-2300	Centrifugal Pump	1.59E-04	
SR-P-2301	Centrifugal Pump	1.97E-04	
SR-P-2302	Centrifugal Pump	1.57E-04	
SR-C-2300	Distillation Column	5.05E+00	
SR-F-2300	Filtration Unit	1.29E-01	

SR-D-2300	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		2.20E+00	Heating requirement

Table A-69. Recovered Solvent from the Solvent Recovery System Implemented to Process 23 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Methanol	10402.92	99.50%
Water	10231.55	99.07%

A.1.24 Process 24 – Cooling Crystallization

The process flow diagram of Process 24 can be found in Figure A-24. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-70 and Table A-71, respectively. The mass of solvent recovered from Process 24 using solvent recovery techniques are reported in Table A-72.

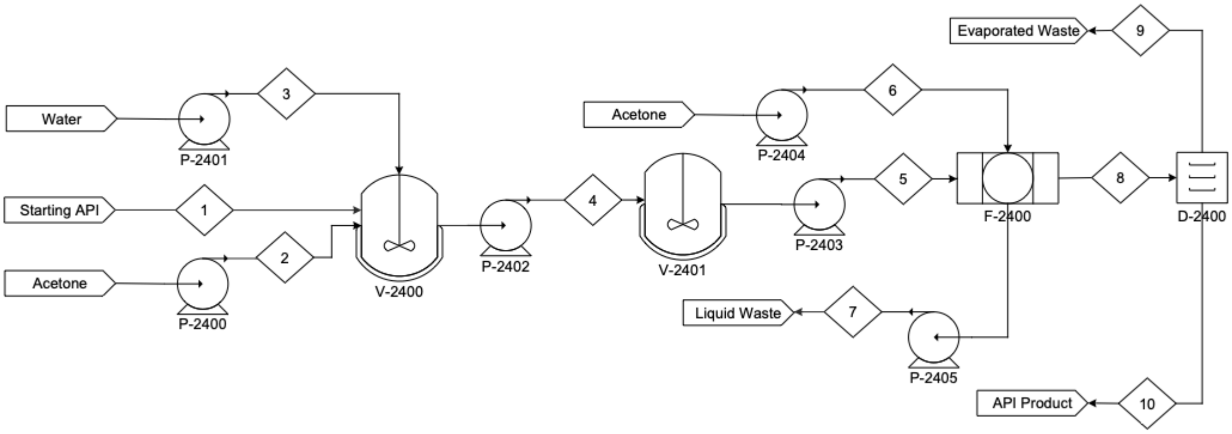

Figure A-24. Process flow diagram of Process 24 – Cooling Crystallization.

Table A-70. Mass of Each Component in Each Stream of Process 24 (According to Figure A-24). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API (g)	Acetone (g)	Water (g)
1	1111.11	0.00	0.00
2	0.00	7840.01	0.00
3	0.00	0.00	299.10

4	1111.11	7840.01	299.10
5	1111.11	7840.01	299.10
6	0.00	1742.22	0.00
7	111.11	7665.79	239.28
8	1000.00	1916.45	59.82
9	0.00	1916.45	59.82
10	1000.00	0.00	0.00
Solvent Recovery System	**---**	**---**	**---**
11	0.00	7589.13	38.14
12	111.11	76.66	201.14
13	0.00	75.89	0.38
14	111.11	0.77	200.76
15	11.11	0.61	160.61
16	100.00	76.04	40.53
17	0.00	76.04	40.53
18	100.00	0.00	1.00

Table A-71. Equipment Description for Process 24 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-2400	Centrifugal Pump	1.20E-04	
P-2401	Centrifugal Pump	4.58E-06	
P-2402	Centrifugal Pump	1.42E-04	
P-2403	Centrifugal Pump	1.42E-04	
P-2404	Centrifugal Pump	2.67E-05	
P-2405	Centrifugal Pump	1.23E-04	
V-2400	Heating Vessel	1.29E-03	Mixing requirement
		1.19E-01	Heating requirement
V-2401	Cooling Vessel	7.52E-03	Mixing requirement
		-1.39E-01	Cooling requirement
V-2302	Solvent Mixture Vessel	0.00E+00	
V-2303	Solvent Wash vessel	0.00E+00	

F-2400	Filtration Unit	3.05E-05	
D-2400	Vacuum Dryer	1.16E+00	Vacuum pump requirement
		1.54E-01	Heating requirement
Solvent Recovery System	---	---	---
SR-P-2400	Centrifugal Pump	1.17E-04	
SR-P-2401	Centrifugal Pump	5.95E-06	
SR-P-2402	Centrifugal Pump	1.17E-06	
SR-P-2403	Centrifugal Pump	4.78E-06	
SR-P-2404	Centrifugal Pump	2.64E-06	
SR-C-2400	Distillation Column	1.69E-01	
SR-C-2401	Distillation Column	3.17E-03	
SR-F-2400	Filtration Unit	3.13E-03	
SR-D-2400	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		3.88E-02	Heating requirement

Table A-72. Recovered Solvent from the Solvent Recovery System Implemented to Process 24 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
Acetone	7703.54	99.50%
Water	172.33	93.20%

A.1.25 Process 25 – Reactive Crystallization

The process flow diagram of Process 25 can be found in Figure A-25. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-73 and Table A-74, respectively. The mass of solvent recovered from Process 25 using solvent recovery techniques are reported in Table A-75.

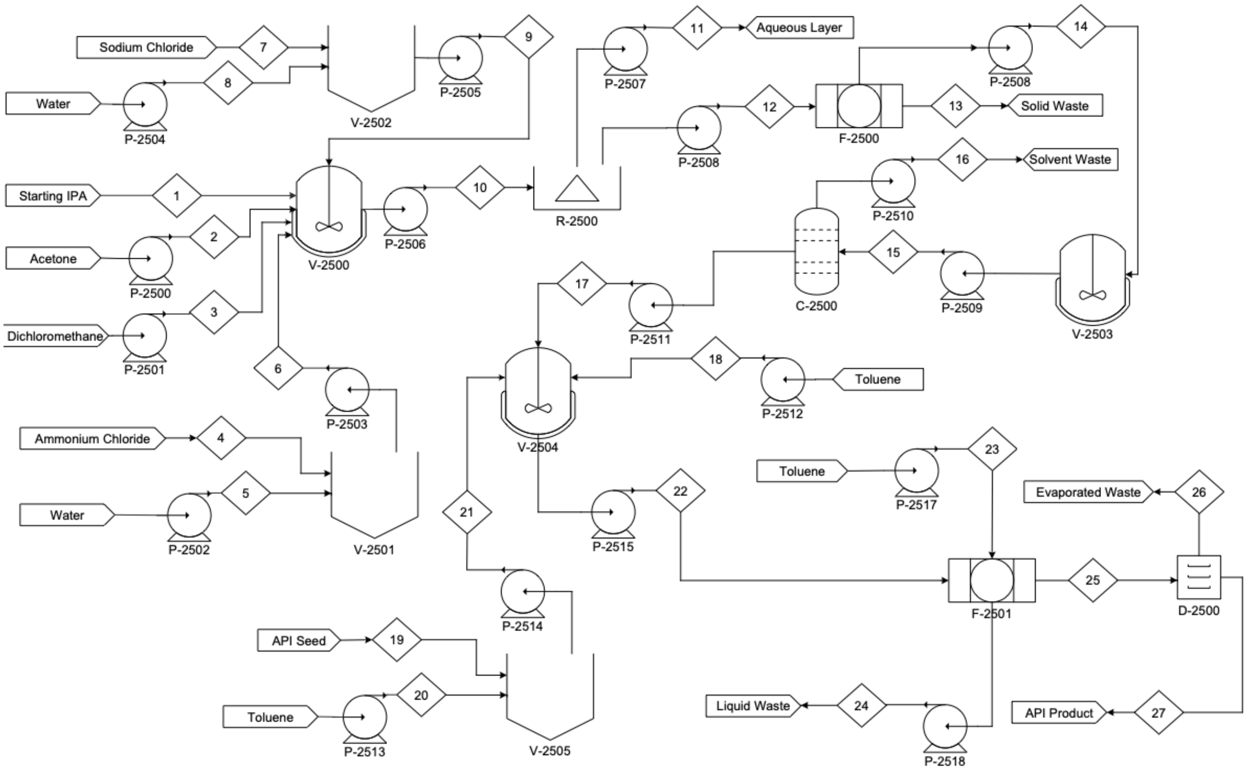

Figure A-25. Process flow diagram of Process 25 – Cooling Crystallization.

Table A-73. Mass of Each Component in Each Stream of Process 25 (According to Figure A-25). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	Starting API (g)	Dichloromethane (g)	Methanol (g)	Ammonium Chloride (g)	Water (g)	Sodium Chloride (g)	API Product (g)	Toluene (g)
1	552.792	0.000	0.000	0.000	0.000	0.000	0.000	0.000
2	0.000	24444.416	0.000	0.000	0.000	0.000	0.000	0.000
3	0.000	0.000	3359.163	0.000	0.000	0.000	0.000	0.000
4	0.000	0.000	0.000	337.203	0.000	0.000	0.000	0.000
5	0.000	0.000	0.000	0.000	1676.064	0.000	0.000	0.000
6	0.000	0.000	0.000	337.203	1676.064	0.000	0.000	0.000
7	0.000	0.000	0.000	0.000	0.000	221.117	0.000	0.000
8	0.000	0.000	0.000	0.000	2211.166	0.000	0.000	0.000
9	0.000	0.000	0.000	0.000	2211.166	221.117	0.000	0.000
10	0.000	24444.416	3359.163	0.000	3887.231	0.000	1111.111	0.000

11	0.000	0.000	0.000	0.000	3887.231	0.000	0.000	0.000
12	0.000	24444.416	3359.163	0.000	0.000	0.000	1111.111	0.000
13	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
14	0.000	24444.416	3359.163	0.000	0.000	0.000	1111.111	0.000
15	0.000	24444.416	3359.163	0.000	0.000	0.000	1111.111	0.000
16	0.000	24444.416	3353.481	0.000	0.000	0.000	0.000	0.000
17	0.000	0.000	5.682	0.000	0.000	0.000	0.000	0.000
18	0.000	0.000	0.000	0.000	0.000	0.000	0.000	840.243
19	0.000	0.000	0.000	0.000	0.000	0.000	0.553	0.000
20	0.000	0.000	0.000	0.000	0.000	0.000	0.000	5527.916
21	0.000	0.000	0.000	0.000	0.000	0.000	0.000	5527.916
22	0.000	0.000	5.682	0.000	0.000	0.000	1111.111	6368.159
23	0.000	0.000	0.000	0.000	0.000	0.000	0.000	4864.566
24	0.000	0.000	4.545	0.000	0.000	0.000	111.111	8986.180
25	0.000	0.000	1.136	0.000	0.000	0.000	1000.000	2246.545
26	0.000	0.000	1.136	0.000	0.000	0.000	0.000	2246.545
27	0.000	0.000	0.000	0.000	0.000	0.000	1000.000	0.000
Solvent Recovery System	---	---	---	---	---	---	---	---
28	0.00	24199.97	121.61	0.00	0.00	0.00	0.00	
29	0.00	244.44	3231.87	0.00	0.00	0.00	0.00	0.00
30	0.00	195.56	2585.50	0.00	0.00	0.00	0.00	0.00
31	0.00	48.89	646.37	0.00	0.00	0.00	0.00	0.00
32	0.00	48.89	646.37	0.00	0.00	0.00	0.00	0.00
33	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00

Table A-74. Equipment Description for Process 25 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-2500	Centrifugal Pump	3.74E-04	
P-2501	Centrifugal Pump	5.14E-05	

P-2502	Centrifugal Pump	2.56E-05	
P-2503	Centrifugal Pump	3.08E-05	
P-2504	Centrifugal Pump	3.38E-05	
P-2505	Centrifugal Pump	3.72E-05	
P-2506	Centrifugal Pump	5.02E-04	
P-2507	Centrifugal Pump	5.95E-05	
P-2508	Centrifugal Pump	4.42E-04	
P-2509	Centrifugal Pump	4.42E-04	
P-2510	Centrifugal Pump	4.25E-04	
P-2511	Centrifugal Pump	8.69E-08	
P-2512	Centrifugal Pump	1.29E-05	
P-2513	Centrifugal Pump	8.46E-09	
P-2514	Centrifugal Pump	8.46E-05	
P-2515	Centrifugal Pump	8.46E-05	
P-2516	Centrifugal Pump	1.15E-04	
P-2517	Centrifugal Pump	7.44E-05	
P-2518	Centrifugal Pump	1.39E-04	
V-2500	Cooling Vessel with Mixing	3.21E-03	Mixing requirement
		-2.05E-01	Cooling requirement
V-2501	Solvent Vessel	0.00E+00	
V-2502	Solvent Vessel	0.00E+00	
V-2503	Heating Vessel with Mixing	3.28E-03	Mixing requirement
		4.16E-01	Heating requirement
V-2504	Cooling Vessel with Mixing	8.53E-03	Mixing requirement
		-9.26E-02	Cooling requirement
V-2505	Solvent Vessel	0.00E+00	
C-2500	Distillation Column	3.47E+00	
F-2500	Polish Filtration Unit	1.58E-08	
F-2501	Filtration Unit	3.43E-05	
D-2500	Vacuum Dryer	1.16E+00	Vacuum pump requirement
		8.46E-02	Heating requirement

Solvent Recovery System	---	---	---
SR-P-2400	Centrifugal Pump	3.72E-04	
SR-P-2401	Centrifugal Pump	5.32E-05	
SR-P-2404	Centrifugal Pump	4.26E-05	
SR-C-2400	Distillation Column	3.42E+00	
SR-F-2400	Filtration Unit	3.48E+03	
SR-D-2400	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		2.67E-01	Heating requirement

Table A-75. Recovered Solvent from the Solvent Recovery System Implemented to Process 25 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Acetone	7703.54	99.50%
Water	172.33	93.20%

A.1.26 Process 26 – Antisolvent Crystallization

The process flow diagram of Process 26 can be found in Figure A-26. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-76 and Table A-77, respectively. The mass of solvent recovered from Process 26 using solvent recovery techniques are reported in Table A-78.

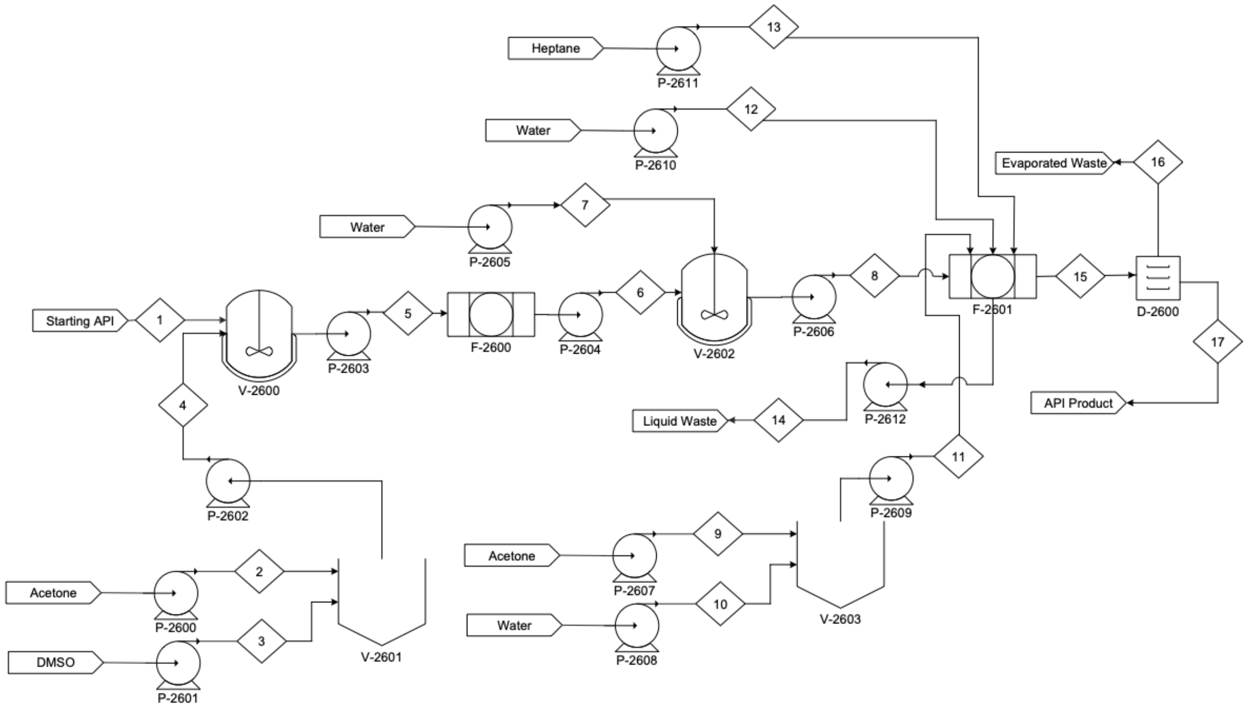

Figure A-26. Process flow diagram of Process 26 – Antisolvent Crystallization.

Table A-76. Mass of Each Component in Each Stream of Process 26 (According to Figure A-26). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API (g)	Acetone (g)	DMSO (g)	Water (g)	Heptane (g)
1	1111.11	0.00	0.00	0.00	0.00
2	0.00	2613.34	0.00	0.00	0.00
3	0.00	0.00	2444.45	0.00	0.00
4	1111.11	2613.34	2444.45	0.00	0.00
5	1111.11	2613.34	2444.45	0.00	0.00
6	1111.11	2613.34	2444.45	0.00	0.00
7	0.00	0.00	0.00	16616.68	0.00
8	1111.11	2613.34	2444.45	16616.68	0.00
9	0.00	261.33	0.00	0.00	0.00
10	0.00	0.00	0.00	1329.33	0.00
11	0.00	261.33	0.00	1329.33	0.00
12	0.00	0.00	0.00	1661.67	0.00
13	0.00	0.00	0.00	0.00	1140.00

14	111.11	2299.74	1955.56	15686.15	912.00
15	1000.00	574.93	488.89	3921.54	228.00
16	0.00	574.93	488.89	3921.54	228.00
17	1000.00	0.00	0.00	0.00	0.00
Solvent Recovery System	---	---	---	---	---
18	0.00	2276.74	0.00	5.72	5.72
19	111.11	23.00	1955.56	15680.43	906.28
20	0.00	2.25	0.00	2.25	897.22
21	111.11	20.74	1955.56	15678.17	9.06
22	0.00	20.74	0.00	15521.39	9.06
23	111.11	0.00	1955.56	156.78	0.00
24	0.00	0.00	0.00	155.21	0.00
25	111.11	0.00	1955.56	1.57	0.00
26	11.11	0.00	1564.45	1.25	0.00
27	100.00	23.00	391.11	0.31	0.00
28	0.00	23.00	391.11	0.31	0.00
29	100.00	0.00	0.00	0.00	0.00

Table A-77. Equipment Description for Process 26 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-2600	Centrifugal Pump	4.00E-05	
P-2601	Centrifugal Pump	3.74E-05	
P-2602	Centrifugal Pump	9.44E-05	
P-2603	Centrifugal Pump	9.44E-05	
P-2604	Centrifugal Pump	9.44E-05	
P-2605	Centrifugal Pump	2.54E-04	
P-2606	Centrifugal Pump	3.49E-04	
P-2607	Centrifugal Pump	4.00E-06	
P-2608	Centrifugal Pump	2.03E-05	
P-2609	Centrifugal Pump	2.43E-05	
P-2610	Centrifugal Pump	2.54E-05	

P-2611	Centrifugal Pump	1.74E-05	
P-2612	Centrifugal Pump	3.21E-04	
V-2600	Heating Vessel with Mixing	2.76E-02	Mixing Requirement
		4.39E-02	Heating requirement
V-2601	Solvent Mixture Vessel	0.00E+00	
V-2602	Cooling Vessel with Mixing	3.60E-02	
		-1.55E-01	
V-2603	Solvent Mixture Vessel	0.00E+00	
V-2505	Solvent Wash vessel	0.00E+00	
F-2600	Polish Filtration Unit	1.71E-05	
F-2601	Filtration Unit	1.22E-05	
D-2600	Vacuum Dryer	3.86E-01	Vacuum pump requirement
		3.55E+00	Heating requirement
Solvent Recovery System	---	---	---
SR-P-2600	Centrifugal Pump	3.50E-05	
SR-P-2601	Centrifugal Pump	2.86E-04	
SR-P-2602	Centrifugal Pump	1.38E-05	
SR-P-2603	Centrifugal Pump	2.72E-04	
SR-P-2604	Centrifugal Pump	2.38E-04	
SR-P-2605	Centrifugal Pump	3.40E-05	
SR-P-2606	Centrifugal Pump	2.37E-06	
SR-P-2607	Centrifugal Pump	3.16E-05	
SR-P-2608	Centrifugal Pump	2.41E-05	
SR-C-2600	Distillation Column	1.73E-01	
SR-C-2601	Distillation Column	1.83E+02	
SR-C-2602	Distillation Column	1.25E+01	
SR-C-2603	Distillation Column	1.38E-01	
SR-F-2600	Filtration Unit	2.07E-02	
SR-D-2600	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		6.20E-02	Heating requirement

Table A-78. Recovered Solvent from the Solvent Recovery System Implemented to Process 26 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Acetone	2288.18	99.50%
Dimethyl sulfoxide	1576.81	99.22%
Water	15706.41	99.81%
Heptane	901.73	99.50%

A.1.27 Process 27 – Reactive Crystallization

The process flow diagram of Process 27 can be found in Figure A-27. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-79 and Table A-80, respectively. The mass of solvent recovered from Process 27 using solvent recovery techniques are reported in Table A-81.

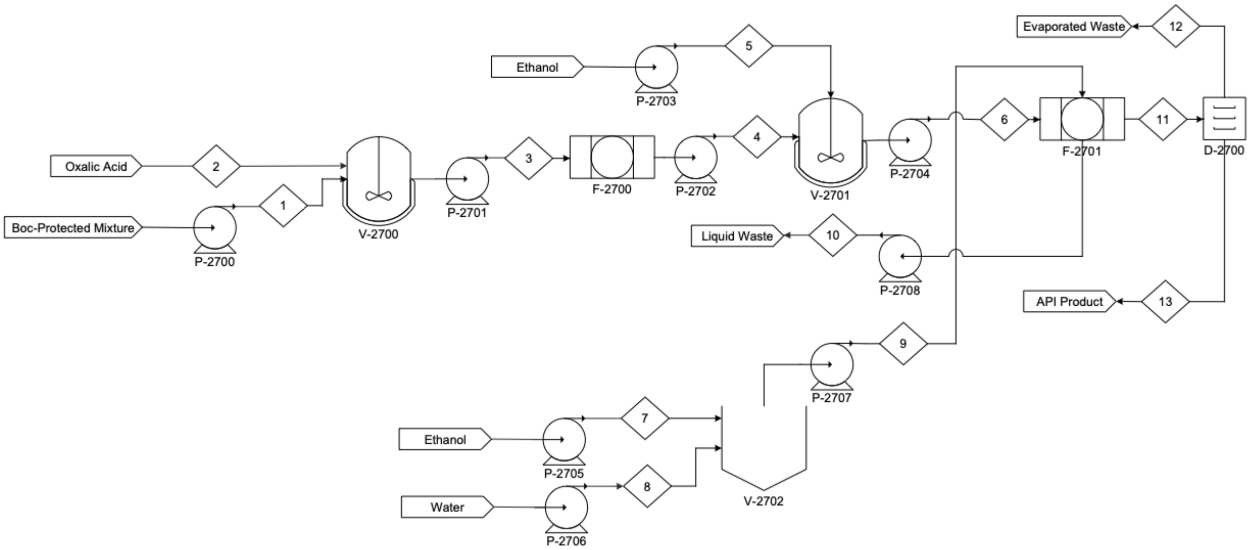

Figure A-27. Process flow diagram of Process 27 – Reactive Crystallization.

Table A-79. Mass of Each Component in Each Stream of Process 27 (According to Figure A-27). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	Starting API (g)	Oxalic Acid (g)	EtOH (g)	Water (g)	API Product (g)
1	357.597	0.000	0.000	34226.277	0.000
2	0.000	753.515	0.000	0.000	0.000

3	0.000	0.000	0.000	34226.277	1111.111
4	0.000	0.000	0.000	34226.277	1111.111
5	0.000	0.000	6771.448	0.000	0.000
6	0.000	0.000	6771.448	34226.277	1111.111
7	0.000	0.000	902.860	0.000	0.000
8	0.000	0.000	0.000	285.219	0.000
9	0.000	0.000	902.860	285.219	0.000
10	0.000	0.000	6139.446	27609.197	111.111
11	0.000	0.000	1534.861	6902.299	1000.000
12	0.000	0.000	1534.861	6902.299	0.000
13	0.000	0.000	0.000	0.000	1000.000
Solvent Recovery System	---	---	---	---	---
14	0.00	0.00	6078.05	30.54	0.00
15	0.00	0.00	61.39	27578.65	111.11
16	0.00	0.00	49.12	22062.92	11.11
17	0.00	0.00	12.28	5515.73	100.00
18	0.00	0.00	12.28	5515.73	0.00
19	0.00	0.00	0.00	0.00	100.00

Table A-80. Equipment Description for Process 27 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-2700	Centrifugal Pump	5.29E-04	
P-2701	Centrifugal Pump	5.41E-04	
P-2702	Centrifugal Pump	5.41E-04	
P-2703	Centrifugal Pump	1.04E-04	
P-2704	Centrifugal Pump	6.44E-04	
P-2705	Centrifugal Pump	1.38E-05	
P-2706	Centrifugal Pump	4.36E-06	
P-2707	Centrifugal Pump	1.82E-05	
P-2708	Centrifugal Pump	5.18E-04	

V-2700	Heating Vessel with Mixing	2.17E-04	Mixing Requirement
		0.00E+00	Heating requirement
V-2701	Cooling Vessel with Mixing	8.44E-03	Mixing Requirement
		-6.65E-01	Cooling requirement
V-2702	Solvent Vessel	0.00E+00	
F-2700	Polish Filtration	9.82E-05	
F-2701	Filtration	1.20E-04	
D-2700	Vacuum Dryer	5.79E-01	
		6.64E+00	
Solvent Recovery System	---	---	---
SR-P-2700	Centrifugal Pump	9.30E-05	
SR-P-2701	Centrifugal Pump	9.39E-07	
SR-P-2702	Centrifugal Pump	7.51E-07	
SR-C-2700	Distillation Column	2.01E+01	
SR-F-2700	Filtration	2.21E+04	
SR-D-2700	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		4.76E+00	Heating requirement

Table A-81. Recovered Solvent from the Solvent Recovery System Implemented to Process 27 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
Ethanol	6108.59	99.50%
Water	22123.15	99.73%

A.1.28 Process 28 – Reactive Crystallization

The process flow diagram of Process 28 can be found in Figure A-28. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-82 and Table A-83, respectively. The mass of solvent recovered from Process 28 using solvent recovery techniques are reported in Table A-84.

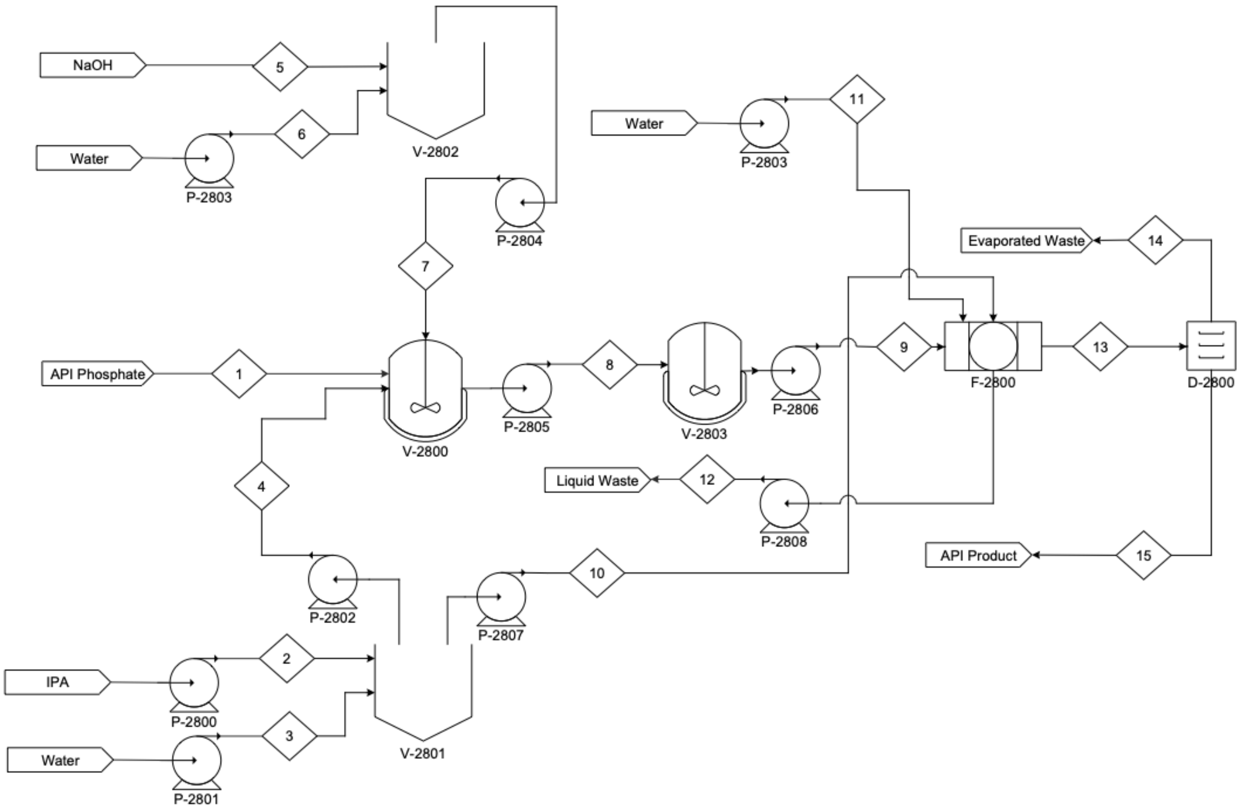

Figure A-28. Process flow diagram of Process 28 – Reactive Crystallization.

Table A-82. Mass of Each Component in Each Stream of Process 28 (According to Figure A-28). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	Starting API (g)	IPA (g)	Water (g)	NaOH (g)	API Product (g)
1	997.79	0.00	0.00	0.00	0.00
2	0.00	3882.12	0.00	0.00	0.00
3	0.00	0.00	11489.95	0.00	0.00
4	0.00	3529.20	10445.41	0.00	0.00
5	0.00	0.00	0.00	113.32	0.00
6	0.00	0.00	2266.34	0.00	0.00
7	0.00	3529.20	12711.75	0.00	1111.11
8	0.00	3529.20	12711.75	0.00	1111.11
9	0.00	3529.20	12711.75	0.00	1111.11
10	0.00	352.92	1044.54	0.00	0.00
11	0.00	0.00	1492.20	0.00	0.00

12	0.00	3105.69	12198.79	0.00	111.11
13	0.00	776.42	3049.70	0.00	1000.00
14	0.00	776.42	3049.70	0.00	0.00
15	0.00	0.00	0.00	0.00	1000.00
Solvent Recovery System	---	---	---	---	---
16	0.00	3074.64	15.45	0.00	0.00
17	0.00	31.06	12183.34	0.00	111.11
18	0.00	24.85	9746.67	0.00	11.11
19	0.00	6.21	2436.67	0.00	100.00
20	0.00	6.21	2436.67	0.00	0.00
21	0.00	0.00	0.00	0.00	100.00

Table A-83. Equipment Description for Process 28 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-2800	Centrifugal Pump	5.94E-05	
P-2801	Centrifugal Pump	1.76E-04	
P-2802	Centrifugal Pump	2.14E-04	
P-2803	Centrifugal Pump	3.47E-05	
P-2804	Centrifugal Pump	2.65E-04	
P-2805	Centrifugal Pump	2.65E-04	
P-2806	Centrifugal Pump	2.65E-04	
P-2807	Centrifugal Pump	2.14E-05	
P-2808	Centrifugal Pump	2.28E-05	
P-2809	Centrifugal Pump	2.36E-04	
V-2800	Heating Vessel with Mixing	3.20E-03	Mixing Requirement
		8.80E-01	Heating requirement
V-2801	Solvent Vessel	0.00E+00	
V-2802	Solvent Vessel	0.00E+00	
V-2803	Cooling Vessel with Mixing	3.20E-03	Mixing Requirement
		-1.22E-01	Cooling requirement

F-2800	Filtration Unit	5.62E-05	
D-2800	Vacuum Dryer	2.41E-01	Vacuum pump requirement
		2.93E+00	Heating requirement
Solvent Recovery System	---	---	---
SR-P-2800	Centrifugal Pump	4.73E-05	
SR-P-2801	Centrifugal Pump	1.89E-04	
SR-P-2802	Centrifugal Pump	1.50E-04	
SR-C-2800	Distillation Column	3.76E-02	
SR-F-2800	Filtration Unit	9.78E+03	
SR-D-2800	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		8.28E-01	Heating requirement

Table A-84. Recovered Solvent from the Solvent Recovery System Implemented to Process 28 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Isopropyl Alcohol	3090.09	99.50%
Water	9782.63	99.63%

A.1.29 Process 29 – Reactive Crystallization

The process flow diagram of Process 29 can be found in Figure A-29. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-85 and Table A-86, respectively. The mass of solvent recovered from Process 29 using solvent recovery techniques are reported in Table A-87.

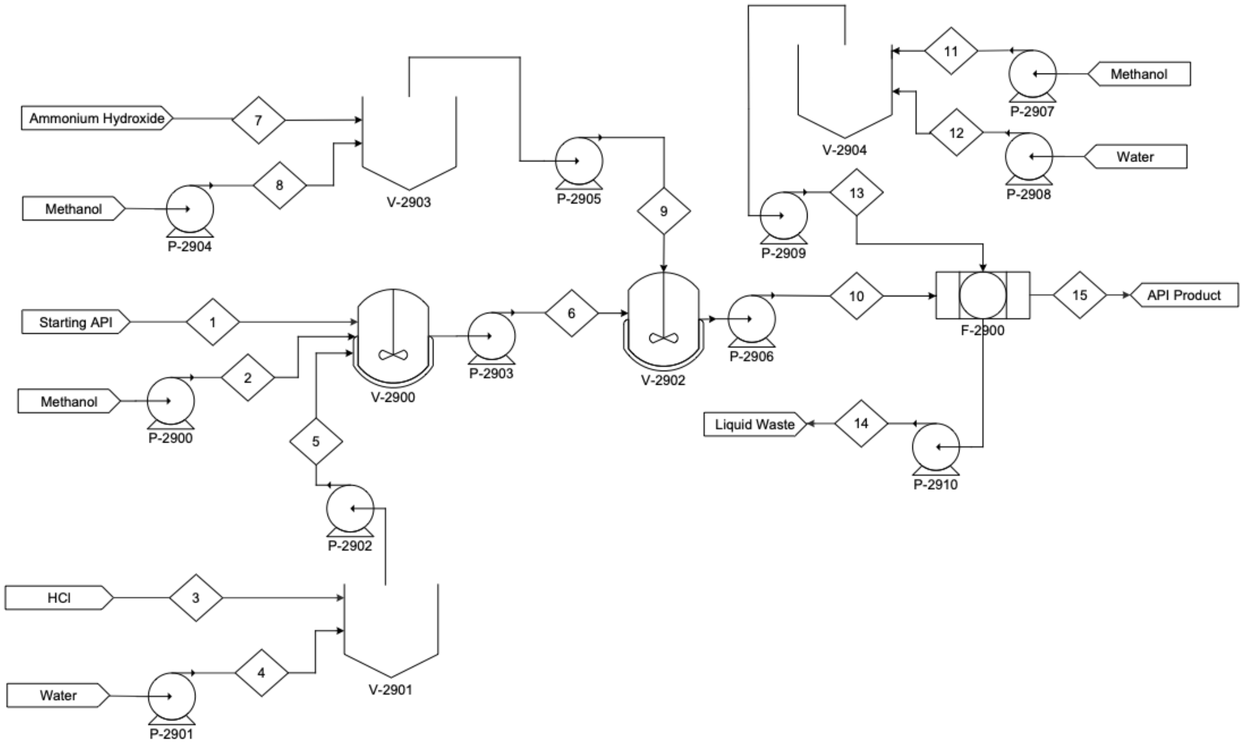

Figure A-29. Process flow diagram of Process 29 – Reactive Crystallization.

Table A-85. Mass of Each Component in Each Stream of Process 29 (According to Figure A-29). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	Starting API (g)	Methanol (g)	Hydrochloric Acid (g)	Water (g)	Ammonium Hydroxide (g)	API Product (g)
1	284.990	0.000	0.000	0.000	0.000	0.000
2	0.000	1128.559	0.000	0.000	0.000	0.000
3	0.000	0.000	26.209	0.000	0.000	0.000
4	0.000	0.000	0.000	649.532	0.000	0.000
5	0.000	0.000	26.209	649.532	0.000	0.000
6	0.000	1128.559	0.000	649.532	0.000	338.907
7	0.000	0.000	0.000	0.000	27.708	0.000
8	0.000	677.136	0.000	0.000	0.000	0.000
9	0.000	0.000	0.000	0.000	0.000	338.907
10	0.000	1805.695	0.000	649.532	0.000	338.907
11	0.000	451.424	0.000	0.000	0.000	0.000
12	0.000	0.000	0.000	568.269	0.000	0.000

13	0.000	451.424	0.000	568.269	0.000	0.000
14	0.000	1805.695	0.000	974.241	0.000	33.891
15	0.000	451.424	0.000	243.560	0.000	305.016
Solvent Recovery System	---	---	---	---	---	---
16	0.00	1787.64	0.00	8.98	0.00	0.00
17	0.00	18.06	0.00	965.26	0.00	33.89
18	0.00	14.45	0.00	772.21	0.00	3.39
19	0.00	3.61	0.00	193.05	0.00	30.50
20	0.00	3.61	0.00	193.05	0.00	0.00
21	0.00	0.00	0.00	0.00	0.00	30.50

Table A-86. Equipment Description for Process 29 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-2900	Centrifugal Pump	1.73E-05	
P-2901	Centrifugal Pump	9.94E-06	
P-2902	Centrifugal Pump	1.03E-05	
P-2903	Centrifugal Pump	3.24E-05	
P-2904	Centrifugal Pump	1.04E-05	
P-2905	Centrifugal Pump	5.19E-06	
P-2906	Centrifugal Pump	4.28E-05	
P-2907	Centrifugal Pump	6.91E-06	
P-2908	Centrifugal Pump	8.69E-06	
P-2909	Centrifugal Pump	1.56E-05	
P-2910	Centrifugal Pump	4.31E-05	
V-2900	Heating Vessel with Mixing	3.82E-04	Mixing Requirement
		3.95E-02	Heating requirement
V-2901	Solvent Vessel	0.00E+00	
V-2902	Cooling Vessel with Mixing	3.90E-04	Mixing Requirement
		-4.58E-03	Cooling requirement

V-2903	Solvent Vessel	0.00E+00	
V-2904	Solvent Vessel	0.00E+00	
F-2900	Filtration Unit	1.06E-05	
Solvent Recovery System	---	---	---
SR-P-2700	Centrifugal Pump	2.75E-05	
SR-P-2401	Centrifugal Pump	1.56E-05	
SR-P-2404	Centrifugal Pump	1.21E-05	
SR-C-2400	Distillation Column	1.63E-02	
SR-F-2400	Filtration Unit	7.87E+02	
SR-D-2400	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		1.67E-01	Heating requirement

Table A-87. Recovered Solvent from the Solvent Recovery System Implemented to Process 29 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
Methanol	1796.62	99.50%
Water	786.65	97.74%

A.1.30 Process 30 – Antisolvent Crystallization

The process flow diagram of Process 30 can be found in Figure A-30. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-88 and Table A-89, respectively. The mass of solvent recovered from Process 30 using solvent recovery techniques are reported in Table A-90.

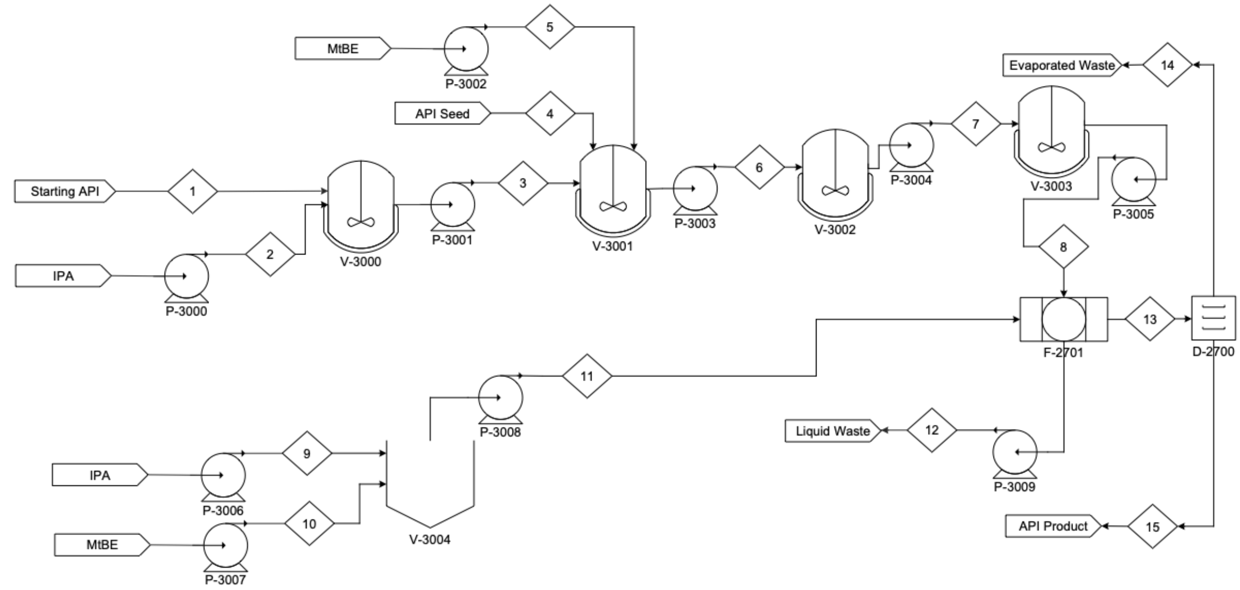

Figure A-30. Process flow diagram of Process 30 – Antisolvent Crystallization.

Table A-88. Mass of Each Component in Each Stream of Process 30 (According to Figure A-30). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**API (g)**	**IPA (g)**	**MTBE (g)**
1	1089.33	0.00	0.00
2	0.00	3424.84	0.00
3	1089.33	3424.84	0.00
4	21.79	0.00	0.00
5	0.00	0.00	8061.01
6	1111.11	3424.84	8061.01
7	1111.11	3424.84	8061.01
8	1111.11	3424.84	8061.01
9	0.00	1027.45	0.00
10	0.00	0.00	2257.08
11	0.00	1027.45	2257.08
12	111.11	3561.83	8254.47
13	1000.00	890.46	2063.62
14	0.00	890.46	2063.62

15	1000.00	0.00	0.00
Solvent Recovery System	---	---	---
16	0.00	41.06	8171.93
17	111.11	3520.77	82.54
18	11.11	2816.61	66.04
19	100.00	704.15	16.51
20	0.00	704.15	16.51
21	100.00	0.00	0.00

Table A-89. Equipment Description for Process 30 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-3000	Centrifugal Pump	5.24E-05	
P-3001	Centrifugal Pump	6.91E-05	
P-3002	Centrifugal Pump	1.23E-04	
P-3003	Centrifugal Pump	1.93E-04	
P-3004	Centrifugal Pump	1.93E-04	
P-3005	Centrifugal Pump	1.93E-04	
P-3006	Centrifugal Pump	1.57E-05	
P-3007	Centrifugal Pump	3.45E-05	
P-3008	Centrifugal Pump	5.03E-05	
P-3009	Centrifugal Pump	1.82E-04	
V-3000	Heating Vessel	3.13E-04	Mixing requirement
		3.47E-01	Heating requirement
V-3001	Cooling Vessel	1.30E-02	Mixing requirement
		-2.79E-01	Cooling requirement
V-3002	Heating Vessel	3.71E-03	Mixing requirement
		1.42E-01	Heating requirement
V-3003	Cooling Vessel	7.42E-03	Mixing requirement
		-2.75E-01	Cooling requirement
V-3003	Solvent Vessel	0.00E+00	
F-3000	Filtration Unit	4.41E-05	

D-3000	Vacuum Dryer	8.69E-01	Vacuum pump requirement
		5.94E-01	Heating requirement
Solvent Recovery System	---	---	
SR-P-3000	Centrifugal Pump	1.26E-04	
SR-P-3001	Centrifugal Pump	5.68E-05	
SR-P-3002	Centrifugal Pump	4.43E-05	
SR-C-3000	Distillation Column	1.68E-01	
SR-F-3000	Filtration Unit	3.71E-02	
SR-D-3000	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		2.41E-01	Heating requirement

Table A-90. Recovered Solvent from the Solvent Recovery System Implemented to Process 30 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
Isopropyl Alcohol	2893.76	97.33%
Methyl tert-Butyl Ether	8212.99	99.50%

A.1.31 Process 31A – Antisolvent Crystallization

The process flow diagram of Process 31A can be found in Figure A-31. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-91 and Table A-92, respectively. The mass of solvent recovered from Process 31A using solvent recovery techniques are reported in Table A-93.

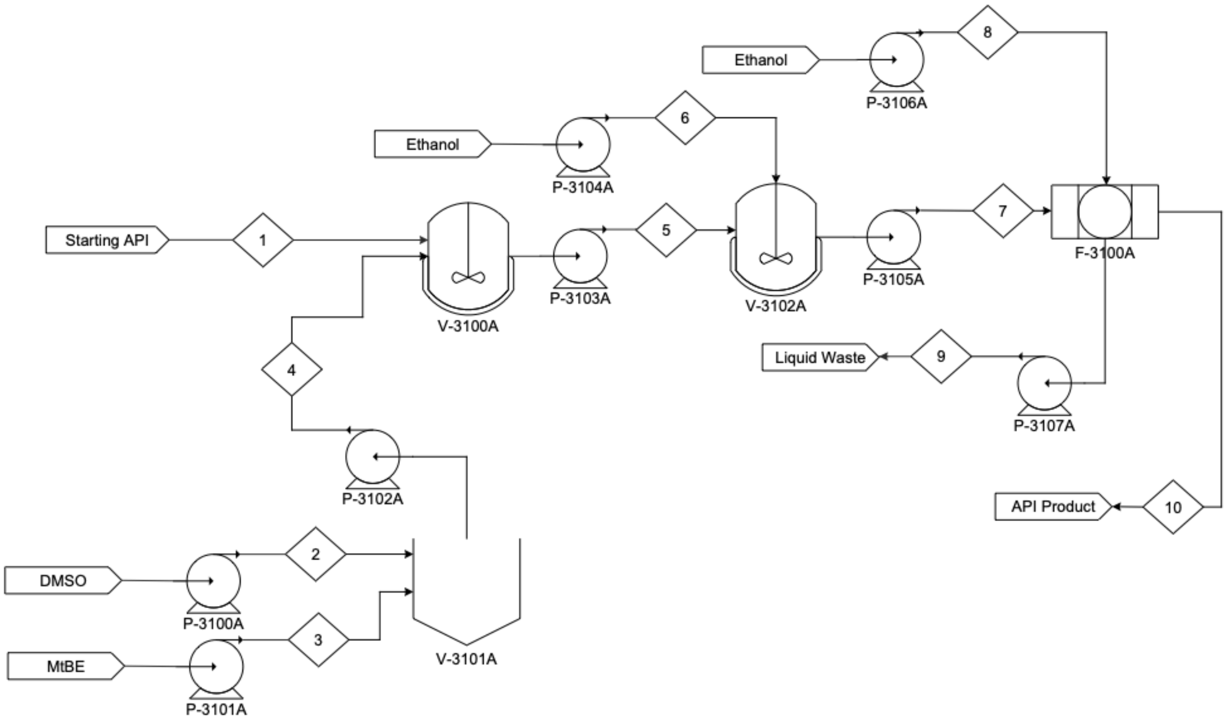

Figure A-31. Process flow diagram of Process 31A – Antisolvent Crystallization.

Table A-91. Mass of Each Component in Each Stream of Process 31A (According to Figure A-31). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**API (g)**	**DMSO (g)**	**EtOH (g)**
1	1037.11	0.00	0.00
2	0.00	2909.09	0.00
3	0.00	0.00	1391.08
4	0.00	2909.09	1391.08
5	1037.11	2909.09	1391.08
6	0.00	0.00	12274.19
7	1037.11	2909.09	13665.27
8	0.00	0.00	2454.84
9	103.71	2898.91	16063.69
10	933.40	10.18	56.42
Solvent Recovery System	**---**	**---**	**---**
11	0.00	79.91	15903.05
12	103.71	2829.18	160.64

13	10.37	2263.34	128.51
14	93.34	565.84	32.13

Table A-92. Equipment Description for Process 31A and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-3100A	Centrifugal Pump	4.45E-05	
P-3101A	Centrifugal Pump	2.13E-05	
P-3102A	Centrifugal Pump	6.58E-05	
P-3103A	Centrifugal Pump	8.17E-05	
P-3104A	Centrifugal Pump	1.88E-04	
P-3105A	Centrifugal Pump	2.69E-04	
P-3106A	Centrifugal Pump	3.76E-05	
P-3107A	Centrifugal Pump	2.92E-04	
V-3100A	Heating Vessel with Mixing	1.21E-03	Mixing requirement
		7.75E-02	Heating requirement
V-3101A	Solvent Mixture Vessel	0.00E+00	
V-3102A	Cooling Vessel with Mixing	1.19E-03	Mixing Requirement
		-7.22E+00	Cooling requirement
F-3100A	Filtration Unit	5.57E-05	
Solvent Recovery System	---	---	
SR-P-3100A	Centrifugal Pump	2.45E-04	
SR-P-3101A	Centrifugal Pump	4.73E-05	
SR-P-3102A	Centrifugal Pump	3.68E-05	
SR-C-3100A	Distillation Column	2.39E-02	
SR-F-3100A	Filter	3.09E-02	

Table A-93. Recovered Solvent from the Solvent Recovery System Implemented to Process 31A with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
Dimethyl Sulfoxide	2402.22	94.22%

Ethanol	15982.97	99.50%

A.1.32 Process 31B – Antisolvent Crystallization

The process flow diagram of Process 31B can be found in Figure A-32. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-94 and Table A-95, respectively. The mass of solvent recovered from Process 31B using solvent recovery techniques are reported in Table A-95.

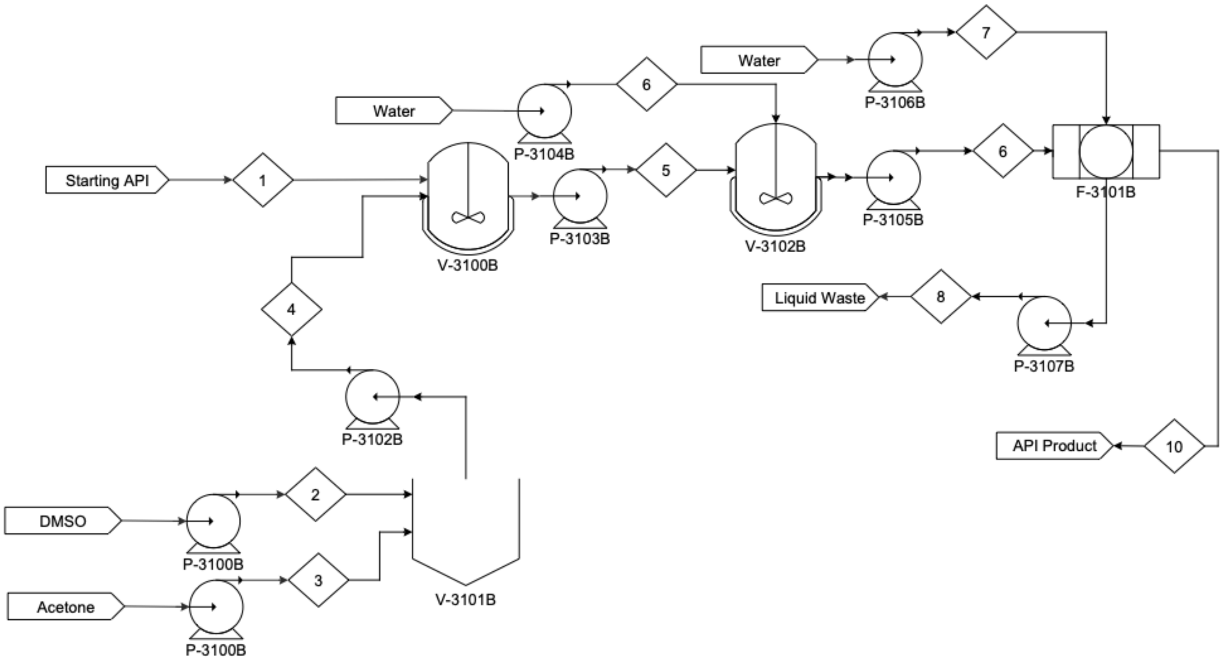

Figure A-32. Process flow diagram of Process 31B – Antisolvent Crystallization.

Table A-94. Mass of Each Component in Each Stream of Process 31B (According to Figure A-32). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**API (g)**	**Acetone (g)**	**DMSO (g)**	**Water (g)**
1	1069.11	0.00	0.00	0.00
2	0.00	6412.10	0.00	0.00
3	0.00	0.00	999.62	0.00
4	0.00	6412.10	999.62	0.00
5	1069.11	6412.10	999.62	0.00

6	0.00	0.00	0.00	12257.90
7	1069.11	6412.10	999.62	12257.90
8	0.00	0.00	0.00	3197.71
9	106.91	6379.40	994.52	15376.78
10	962.20	32.70	5.10	78.82
Solvent Recovery System	---	---	---	---
11	0.00	6315.61	15.87	15.87
12	106.91	96.50	978.65	15360.92
13	0.00	38.21	38.21	15207.31
14	106.91	58.29	940.44	153.61
15	0.00	0.38	0.38	152.07
16	106.91	57.90	940.06	1.54
17	10.69	46.32	752.05	1.23
18	96.22	11.58	188.01	0.31

Table A-95. Equipment Description for Process 31B and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-3100B	Pump	9.81E-05	
P-3101B	Pump	1.53E-05	
P-3102B	Pump	1.13E-04	
P-3103B	Pump	1.30E-04	
P-3104B	Pump	1.88E-04	
P-3105B	Pump	3.17E-04	
P-3106B	Pump	4.89E-05	
P-3107B	Pump	3.50E-04	
V-3100B	Heating Vessel with Mixing	1.08E-03	Mixing requirement
		1.12E-01	Heating requirement
V-3101B	Solvent Mixture Vessel	0.00E+00	
V-3102B	Cooling Vessel with Mixing	1.01E-02	Mixing requirement
		-5.59E-02	Cooling requirement
F-3100B	Filtration Unit	2.36E-05	

Solvent Recovery System	**---**	**---**	**---**
SR-P-3100B	Pump	9.69E-05	
SR-P-3101B	Pump	1.81E-05	
SR-P-3102B	Pump	1.24E-05	
SR-C-3100B	Distillation Column	1.03E-01	
SR-C-3100B	Distillation Column	8.53E-02	
SR-C-3100B	Distillation Column	4.91E-02	
SR-F-3100B	Filter	1.11E-02	

Table A-96. Recovered Solvent from the Solvent Recovery System Implemented to Process 31B with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Acetone	6347.34	99.50%
Dimethyl Sulfoxide	810.29	92.81%
Water	15436.56	99.50%

A.1.33 Process 32 – Reactive Crystallization

The process flow diagram of Process 32 can be found in Figure A-33. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-97 and Table A-98, respectively. The mass of solvent recovered from Process 32 using solvent recovery techniques are reported in Table A-99.

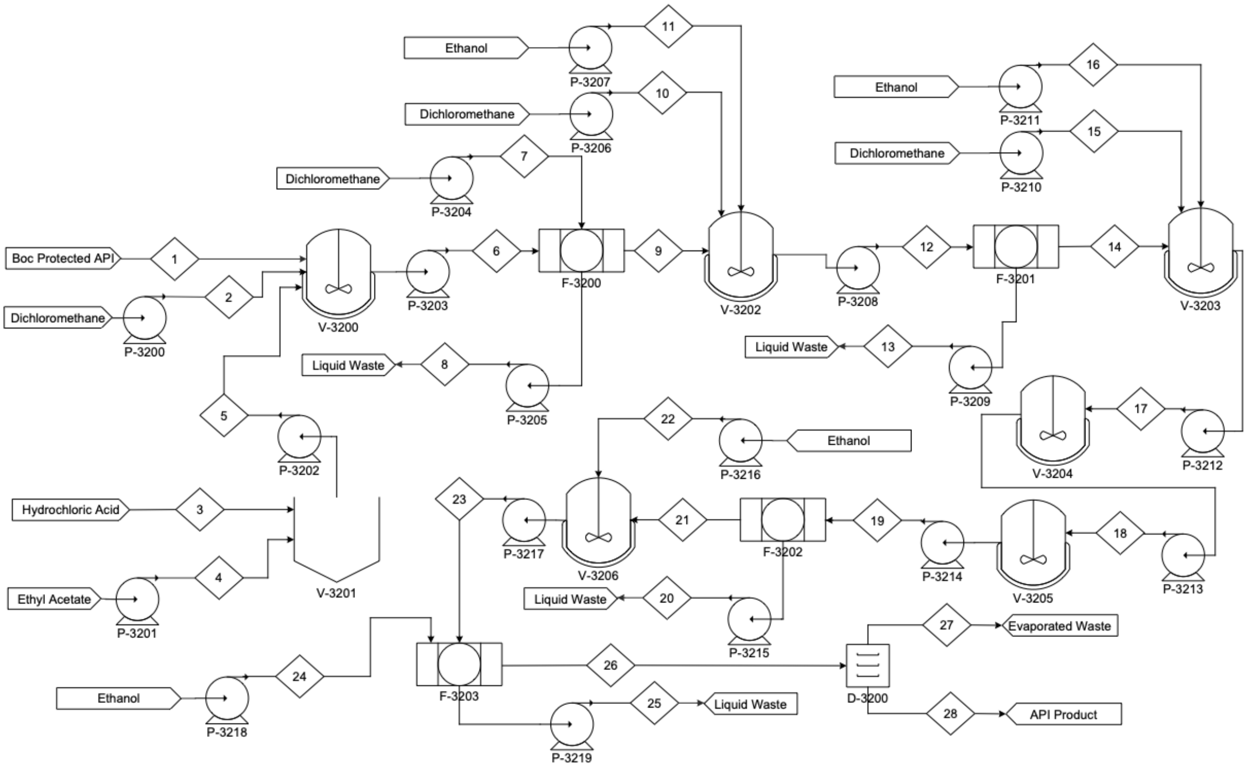

Figure A-33. Process flow diagram of Process 32 – Reactive Crystallization.

Table A-97. Mass of Each Component in Each Stream of Process 32 (According to Figure A-33). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API (g)	Acetone (g)	DMSO (g)	Water (g)
1	1069.11	0.00	0.00	0.00
2	0.00	6412.10	0.00	0.00
3	0.00	0.00	999.62	0.00
4	0.00	6412.10	999.62	0.00
5	1069.11	6412.10	999.62	0.00
6	0.00	0.00	0.00	12257.90
7	1069.11	6412.10	999.62	12257.90
8	0.00	0.00	0.00	3197.71
9	106.91	6379.40	994.52	15376.78
10	962.20	32.70	5.10	78.82
Solvent Recovery System	---	---	---	---
11	0.00	6315.61	15.87	15.87

12	106.91	96.50	978.65	15360.92
13	0.00	38.21	38.21	15207.31
14	106.91	58.29	940.44	153.61
15	0.00	0.38	0.38	152.07
16	106.91	57.90	940.06	1.54
17	10.69	46.32	752.05	1.23
18	96.22	11.58	188.01	0.31

Table A-98. Equipment Description for Process 32 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-3100B	Pump	9.81E-05	
P-3101B	Pump	1.53E-05	
P-3102B	Pump	1.13E-04	
P-3103B	Pump	1.30E-04	
P-3104B	Pump	1.88E-04	
P-3105B	Pump	3.17E-04	
P-3106B	Pump	4.89E-05	
P-3107B	Pump	3.50E-04	
V-3100B	Heating Vessel with Mixing	1.08E-03	Mixing requirement
		1.12E-01	Heating requirement
V-3101B	Solvent Mixture Vessel	0.00E+00	
V-3102B	Cooling Vessel with Mixing	1.01E-02	Mixing requirement
		-5.59E-02	Cooling requirement
F-3100B	Filtration Unit	2.36E-05	
Solvent Recovery System	---	---	---
SR-P-3100B	Pump	9.69E-05	
SR-P-3101B	Pump	1.81E-05	
SR-P-3102B	Pump	1.24E-05	
SR-C-3100B	Distillation Column	1.03E-01	
SR-C-3100B	Distillation Column	8.53E-02	

SR-C-3100B	Distillation Column	4.91E-02	
SR-F-3100B	Filter	1.11E-02	

Table A-99. Recovered Solvent from the Solvent Recovery System Implemented to Process 32 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
Acetone	6347.34	99.50%
Dimethyl Sulfoxide	810.29	92.81%
Water	15436.56	99.50%

A.1.34 Process 33 – Cooling Crystallization

The process flow diagram of Process 33 can be found in Figure A-34. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-100 and Table A-101, respectively. The mass of solvent recovered from Process 33 using solvent recovery techniques are reported in Table A-102.

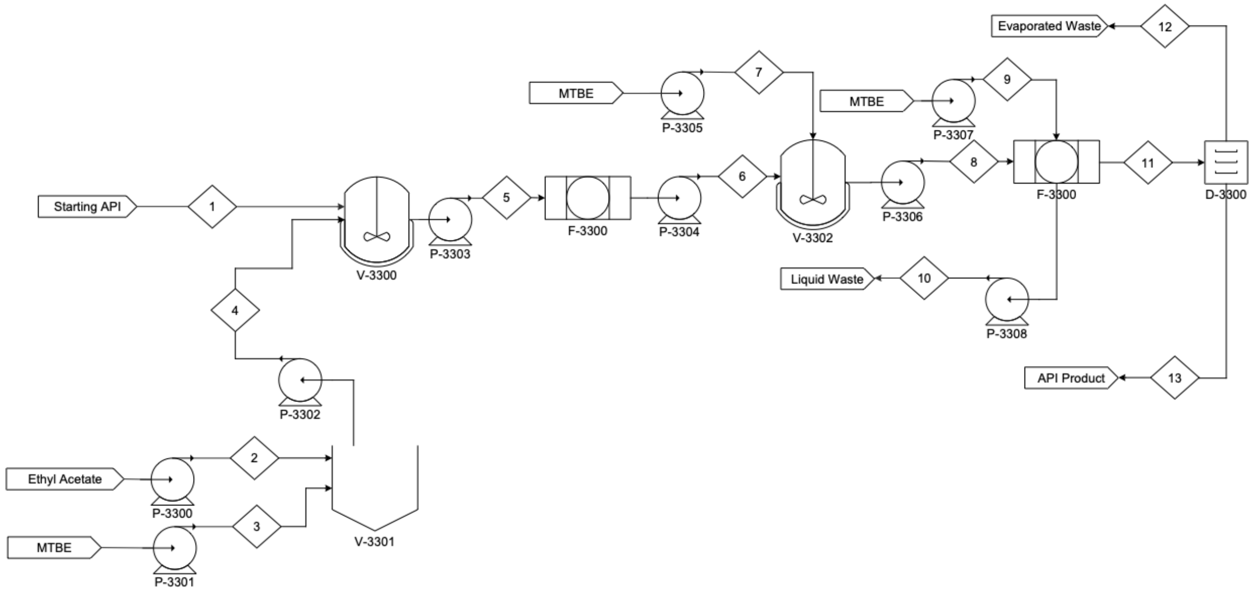

Figure A-34. Process flow diagram of Process 33 – Cooling Crystallization.

Table A-100. Mass of Each Component in Each Stream of Process 33 (According to Figure A-34). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**Starting API (g)**	**Ethyl Acetate (g)**	**MtBE (g)**

1	1111.11	0.00	0.00
2	0.00	3157.00	0.00
3	0.00	0.00	1110.00
4	0.00	3157.00	1110.00
5	1111.11	3157.00	1110.00
6	1111.11	3157.00	1110.00
7	0.00	0.00	12744.46
8	1111.11	3157.00	13854.46
9	0.00	0.00	1233.33
10	111.11	2525.60	12070.23
11	1000.00	631.40	3017.56
12	0.00	631.40	3017.56
13	1000.00	0.00	0.00
Solvent Recovery System	---	---	---
14	0.00	2500.35	12.56
15	111.11	25.26	12057.67
16	11.11	20.20	9646.14
17	100.00	5.05	2411.53
18	0.00	5.05	2411.53
19	100.00	0.00	0.00

Table A-101. Equipment Description for Process 33 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-3300	Centrifugal Pump	4.83E-05	
P-3301	Centrifugal Pump	1.70E-05	
P-3302	Centrifugal Pump	6.53E-05	
P-3303	Centrifugal Pump	8.23E-05	
P-3304	Centrifugal Pump	8.23E-05	
P-3305	Centrifugal Pump	1.95E-04	
P-3306	Centrifugal Pump	2.77E-04	
P-3307	Centrifugal Pump	1.89E-05	

P-3308	Centrifugal Pump	2.25E-04	
V-3300	Heating Vessel with Mixing	2.56E-04	Mixing requirement
		2.54E-01	Heating requirement
V-3301	Solvent Mixture Vessel	0.00E+00	
V-3302	Cooling Vessel with Mixture	1.40E-02	Mixing requirement
		-2.55E-01	Cooling requirement
F-3300	Polish Filtration Unit	1.49E-05	
F-3301	Filtration Unit	5.38E-05	
F-3300	Vacuum Dryer	5.79E-01	Heating requirement
		5.44E-01	Vacuum pump requirement
Solvent Recovery System	---	---	---
SR-P-3300	Centrifugal Pump	3.84E-05	
SR-P-3301	Centrifugal Pump	1.87E-04	
SR-P-3302	Centrifugal Pump	1.48E-04	
SR-C-3300	Distillation Column	9.78E-01	
SR-F-3300	Filtration Unit	1.22E-01	
SR-D-3300	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		3.17E-01	Heating requirement

Table A-102. Recovered Solvent from the Solvent Recovery System Implemented to Process 33 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
Ethyl Acetate	2512.91	99.50%
Methyl tert-Butyl Ether	9677.45	99.68%

A.1.35 Process 34 – Cooling Crystallization

The process flow diagram of Process 34 can be found in Figure A-35. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-103 and Table A-104, respectively. The mass of solvent recovered from Process 34 using solvent recovery techniques are reported in Table A-105.

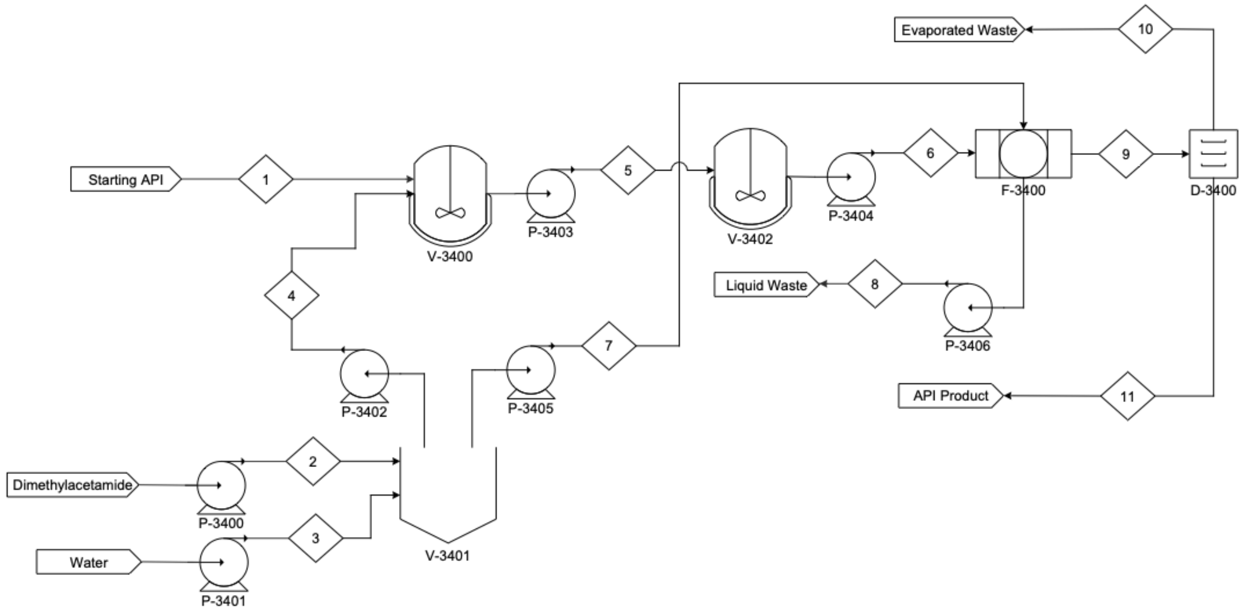

Figure A-35. Process flow diagram of Process 34 – Cooling Crystallization.

Table A-103. Mass of Each Component in Each Stream of Process 34 (According to Figure A-35). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**API (g)**	**DMAc (g)**	**Water (g)**
1	1111.11	0.00	0.00
2	0.00	14337.51	0.00
3	0.00	0.00	1717.06
4	0.00	11562.51	1384.72
5	1111.11	11562.51	1384.72
6	1111.11	11562.51	1384.72
7	0.00	2775.00	332.33
8	1111.11	0.00	0.00
9	0.00	14337.51	0.00
10	0.00	0.00	1717.06
11	0.00	11562.51	1384.72
Solvent Recovery System	---	---	---
12	0.00	6.83	1359.91
13	111.11	11463.18	13.74
14	11.11	9170.54	10.99

15	100.00	2292.64	2.75
16	0.00	2292.64	2.75
17	100.00	0.00	0.00

Table A-104. Equipment Description for Process 34 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-3400	Centrifugal Pump	2.19E-04	
P-3401	Centrifugal Pump	2.63E-05	
P-3402	Centrifugal Pump	1.98E-04	
P-3403	Centrifugal Pump	2.15E-04	
P-3404	Centrifugal Pump	2.15E-04	
P-3405	Centrifugal Pump	4.75E-05	
P-3406	Centrifugal Pump	1.98E-04	
V-3400	Heating Vessel with Mixing	3.87E-03	Mixing requirement
		3.27E-01	Heating requirement
V-3401	Solvent Vessel	0.00E+00	
V-3402	Cooling Vessel with Mixing	7.66E-02	Mixing requirement
		-3.68E-01	Cooling requirement
F-3400	Filtration Unit	1.72E-01	
D-3400	Vacuum Dryer	2.90E-01	Vacuum pump requirement
		4.25E-01	Heating requirement
Solvent Recovery System	---	---	---
SR-P-3500	Centrifugal Pump	2.09E-05	
SR-P-3501	Centrifugal Pump	1.77E-04	
SR-P-3502	Centrifugal Pump	1.41E-04	
SR-C-3500	Distillation Column	1.31E+00	
SR-F-3500	Filtration Unit	1.16E-01	
SR-D-3500	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		9.53E-02	Heating requirement

Table A-105. Recovered Solvent from the Solvent Recovery System Implemented to Process 34 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Dimethyl Acetamide	9192.64	99.76%
Water	1366.74	99.50%

A.1.36 Process 35 – Antisolvent Crystallization

The process flow diagram of Process 35 can be found in Figure A-36. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-106 and Table A-107, respectively. The mass of solvent recovered from Process 35 using solvent recovery techniques are reported in Table A-108.

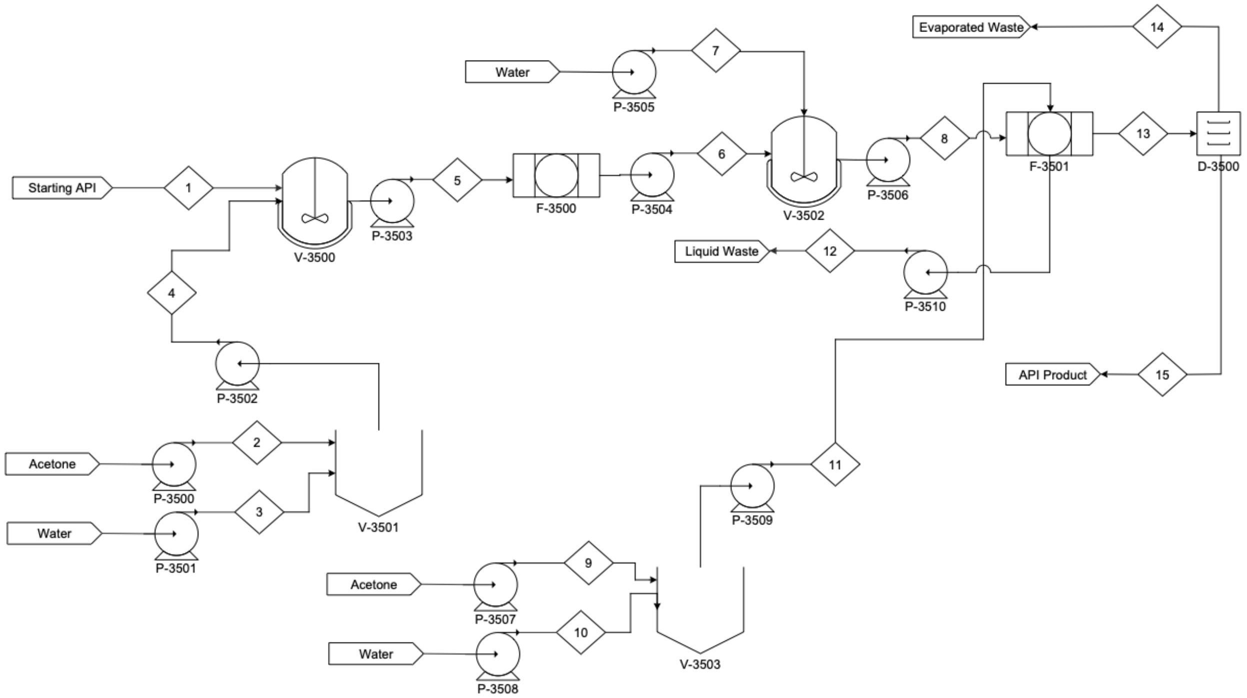

Figure A-36. Process flow diagram of Process 35 – Antisolvent Crystallization.

Table A-106. Mass of Each Component in Each Stream of Process 35 (According to Figure A-36). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	Starting API (g)	Acetone (g)	Water (g)
1	1111.11	0.00	0.00

2	0.00	3136.00	0.00
3	0.00	0.00	2658.67
4	0.00	3136.00	2658.67
5	1111.11	3136.00	2658.67
6	1111.11	3136.00	2658.67
7	0.00	0.00	13293.35
8	1111.11	3136.00	15952.02
9	0.00	696.89	0.00
10	0.00	0.00	3544.89
11	0.00	696.89	3544.89
12	111.11	3066.31	15597.53
13	1000.00	766.58	3899.38
14	0.00	766.58	3899.38
15	1000.00	0.00	0.00
Solvent Recovery System	---	---	---
16	0.00	3035.65	15.25
17	111.11	30.66	15582.27
18	11.11	24.53	12465.82
19	100.00	6.13	3116.45
20	0.00	6.13	3116.45
21	100.00	0.00	0.00

Table A-107. Equipment Description for Process 35 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-3500	Centrifugal Pump	4.80E-05	
P-3501	Centrifugal Pump	4.07E-05	
P-3502	Centrifugal Pump	8.87E-05	
P-3503	Centrifugal Pump	1.06E-04	
P-3504	Centrifugal Pump	1.06E-04	
P-3505	Centrifugal Pump	2.03E-04	
P-3506	Centrifugal Pump	3.09E-04	

P-3507	Centrifugal Pump	1.07E-05	
P-3508	Centrifugal Pump	5.42E-05	
P-3509	Centrifugal Pump	6.49E-05	
P-3510	Centrifugal Pump	2.87E-04	
V-3500	Heating Vessel with Mixing	2.22E-04	Mixing requirement
		1.00E-01	Heating requirement
V-3501	Solvent Mixture Vessel	0.00E+00	
V-3502	Cooling Vessel with Mixing	6.27E-03	Mixing requirement
		-1.00E-01	Cooling requirement
V-3503	Solvent Mixture Vessel	0.00E+00	
F-3501	Polish Filtration Unit	1.92E-05	
F-3502	Filtration Unit	6.79E-05	
D-3500	Vacuum dryer	5.79E-01	Heating requirement
		3.40E+00	Vacuum pump requirement
Solvent Recovery System	---	---	---
SR-P-3500	Centrifugal Pump	4.67E-05	
SR-P-3501	Centrifugal Pump	2.41E-04	
SR-P-3502	Centrifugal Pump	1.91E-04	
SR-C-3500	Distillation Column	1.64E-01	
SR-F-3500	Filtration Unit	1.57E-01	
SR-D-3500	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		2.69E+00	Heating requirement

Table A-108. Recovered Solvent from the Solvent Recovery System Implemented to Process 35 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
Acetone	3050.91	99.50%
Water	12501.46	99.71%

A.1.37 Process 36 – Evaporative Crystallization

The process flow diagram of Process 36 can be found in Figure A-37. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-109 and Table A-110, respectively. The mass of solvent recovered from Process 36 using solvent recovery techniques are reported in Table A-111.

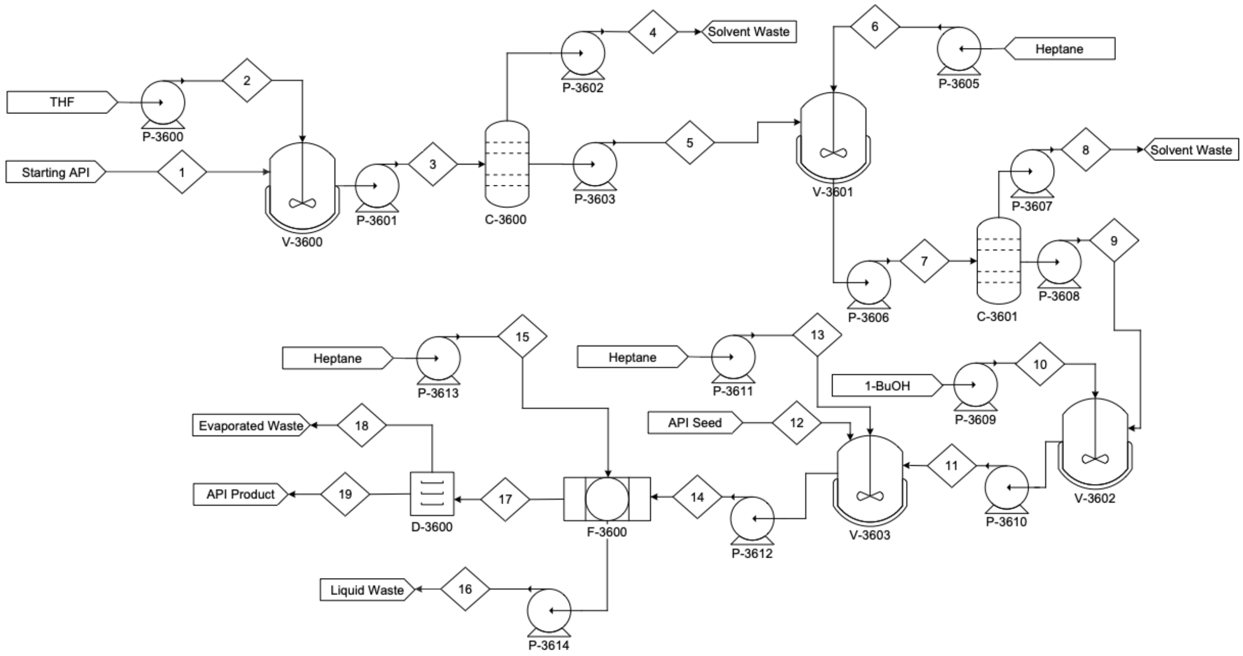

Figure A-37. Process flow diagram of Process 36 – Evaporative Crystallization.

Table A-109. Mass of Each Component in Each Stream of Process 36 (According to Figure A-37). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**API (g)**	**Tetrahydrofuran (g)**	**Heptane (g)**	**1-Butanol (g)**
1	1107.79	0.00	0.00	0.00
2	0.00	4918.58	0.00	0.00
3	1107.79	4918.58	0.00	0.00
4	0.00	2951.15	0.00	0.00
5	1107.79	1967.43	0.00	0.00
6	0.00	0.00	3030.91	0.00

7	1107.79	1967.43	3030.91	0.00
8	0.00	1967.43	1063.48	0.00
9	1107.79	0.00	1967.43	0.00
10	0.00	0.00	0.00	4845.46
11	1107.79	0.00	1967.43	4845.46
12	3.32	0.00	0.00	0.00
13	0.00	0.00	8789.63	0.00
14	1111.11	0.00	10757.06	4845.46
15	0.00	0.00	1515.45	0.00
16	111.11	0.00	9818.01	3876.37
17	1000.00	0.00	2454.50	969.09
18	0.00	0.00	2454.50	969.09
19	1000.00	0.00	0.00	0.00
Solvent Recovery System	---	---	---	---
20	0.00	4869.39	12.23	12.23
21	111.11	49.19	10869.25	3864.136
22	0.00	49.19	10760.56	4.89
23	111.11	0.00	108.69	964.205
24	0.00	0.00	107.61	0.54
25	111.11	0.00	1.09	963.66
26	11.11	0.00	0.87	770.9316735
27	100.00	0.00	0.217	192.733
28	0.00	0.00	0.22	192.733
29	100.00	0.00	0.00	0.000

Table A-110. Equipment Description for Process 36 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-3600	Centrifugal Pump	7.53E-05	
P-3601	Centrifugal Pump	9.22E-05	
P-3602	Centrifugal Pump	4.52E-05	
P-3603	Centrifugal Pump	4.71E-05	

P-3604	Centrifugal Pump	4.64E-05	
P-3605	Centrifugal Pump	9.34E-05	
P-3606	Centrifugal Pump	4.64E-05	
P-3607	Centrifugal Pump	4.71E-05	
P-3608	Centrifugal Pump	7.41E-05	
P-3609	Centrifugal Pump	1.21E-04	
P-3610	Centrifugal Pump	5.08E-08	
P-3611	Centrifugal Pump	1.34E-04	
P-3612	Centrifugal Pump	2.56E-04	
P-3613	Centrifugal Pump	2.32E-05	
P-3614	Centrifugal Pump	2.11E-04	
V-3600	Heating Vessel with Mixing	3.26E-04	Mixing requirement
		1.24E-01	Heating requirement
V-3601	Heating Vessel with Mixing	2.82E-04	Mixing requirement
		1.38E-01	Heating requirement
V-3602	Heating Vessel with Mixing	9.98E-05	Mixing requirement
		2.49E-01	Heating requirement
V-3603	Cooling Vessel with Mixing	1.70E-02	Mixing requirement
		-8.26E-02	Cooling requirement
C-3600	Distillation Column	3.33E-01	
C-3601	Distillation Column	2.10E-01	
F-3600	Filtration Unit	4.64E-05	
D-3600	Vacuum dryer	1.16E+00	Heating requirement
		5.96E-01	Vacuum pump requirement
Solvent Recovery System	---	---	---
SR-P-3600	Centrifugal Pump	7.47E-05	
SR-P-3601	Centrifugal Pump	1.69E-04	
SR-P-3602	Centrifugal Pump	1.65E-04	
SR-P-3603	Centrifugal Pump	3.36E-06	
SR-P-3604	Centrifugal Pump	1.65E-06	
SR-P-3605	Centrifugal Pump	1.72E-06	
SR-P-3606	Centrifugal Pump	1.83E-07	

SR-C-3600	Distillation Column	1.19E+00	
SR-C-3601	Distillation Column	2.97E+00	
SR-C-3602	Distillation Column	1.73E-01	
SR-F-3500	Filtration Unit	1.08E-02	
SR-D-3500	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		5.02E-02	Heating requirement

Table A-111. Recovered Solvent from the Solvent Recovery System Implemented to Process 36 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Tetrahydrofuran	4893.86	99.50%
Heptane	10922.78	99.50%
1-Butanol	782.91	98.47%

A.1.38 Process 37 – Reactive Crystallization

The process flow diagram of Process 37 can be found in Figure A-38. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-112 and Table A-113, respectively. The mass of solvent recovered from Process 37 using solvent recovery techniques are reported in Table A-114.

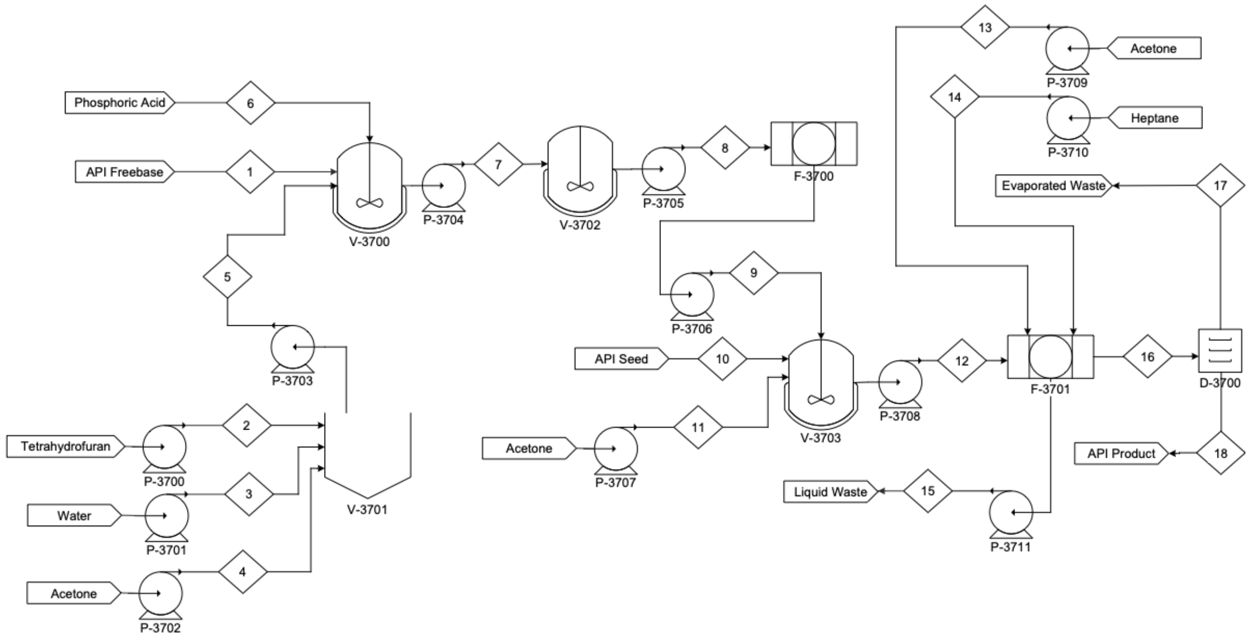

Figure A-38. Process flow diagram of Process 37 – Reactive Crystallization.

Table A-112. Mass of Each Component in Each Stream of Process 37 (According to Figure A-38). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**Starting API (g)**	**Tetrahydrofuran (g)**	**Water (g)**	**Acetone (g)**	**Phosphoric Acid (g)**	**API Product (g)**	**Heptane (g)**
1	915.213	0.000	0.000	0.000	0.000	0.000	0.000
2	0.000	1422.242	0.000	0.000	0.000	0.000	0.000
3	0.000	0.000	1596.819	0.000	0.000	0.000	0.000
4	0.000	0.000	0.000	1076.291	0.000	0.000	0.000
5	0.000	1422.242	1596.819	1076.291	0.000	0.000	0.000
6	0.000	0.000	0.000	0.000	186.746	0.000	0.000
7	0.000	1422.242	1596.819	1076.291	0.000	1101.959	0.000
8	0.000	1422.242	1596.819	1076.291	0.000	1101.959	0.000
9	0.000	1422.242	1596.819	1076.291	0.000	1101.959	0.000
10	0.000	0.000	0.000	0.000	0.000	9.152	0.000
11	0.000	0.000	0.000	13130.749	0.000	0.000	0.000
12	0.000	1422.242	1596.819	14207.040	0.000	1111.111	0.000
13	0.000	0.000	0.000	2152.582	0.000	0.000	0.000
14	0.000	0.000	0.000	0.000	0.000	0.000	1878.018
15	0.000	1137.793	1277.455	13087.698	0.000	111.111	1502.414
16	0.000	284.448	319.364	3271.924	0.000	1000.000	375.604
17	0.000	284.448	319.364	3271.924	0.000	0.000	375.604
18	0.000	0.000	0.000	0.000	0.000	1000.000	0.000
Solvent Recovery System	---	---	---	---	---	---	---
19	0.00	21.70	21.70	12956.82	0.00	0.00	21.70
20	0.00	1116.09	1255.75	130.88	0.00	111.11	1480.71
21	0.00	1104.93	1.85	1.85	0.00	0.00	1.85
22	0.00	11.16	1253.90	129.03	0.00	111.11	1478.86
23	0.00	2.45	2.45	2.45	0.00	0.00	1464.07
24	0.00	8.71	1251.45	126.57	0.00	111.11	14.79

25	0.00	6.97	1001.16	101.26	0.00	88.89	11.83
26	0.00	1.74	250.29	25.31	0.00	22.22	2.96
27	0.00	1.74	250.29	25.31	0.00	0.00	2.96
28	0.00	0.00	0.00	0.00	0.00	22.22	0.00

Table A-113. Equipment Description for Process 37 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-3700	Centrifugal Pump	2.18E-05	
P-3701	Centrifugal Pump	2.44E-05	
P-3702	Centrifugal Pump	1.65E-05	
P-3703	Centrifugal Pump	6.27E-05	
P-3704	Centrifugal Pump	7.95E-05	
P-3705	Centrifugal Pump	7.95E-05	
P-3706	Centrifugal Pump	7.95E-05	
P-3707	Centrifugal Pump	2.01E-04	
P-3708	Centrifugal Pump	2.81E-04	
P-3709	Centrifugal Pump	3.29E-05	
P-3710	Centrifugal Pump	2.87E-05	
P-3711	Centrifugal Pump	2.62E-04	
V-3700	Heating Vessel with Mixing	4.27E-04	Mixing requirement
		8.03E-02	Heating requirement
V-3701	Solvent Vessel	0.00E+00	
V-3702	Cooling Vessel with Mixing	6.41E-05	Mixing requirement
		-9.72E-03	Cooling requirement
V-3703	Cooling Vessel with Mixing	2.55E-04	Mixing requirement
		-7.38E-02	Cooling requirement
F-3700	Polish Filtration Unit	1.44E-05	
F-3701	Filtration Unit	6.21E-05	
D-3700	Vacuum Dryer	7.24E-01	Mixing requirement
		4.89E-01	Vacuum pump requirement

Solvent Recovery System	---	---	---
SR-P-3700	Centrifugal Pump	1.99E-04	
SR-P-3701	Centrifugal Pump	6.26E-05	
SR-P-3702	Centrifugal Pump	1.70E-05	
SR-P-3703	Centrifugal Pump	4.57E-05	
SR-P-3704	Centrifugal Pump	2.25E-05	
SR-P-3705	Centrifugal Pump	2.31E-05	
SR-P-3706	Centrifugal Pump	1.85E-05	
SR-C-3700	Distillation Column	1.03E+00	
SR-C-3701	Distillation Column	3.79E-01	
SR-C-3702	Distillation Column	1.77E+01	
SR-F-3700	Filtration Unit	1.51E-02	
SR-D-3700	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		2.18E-01	Heating requirement

Table A-114. Recovered Solvent from the Solvent Recovery System Implemented to Process 37 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
Tetrahydrofuran	1110.48	99.50%
Water	1210.10	82.73%
Acetone	13021.93	99.50%
Heptane	1471.43	99.50%

A.1.39 Process 38A – Reactive Crystallization

The process flow diagram of Process 38A can be found in Figure A-39. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-115 and Table A-116, respectively. The mass of solvent recovered from Process 38A using solvent recovery techniques are reported in Table A-117.

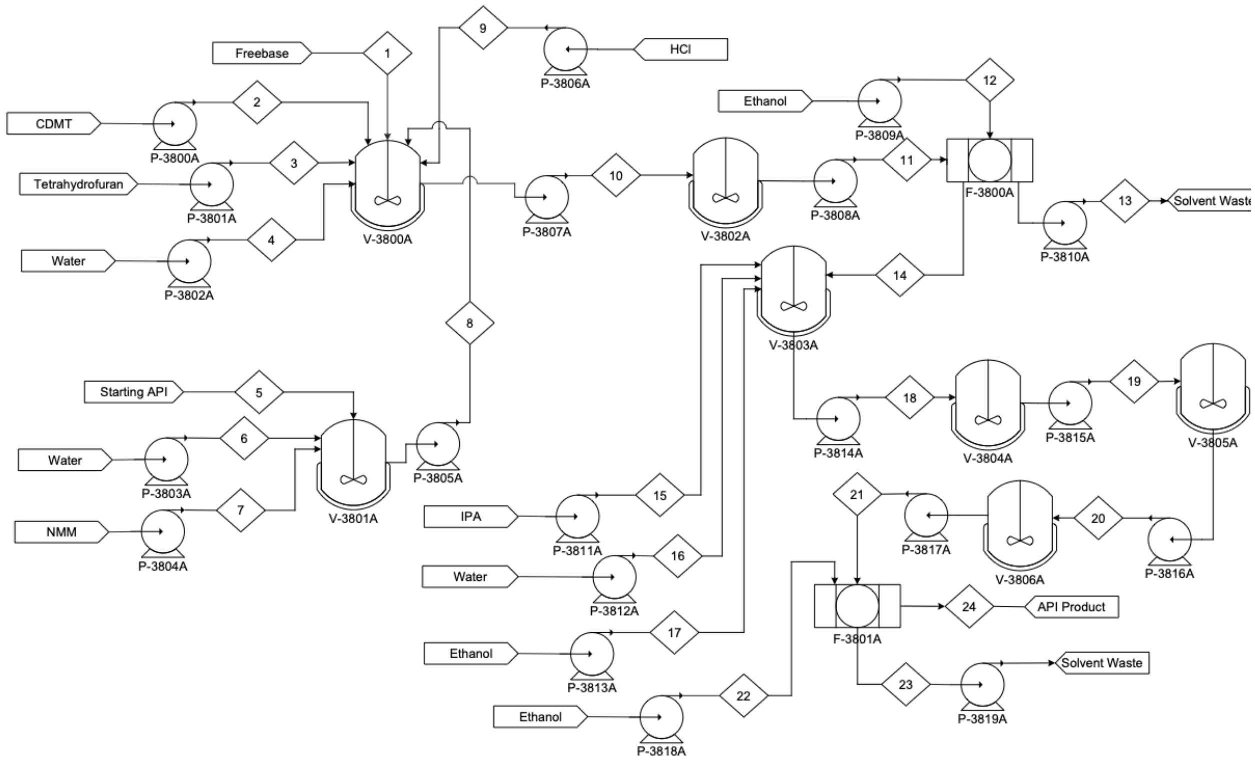

Figure A-39. Process flow diagram of Process 38A – Reactive Crystallization.

Table A-115. Mass of Each Component in Each Stream of Process 38A (According to Figure A-39). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	Starting API (g)	CMDT (g)	Tetrahydrofuran (g)	Water (g)	NMM (g)	HCl (g)	API Product (g)	Ethanol (g)	Isopropyl Alcohol (g)
1	117.66	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	0.00	105.69	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3	0.00	0.00	835.85	0.00	0.00	0.00	0.00	0.00	0.00
4	0.00	0.00	0.00	117.31	0.00	0.00	0.00	0.00	0.00
5	129.42	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
6	0.00	0.00	0.00	821.14	0.00	0.00	0.00	0.00	0.00
7	0.00	0.00	0.00	0.00	234.19	0.00	0.00	0.00	0.00
8	247.08	0.00	0.00	821.14	234.19	0.00	0.00	0.00	0.00
9	0.00	0.00	0.00	0.00	0.00	81.04	0.00	0.00	0.00
10	0.00	0.00	835.85	938.45	0.00	0.00	667.99	0.00	0.00
11	0.00	0.00	835.85	938.45	0.00	0.00	667.99	0.00	0.00

12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	278.50	0.00
13	0.00	0.00	668.68	750.76	0.00	0.00	66.80	222.80	0.00
14	0.00	0.00	167.17	187.69	0.00	0.00	601.19	55.70	0.00
15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	554.88
16	0.00	0.00	0.00	586.53	0.00	0.00	0.00	0.00	0.00
17	0.00	0.00	0.00	0.00	0.00	0.00	0.00	464.16	0.00
18	0.00	0.00	167.17	774.22	0.00	0.00	601.19	519.86	554.88
19	0.00	0.00	167.17	774.22	0.00	0.00	601.19	519.86	554.88
20	0.00	0.00	167.17	774.22	0.00	0.00	601.19	519.86	554.88
21	0.00	0.00	167.17	774.22	0.00	0.00	601.19	519.86	554.88
22	0.00	0.00	0.00	0.00	0.00	0.00	0.00	278.50	0.00
23	0.00	0.00	133.74	619.37	0.00	0.00	60.12	638.69	443.90
24	0.00	0.00	33.43	154.84	0.00	0.00	541.07	159.67	110.98
Solvent Recovery System	---	---	---	---	---	---	---	---	---
25	0.00	0.00	794.39	1.33	0.00	0.00	0.00	1.33	1.33
26	0.00	0.00	8.02	1368.80	0.00	0.00	126.92	860.16	442.57
27	0.00	0.00	1.43	1.43	0.00	0.00	0.00	851.56	1.43
28	0.00	0.00	6.60	1367.37	0.00	0.00	126.92	8.60	441.15
29	0.00	0.00	0.73	0.73	0.00	0.00	0.00	0.73	436.73
30	0.00	0.00	5.87	1366.64	0.00	0.00	126.92	7.87	4.41
31	0.00	0.00	4.69	1093.31	0.00	0.00	12.69	6.30	3.53
32	0.00	0.00	1.17	273.33	0.00	0.00	114.23	1.57	0.88

Table A-116. Equipment Description for Process 38A and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-3800A	Centrifugal Pump	1.62E-06	
P-3801A	Centrifugal Pump	1.28E-05	
P-3802A	Centrifugal Pump	1.79E-06	
P-3803A	Centrifugal Pump	1.98E-06	

P-3804A	Centrifugal Pump	1.26E-05	
P-3805A	Centrifugal Pump	3.58E-06	
P-3806A	Centrifugal Pump	1.99E-05	
P-3807A	Centrifugal Pump	3.74E-05	
P-3808A	Centrifugal Pump	3.74E-05	
P-3809A	Centrifugal Pump	4.26E-06	
P-3810A	Centrifugal Pump	2.61E-05	
P-3811A	Centrifugal Pump	8.49E-06	
P-3812A	Centrifugal Pump	8.97E-06	
P-3813A	Centrifugal Pump	7.10E-06	
P-3814A	Centrifugal Pump	4.00E-05	
P-3815A	Centrifugal Pump	4.00E-05	Mixing requirement
P-3816A	Centrifugal Pump	4.00E-05	Cooling requirement
P-3817A	Centrifugal Pump	4.00E-05	Mixing requirement
P-3818A	Centrifugal Pump	4.26E-06	Cooling requirement
P-3819A	Centrifugal Pump	2.90E-05	
V-3800A	Cooling Vessel with Mixing	6.80E-03	Mixing requirement
		-1.61E-02	Cooling requirement
V-3801A	Heating Vessel with Mixing	1.70E-03	Mixing requirement
		3.27E-03	Heating requirement
V-3802A	Heating Vessel with Mixing	1.24E-03	Mixing requirement
		4.48E-02	Heating requirement
V-3803A	Heating Vessel with Mixing	2.43E-03	Mixing requirement
		1.38E-01	Heating requirement
V-3804A	Cooling Vessel with Mixing	1.21E-03	Mixing requirement
		-1.01E-01	Cooling requirement
V-3805A	Heating Vessel with Mixing	1.21E-03	Mixing requirement
		1.12E-01	Heating requirement
V-3806A	Cooling Vessel with Mixing	9.72E-03	Mixing requirement
		-1.13E-02	Cooling requirement
F-3800A	Filtration Unit	7.56E-06	
F-3801A	Filtration Unit	8.04E-06	
Solvent Recovery System	**---**	**---**	**---**

SR-P-3800A	Centrifugal Pump	1.22E-05	
SR-P-3801A	Centrifugal Pump	4.29E-05	
SR-P-3802A	Centrifugal Pump	1.31E-05	
SR-P-3803A	Centrifugal Pump	2.98E-05	
SR-P-3804A	Centrifugal Pump	6.72E-06	
SR-P-3805A	Centrifugal Pump	2.31E-05	
SR-P-3806A	Centrifugal Pump	1.71E-05	
SR-C-3800A	Distillation Column	6.36E-01	
SR-C-3801A	Distillation Column	8.23E+00	
SR-C-3802A	Distillation Column	1.18E+00	
SR-F-3800A	Filtration Unit	1.51E-02	

Table A-117. Recovered Solvent from the Solvent Recovery System Implemented to Process 38A with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
Tetrahydrofuran	798.38	99.50%
Water	1511.71	90.40%
Ethanol	855.84	99.50%
Isopropyl Alcohol	438.93	99.50%

A.1.40 Process 38B – Reactive Crystallization

The process flow diagram of Process 38B can be found in Figure A-40. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-118 and Table A-119, respectively. The mass of solvent recovered from Process 38B using solvent recovery techniques are reported in Table A-120.

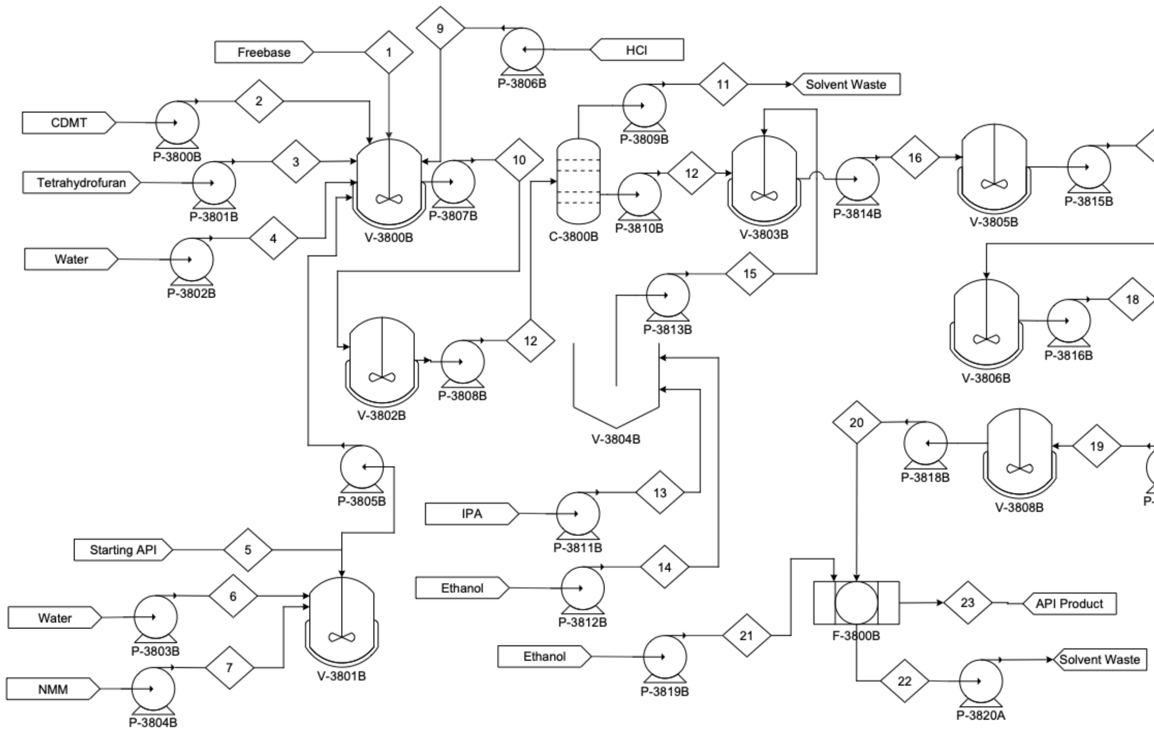

Figure A-40. Process flow diagram of Process 38B – Reactive Crystallization.

Table A-118. Mass of Each Component in Each Stream of Process 38B (According to Figure A-40). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	Starting API (g)	CMDT (g)	Tetrahydrofuran (g)	Water (g)	NMM (g)	HCl (g)	API Product (g)	Ethanol (g)	Isopropyl Alcohol (g)
1	106.12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	0.00	95.32	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3	0.00	0.00	753.87	0.00	0.00	0.00	0.00	0.00	0.00
4	0.00	0.00	0.00	105.80	0.00	0.00	0.00	0.00	0.00
5	116.73	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
6	0.00	0.00	0.00	740.60	0.00	0.00	0.00	0.00	0.00
7	0.00	0.00	0.00	0.00	211.22	0.00	0.00	0.00	0.00
8	116.73	0.00	0.00	740.60	211.22	0.00	0.00	0.00	0.00
9	0.00	0.00	0.00	0.00	0.00	34.80	0.00	0.00	0.00
10	0.00	0.00	753.87	846.40	0.00	0.00	602.47	0.00	0.00
	0.00	0.00	753.87	846.40	0.00	0.00	602.47	0.00	0.00

11	0.00	0.00	565.40	0.00	0.00	0.00	0.00	0.00	0.00
12	0.00	0.00	188.47	846.40	0.00	0.00	0.00	0.00	0.00
13	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	500.45
14	0.00	0.00	0.00	0.00	0.00	0.00	0.00	502.36	0.00
15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	502.36	500.45
16	0.00	0.00	188.47	846.40	0.00	0.00	602.47	502.36	500.45
18	0.00	0.00	188.47	846.40	0.00	0.00	602.47	502.36	500.45
19	0.00	0.00	188.47	846.40	0.00	0.00	602.47	502.36	500.45
20	0.00	0.00	188.47	846.40	0.00	0.00	602.47	502.36	500.45
21	0.00	0.00	188.47	846.40	0.00	0.00	602.47	502.36	500.45
22	0.00	0.00	0.00	0.00	0.00	0.00	0.00	251.18	0.00
23	0.00	0.00	150.77	677.12	0.00	0.00	60.25	602.84	400.36
24	0.00	0.00	37.69	169.28	0.00	0.00	542.23	150.71	100.09
Solvent Recovery System	---	---	---	---	---	---	---	---	---
25	0.00	0.00	335.85	0.56	0.00	0.00	0.00	0.56	0.56
26	0.00	0.00	3.39	1522.96	0.00	0.00	60.25	602.27	399.80
27	0.00	0.00	1.00	1.00	0.00	0.00	0.00	596.25	1.00
28	0.00	0.00	2.39	1521.96	0.00	0.00	60.25	6.02	398.80
29	0.00	0.00	0.66	0.66	0.00	0.00	0.00	0.66	394.81
30	0.00	0.00	1.73	1521.30	0.00	0.00	60.25	5.36	3.99
31	0.00	0.00	1.39	1217.04	0.00	0.00	6.02	4.29	3.19
32	0.00	0.00	0.35	304.26	0.00	0.00	54.22	1.07	0.80

Table A-119. Equipment Description for Process 38B and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-3800B	Centrifugal Pump	1.46E-06	
P-3801B	Centrifugal Pump	1.15E-05	
P-3802B	Centrifugal Pump	1.62E-06	
P-3803B	Centrifugal Pump	1.13E-05	

P-3804B	Centrifugal Pump	3.23E-06	
P-3805B	Centrifugal Pump	1.63E-05	
P-3806B	Centrifugal Pump	5.33E-07	
P-3807B	Centrifugal Pump	3.37E-05	
P-3808B	Centrifugal Pump	3.37E-05	
P-3809B	Centrifugal Pump	8.65E-06	
P-3810B	Centrifugal Pump	1.58E-05	
P-3811B	Centrifugal Pump	7.66E-06	
P-3812B	Centrifugal Pump	7.69E-06	
P-3813B	Centrifugal Pump	1.53E-05	
P-3814B	Centrifugal Pump	4.04E-05	
P-3815B	Centrifugal Pump	4.04E-05	
P-3816B	Centrifugal Pump	4.04E-05	
P-3817B	Centrifugal Pump	4.04E-05	
P-3818B	Centrifugal Pump	4.04E-05	
P-3819B	Centrifugal Pump	3.84E-06	
P-3820B	Centrifugal Pump	2.89E-05	
V-3800B	Cooling Vessel with Mixing	8.04E-03	Mixing requirement
		-1.45E-02	Cooling requirement
V-3801B	Heating Vessel with Mixing	1.24E-03	Mixing requirement
		5.16E-03	Heating requirement
V-3802B	Heating Vessel with Mixing	6.18E-04	Mixing requirement
		8.15E-02	Heating requirement
V-3803B	Solvent Vessel	0.00E+00	
V-3804B	Cooling Vessel with Mixing	6.14E-04	Mixing requirement
		-5.39E-02	Cooling requirement
V-3805B	Heating Vessel with Mixing	1.84E-03	Mixing requirement
		9.63E-02	Heating requirement
V-3806B	Cooling Vessel with Mixing	1.23E-03	Mixing requirement
		-1.14E-01	Cooling requirement
V-3807B	Heating Vessel with Mixing	1.23E-03	Mixing requirement
		1.14E-01	Heating requirement
V-3808B	Cooling Vessel with Mixing	9.82E-03	Mixing requirement

		-5.97E-02	Cooling requirement
C-3800B	Distillation Column	9.52E-02	
F-3800B	Filtration Unit	8.03E-06	
Solvent Recovery System	---	---	---
SR-P-3800A	Centrifugal Pump	5.16E-06	
SR-P-3801A	Centrifugal Pump	3.96E-05	
SR-P-3802A	Centrifugal Pump	9.17E-06	
SR-P-3803A	Centrifugal Pump	3.04E-05	
SR-P-3804A	Centrifugal Pump	6.07E-06	
SR-P-3805A	Centrifugal Pump	2.44E-05	
SR-P-3806A	Centrifugal Pump	1.88E-05	
SR-C-3800A	Distillation Column	5.51E-01	
SR-C-3801A	Distillation Column	8.33E+00	
SR-C-3802A	Distillation Column	1.27E+00	
SR-F-3800A	Filtration Unit	1.59E-02	

Table A-120. Recovered Solvent from the Solvent Recovery System Implemented to Process 38B with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Tetrahydrofuran	902.93	99.81%
Water	1592.63	95.52%
Ethanol	599.25	99.50%
Isopropyl Alcohol	396.80	99.50%

A.1.41 Process 39 – Reactive Crystallization

The process flow diagram of Process 39 can be found in Figure A-41. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-121 and Table A-122, respectively. The mass of solvent recovered from Process 39 using solvent recovery techniques are reported in Table A-123.

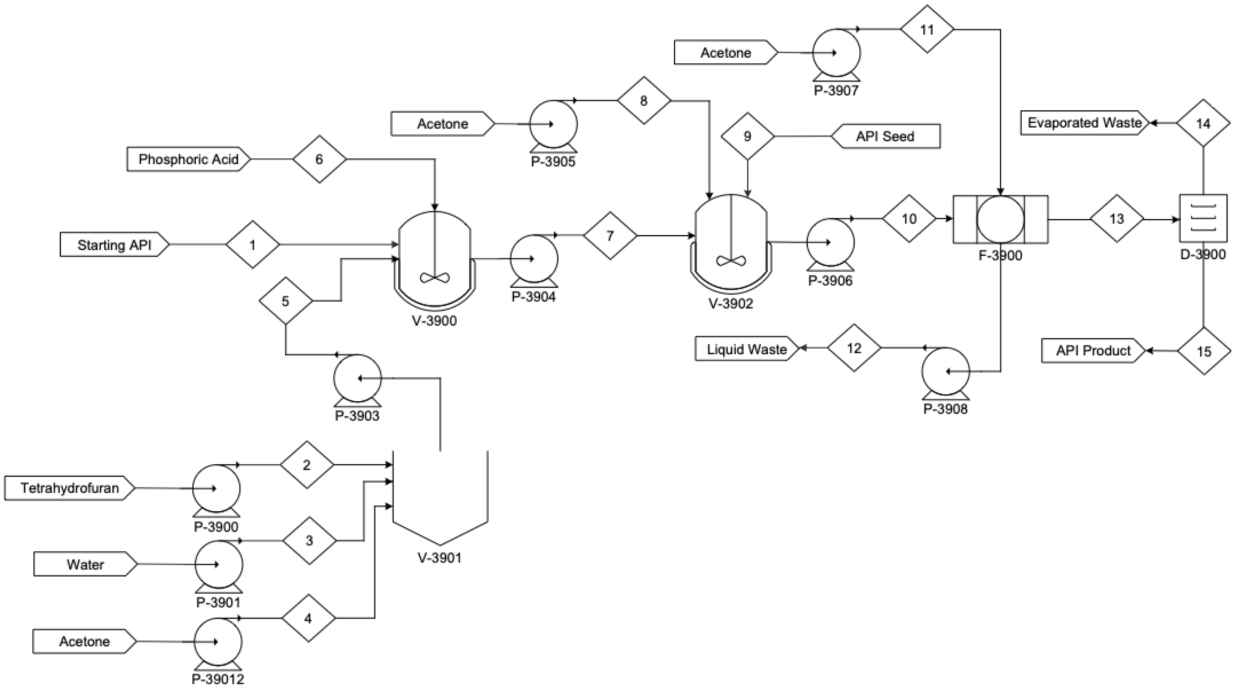

Figure A-41. Process flow diagram of Process 39 – Reactive Crystallization.

Table A-121. Mass of Each Component in Each Stream of Process 39 (According to Figure A-41). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	Starting API (g)	Tetrahydrofuran (g)	Water (g)	Acetone (g)	Phosphoric Acid (g)	API Product (g)
1	915.21	0.00	0.00	0.00	0.00	0.00
2	0.00	1625.42	0.00	0.00	0.00	0.00
3	0.00	0.00	1824.94	0.00	0.00	0.00
4	0.00	0.00	0.00	717.53	0.00	0.00
5	0.00	1625.42	1824.94	717.53	0.00	0.00
6	0.00	0.00	0.00	0.00	186.75	0.00
7	0.00	1625.42	1824.94	717.53	0.00	1101.96
8	0.00	0.00	0.00	717.53	0.00	0.00
9	0.00	0.00	0.00	0.00	0.00	9.15
10	0.00	1625.42	1824.94	1435.05	0.00	1111.11
11	0.00	0.00	0.00	2152.58	0.00	0.00
12	0.00	1300.34	1459.95	2870.11	0.00	111.11
13	0.00	325.08	364.99	717.53	0.00	1000.00

14	0.00	325.08	364.99	717.53	0.00	0.00
15	0.00	0.00	0.00	0.00	0.00	1000.00
Solvent Recovery System	---	---	---	---	---	---
16	0.00	7.14	7.14	2841.41	0.00	0.00
17	0.00	1293.20	1452.81	28.70	0.00	111.11
18	0.00	1280.26	3.22	3.22	0.00	0.00
19	0.00	12.93	1449.59	25.48	0.00	111.11
20	0.00	10.35	1159.67	20.39	0.00	11.11
21	0.00	2.59	289.92	5.10	0.00	100.00
22	0.00	2.59	289.92	5.10	0.00	0.00
23	0.00	0.00	0.00	0.00	0.00	100.00

Table A-122. Equipment Description for Process 39 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-3900	Centrifugal Pump	2.49E-05	
P-3901	Centrifugal Pump	2.79E-05	
P-3902	Centrifugal Pump	1.10E-05	
P-3903	Centrifugal Pump	6.38E-05	
P-3904	Centrifugal Pump	8.06E-05	
P-3905	Centrifugal Pump	1.10E-05	
P-3906	Centrifugal Pump	9.17E-05	
P-3907	Centrifugal Pump	3.29E-05	
P-3908	Centrifugal Pump	8.78E-05	
V-3900	Heating Vessel with Mixing	2.72E-04	Mixing requirement
		8.39E-02	Heating requirement
V-3901	Solvent Vessel	0	
V-3902	Cooling Vessel with Mixing	8.56E-03	Mixing requirement
		-1.03E-01	Cooling requirement
F-3900	Filtration Unit	2.26E-05	

D-3900	Vacuum Dryer	3.86E-01	Vacuum pump requirement
		4.10E-01	Heating requirement
Solvent Recovery System	---	---	---
SR-P-3900	Centrifugal Pump	4.37E-05	
SR-P-3901	Centrifugal Pump	4.42E-05	
SR-P-3902	Centrifugal Pump	1.97E-05	
SR-P-3903	Centrifugal Pump	2.45E-05	
SR-P-3904	Centrifugal Pump	1.84E-05	
SR-C-3900	Distillation Column	3.93E-01	
SR-C-3901	Distillation Column	3.96E-01	
SR-F-3900	Filtration Unit	1.20E-02	
SR-D-3900	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		2.51E-01	Heating requirement

Table A-123. Recovered Solvent from the Solvent Recovery System Implemented to Process 39 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Tetrahydrofuran	1286.70	99.50%
Water	1201.52	96.52%
Acetone	2855.69	99.50%

A.1.42 Process 40 – Evaporative Crystallization

The process flow diagram of Process 40 can be found in Figure A-42. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-124 and Table A-125, respectively. The mass of solvent recovered from Process 40 using solvent recovery techniques are reported in Table A-126.

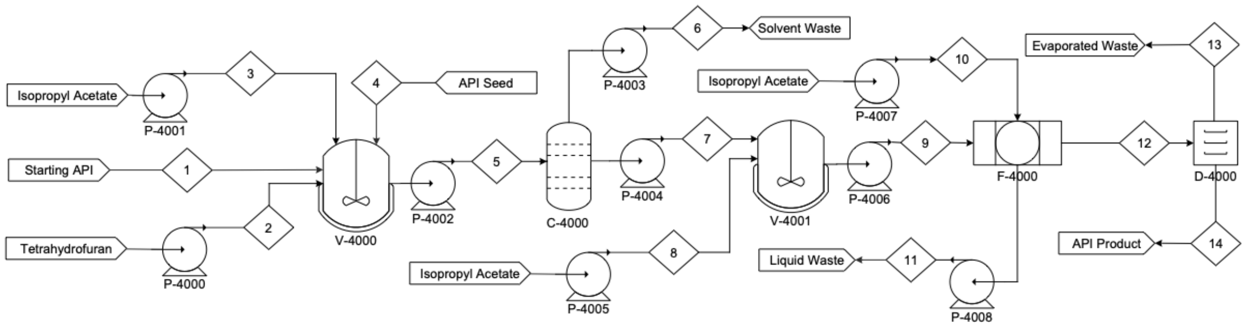

Figure A-42. Process flow diagram of Process 40 – Evaporative Crystallization.

Table A-124. Mass of Each Component in Each Stream of Process 40 (According to Figure A-42). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**API (g)**	**Tetrahydrofuran (g)**	**Isopropyl Acetate (g)**
1	1105.58	0.00	0.00
2	0.00	4908.79	0.00
3	0.00	0.00	6733.01
4	5.53	0.00	0.00
5	1111.11	4908.79	6733.01
6	0.00	4908.79	1923.72
7	1111.11	0.00	4809.29
8	0.00	0.00	5771.15
9	1111.11	0.00	10580.44
10	0.00	0.00	2885.57
11	111.11	0.00	10772.81
12	1000.00	0.00	2693.20
13	0.00	0.00	2693.20
14	1000.00	0.00	0.00
Solvent Recovery System	---	---	---
14	0.00	0.00	10665.08
15	111.11	0.00	107.73
16	0.00	4859.71	24.42
17	0.00	49.09	1899.30
18	11.11	0.00	86.18

19	100.00	0.00	21.55
20	0.00	0.00	21.55
21	100.00	0.00	0.00

Table A-125. Equipment Description for Process 40 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-4000	Centrifugal Pump	7.51E-05	
P-4001	Centrifugal Pump	1.03E-04	
P-4002	Centrifugal Pump	1.95E-04	
P-4003	Centrifugal Pump	1.05E-04	
P-4004	Centrifugal Pump	9.06E-05	
P-4005	Centrifugal Pump	8.83E-05	
P-4006	Centrifugal Pump	1.79E-04	
P-4007	Centrifugal Pump	4.41E-05	
P-4008	Centrifugal Pump	1.67E-04	
V-4000	Heating Vessel with Mixing	6.64E-03	Mixing requirement
		1.85E-01	Heating requirement
V-4001	Cooling Vessel with Mixing	3.79E-03	Mixing requirement
		-2.04E-01	Cooling requirement
C-4000	Distillation Column	5.67E-01	
F-4000	Filtration Unit	4.05E-05	
D-4000	Vacuum Dryer	7.72E-01	Vacuum pump requirement
		4.03E-01	Heating requirement
Solvent Recovery System	---	---	---
SR-P-4000	Centrifugal Pump	1.63E-04	
SR-P-4001	Centrifugal Pump	3.35E-06	
SR-P-4002	Centrifugal Pump	7.47E-05	
SR-P-4003	Centrifugal Pump	2.98E-05	
SR-P-4004	Centrifugal Pump	1.49E-06	

SR-C-4000	Distillation Column	1.26E+00	
SR-C-4001	Distillation Column	1.05E+00	
SR-F-4000	Filtration Unit	2.19E-03	
SR-D-4000	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		3.15E-03	Heating requirement

Table A-126. Recovered Solvent from the Solvent Recovery System Implemented to Process 40 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Tetrahydrofuran	12613.47	99.61%
Isopropyl Acetate	4884.13	99.50%

A.1.43 Process 41 – Reactive Crystallization

The process flow diagram of Process 41 can be found in Figure A-43. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-127 and Table A-128, respectively. Please note that for this process, no solvent recovery system was needed because the purity of the solvents collected were already high enough for reuse. The mass of solvent recovered from Process 41 using solvent recovery techniques are reported in Table A-129.

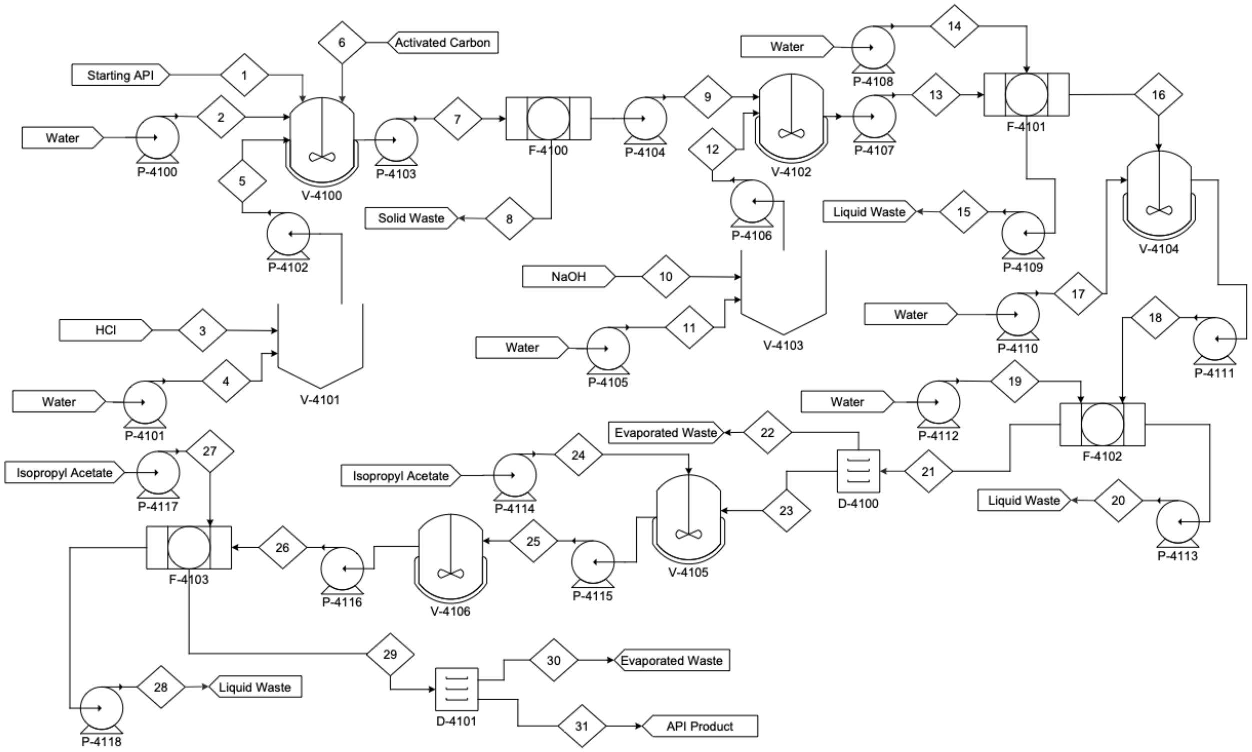

Figure A-43. Process flow diagram of Process 41 – Reactive Crystallization.

Table A-127. Mass of Each Component in Each Stream of Process 41 (According to Figure A-43). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	Starting API (g)	Water (g)	Hydrochloric Acid (g)	Activated Carbon (g)	API Product (g)	Sodium Hydroxide (g)	Isopropyl Acetate (g)
1	781.09	0.00	0.00	0.00	0.00	0.00	0.00
2	0.00	7787.43	0.00	0.00	0.00	0.00	0.00
3	0.00	0.00	569.57	0.00	0.00	0.00	0.00
4	0.00	3114.97	0.00	0.00	0.00	0.00	0.00
5	781.09	3114.97	569.57	0.00	0.00	0.00	0.00
6	0.00	0.00	0.00	446.56	0.00	0.00	0.00
7	0.00	3114.97	0.00	446.56	1371.74	0.00	0.00
8	0.00	0.00	0.00	446.56	0.00	0.00	0.00
9	0.00	10902.40	0.00	0.00	1371.74	0.00	0.00
10	0.00	0.00	0.00	0.00	0.00	21.09	0.00
11	0.00	10513.03	0.00	0.00	0.00	0.00	0.00

12	0.00	10513.03	0.00	0.00	0.00	21.09	0.00
13	0.00	21415.43	0.00	0.00	1371.74	0.00	0.00
14	0.00	6229.94	0.00	0.00	0.00	0.00	0.00
15	0.00	22116.30	0.00	0.00	137.17	0.00	0.00
16	0.00	5529.08	0.00	0.00	1234.57	0.00	0.00
17	0.00	11716.29	0.00	0.00	0.00	0.00	0.00
18	0.00	17245.37	0.00	0.00	1234.57	0.00	0.00
19	0.00	4672.46	0.00	0.00	0.00	0.00	0.00
20	0.00	17534.26	0.00	0.00	123.46	0.00	0.00
21	0.00	4383.57	0.00	0.00	1111.11	0.00	0.00
22	0.00	4383.57	0.00	0.00	0.00	0.00	0.00
23	0.00	0.00	0.00	0.00	1111.11	0.00	0.00
24	0.00	0.00	0.00	0.00	0.00	0.00	10193.18
25	0.00	0.00	0.00	0.00	1111.11	0.00	10193.18
26	0.00	0.00	0.00	0.00	1111.11	0.00	10193.18
27	0.00	0.00	0.00	0.00	0.00	0.00	2718.18
28	0.00	0.00	0.00	0.00	111.11	0.00	10329.08
29	0.00	0.00	0.00	0.00	1000.00	0.00	2582.27
30	0.00	0.00	0.00	0.00	0.00	0.00	2582.27
31	0.00	0.00	0.00	0.00	1000.00	0.00	0.00

Table A-128. Equipment Description for Process 41 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-4100	Centrifugal Pump	1.19E-04	
P-4101	Centrifugal Pump	4.77E-05	
P-4102	Centrifugal Pump	6.83E-05	
P-4103	Centrifugal Pump	7.55E-05	
P-4104	Centrifugal Pump	1.88E-04	
P-4105	Centrifugal Pump	1.61E-04	
P-4106	Centrifugal Pump	1.61E-04	
P-4107	Centrifugal Pump	3.49E-04	

P-4108	Centrifugal Pump	9.53E-05	
P-4109	Centrifugal Pump	3.40E-04	
P-4110	Centrifugal Pump	1.79E-04	
P-4111	Centrifugal Pump	2.83E-04	
P-4112	Centrifugal Pump	7.15E-05	
P-4113	Centrifugal Pump	2.70E-04	
P-4114	Centrifugal Pump	1.56E-04	
P-4115	Centrifugal Pump	1.73E-04	
P-4116	Centrifugal Pump	1.73E-04	
P-4117	Centrifugal Pump	4.16E-05	
P-4118	Centrifugal Pump	1.60E-04	
V-4100	Heating Vessel with Mixing	6.80E-03	Mixing requirement
		7.24E-03	Heating requirement
V-4101	Solvent Vessel	0	
V-4102	Cooling Vessel with Mixing	4.08E-03	Mixing requirement
		-4.24E-01	Cooling requirement
V-4103	Solvent Vessel	0	
V-4104	Heating Vessel with Mixing	3.77E-03	Mixing requirement
		6.01E-01	Heating requirement
V-4105	Heating Vessel with Mixing	3.15E-03	Mixing requirement
		2.72E-01	Heating requirement
V-4106	Cooling Vessel with Mixing	1.65E-03	Mixing requirement
		-1.03E-01	Cooling requirement
F-4100	Filtration Unit	0.049332768	
F-4101	Filtration Unit	0.227871747	
F-4102	Filtration Unit	0.184799372	
F-4103	Filtration Unit	0.14022467	
D-4100	Vacuum Dryer	7.72E-01	Vacuum pump requirement
		3.63E+00	Heating requirement
D-4101	Vacuum Dryer	7.72E-01	Vacuum pump requirement
		4.03E-01	Heating requirement

Table A-129. Recovered Solvent from the Solvent Recovery System Implemented to Process 41 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Tetrahydrofuran	12613.47	99.61%
Isopropyl Acetate	4884.13	99.50%

A.1.44 Process 42 – Antisolvent Crystallization

The process flow diagram of Process 42 can be found in Figure A-44. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-130 and Table A-131, respectively. The mass of solvent recovered from Process 42 using solvent recovery techniques are reported in Table A-132.

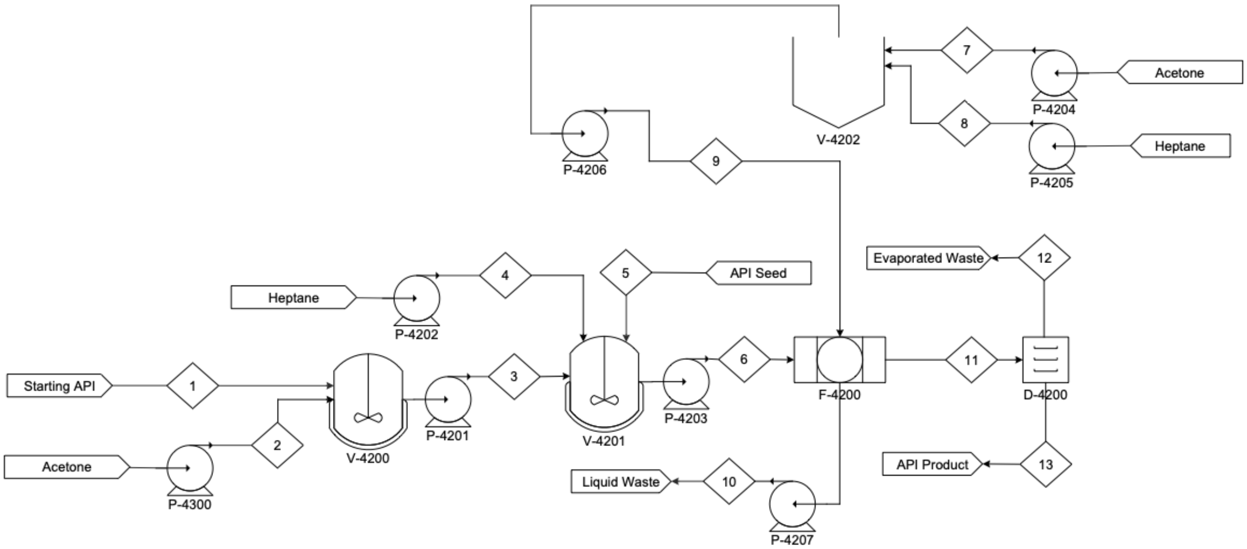

Figure A-44. Process flow diagram of Process 42 – Antisolvent Crystallization.

Table A-130. Mass of Each Component in Each Stream of Process 42 (According to Figure A-44). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API (g)	Acetone (g)	Heptane (g)
1	1105.58	0.00	0.00
2	0.00	7367.61	0.00
3	1105.58	7367.61	0.00
4	0.00	0.00	11721.40

5	5.53	0.00	0.00
6	1111.11	7367.61	11721.40
7	0.00	693.42	0.00
8	0.00	0.00	907.46
9	0.00	693.42	907.46
10	111.11	6448.83	10103.09
11	1000.00	1612.21	2525.77
12	0.00	1612.21	2525.77
13	1000.00	0.00	0.00
Solvent Recovery System	---	---	---
14	0.00	6384.34	32.08
15	111.11	64.49	10071.01
16	11.11	51.59	8056.81
17	100.00	12.90	2014.20
18	0.00	12.90	2014.20
19	100.00	0.00	0.00

Table A-131. Equipment Description for Process 42 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-4200	Centrifugal Pump	1.13E-04	
P-4201	Centrifugal Pump	1.30E-04	
P-4202	Centrifugal Pump	1.79E-04	
P-4203	Centrifugal Pump	3.09E-04	
P-4204	Centrifugal Pump	1.06E-05	
P-4205	Centrifugal Pump	1.39E-05	
P-4206	Centrifugal Pump	2.45E-05	
P-4207	Centrifugal Pump	2.55E-04	
V-4200	Heating Vessel with Mixing	3.07E-04	Mixing requirement
		1.37E-01	Heating requirement
V-4201	Cooling Vessel with Mixing	1.97E-02	Mixing requirement

		-7.96E-02	Cooling requirement
V-4202	Solvent Mixture Vessel	0.00E+00	
F-4200	Filtration Unit	6.06E-05	
D-4200	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		6.08E-01	Heating requirement
Solvent Recovery System	---	---	---
SR-P-4200	Centrifugal Pump	9.82E-05	
SR-P-4201	Centrifugal Pump	1.57E-04	
SR-P-4202	Centrifugal Pump	1.24E-04	
SR-C-4200	Distillation Column	1.97E-01	
SR-F-4200	Filtration Unit	1.02E-01	
SR-D-4200	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		2.83E-01	Heating requirement

Table A-132. Recovered Solvent from the Solvent Recovery System Implemented to Process 42 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
Acetone	6416.42	99.50%
Heptane	8119.51	99.23%

A.1.45 Process 43 – Evaporative Crystallization

The process flow diagram of Process 43 can be found in Figure A-45. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-133 and Table A-134, respectively. The mass of solvent recovered from Process 43 using solvent recovery techniques are reported in Table A-135.

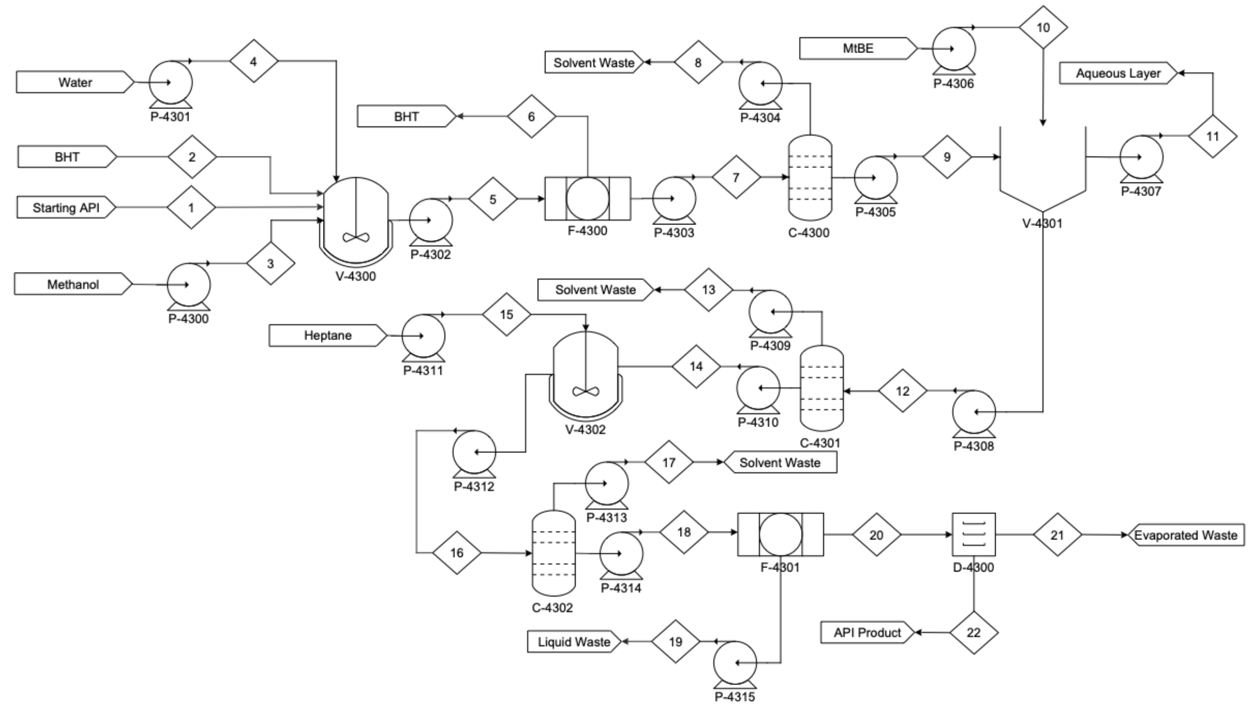

Figure A-45. Process flow diagram of Process 43 – Evaporative Crystallization.

Table A-133. Mass of Each Component in Each Stream of Process 43 (According to Figure A-45). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API (g)	BHT (g)	Methanol (g)	Water (g)	MtBE (g)	Heptane (g)
1	1111.11	0.00	0.00	0.00	0.00	0.00
2	0.00	5555.56	0.00	0.00	0.00	0.00
3	0.00	0.00	8800.00	0.00	0.00	0.00
4	0.00	0.00	0.00	4431.11	0.00	0.00
5	1111.11	5555.56	8800.00	4431.11	0.00	0.00
6	0.00	5555.56	0.00	0.00	0.00	0.00
7	1111.11	0.00	8800.00	4431.11	0.00	0.00
8	0.00	0.00	6160.00	0.00	0.00	0.00
9	1111.11	0.00	2640.00	4431.11	0.00	0.00
10	0.00	0.00	0.00	0.00	20555.56	0.00
11	0.00	0.00	0.00	4431.11	0.00	0.00
12	1111.11	0.00	2640.00	0.00	20555.56	0.00
13	0.00	0.00	0.00	0.00	20555.56	0.00

14	1111.11	0.00	2640.00	0.00	0.00	0.00
15	0.00	0.00	0.00	0.00	0.00	21280.00
16	1111.11	0.00	2640.00	0.00	0.00	21280.00
17	0.00	0.00	2640.00	0.00	0.00	12160.00
18	1111.11	0.00	0.00	0.00	0.00	9120.00
19	111.11	0.00	0.00	0.00	0.00	7296.00
20	1000.00	0.00	0.00	0.00	0.00	1824.00
21	0.00	0.00	0.00	0.00	0.00	1824.00
22	1000.00	0.00	0.00	0.00	0.00	0.00
Solvent Recovery System	---	---	---	---	---	---
23	0.00	0.00	2613.60	0.00	0.00	13.13
24	0.00	0.00	26.40	0.00	0.00	12146.87
25	0.00	0.00	21.12	0.00	0.00	9717.49
26	0.00	0.00	5.28	0.00	0.00	2429.37
27	0.00	0.00	5.28	0.00	0.00	2429.37
28	0.00	0.00	0.00	0.00	0.00	0.00

Table A-134. Equipment Description for Process 43 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-4300	Centrifugal Pump	1.35E-04	
P-4301	Centrifugal Pump	6.78E-05	
P-4302	Centrifugal Pump	3.04E-04	
P-4303	Centrifugal Pump	2.19E-04	
P-4304	Centrifugal Pump	9.42E-05	
P-4305	Centrifugal Pump	1.25E-04	
P-4306	Centrifugal Pump	3.15E-04	
P-4307	Centrifugal Pump	6.78E-05	
P-4308	Centrifugal Pump	3.72E-04	
P-4309	Centrifugal Pump	3.15E-04	
P-4310	Centrifugal Pump	5.74E-05	

P-4311	Centrifugal Pump	3.26E-04	
P-4312	Centrifugal Pump	3.83E-04	
P-4313	Centrifugal Pump	2.26E-04	
P-4314	Centrifugal Pump	1.57E-04	
P-4315	Centrifugal Pump	1.13E-04	
V-4300	Mixing Vessel	2.06E-03	Mixing requirement
V-4301	Separatory Vessel	0	
V-4302	Cooling Vessel with Mixing	5.99E-03	Mixing requirement
		-1.33E-01	Cooling requirement
C-4300	Distillation Column	2.02E+00	
C-4301	Distillation Column	2.89E+00	
C-4302	Distillation Column	2.85E+00	
F-4300	Filtration Unit	5.53E-05	
F-4301	Filtration Unit	2.84E-05	
D-4300	Vacuum Dryer	5.31E-01	Vacuum pump requirement
		2.51E-01	Heating requirement
Solvent Recovery System	---	---	---
SR-P-4300	Centrifugal Pump	4.02E-05	
SR-P-4301	Centrifugal Pump	1.86E-04	
SR-P-4302	Centrifugal Pump	1.49E-04	
SR-C-3600	Distillation Column	1.54E+00	
SR-F-3500	Filtration Unit	1.22E-01	
SR-D-3500	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		3.42E-01	Heating requirement

Table A-135. Recovered Solvent from the Solvent Recovery System Implemented to Process 43 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
Methanol	8786.73	99.85%
Water	4431.11	100.00%
Methyl tert-Butyl Ether	20555.56	100.00%
Heptane	17145.72	99.23%

A.1.46 Process 44A – Evaporative Crystallization

The process flow diagram of Process 44A can be found in Figure A-46. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-136 and Table A-137, respectively. The mass of solvent recovered from Process 44A using solvent recovery techniques are reported in Table A-138.

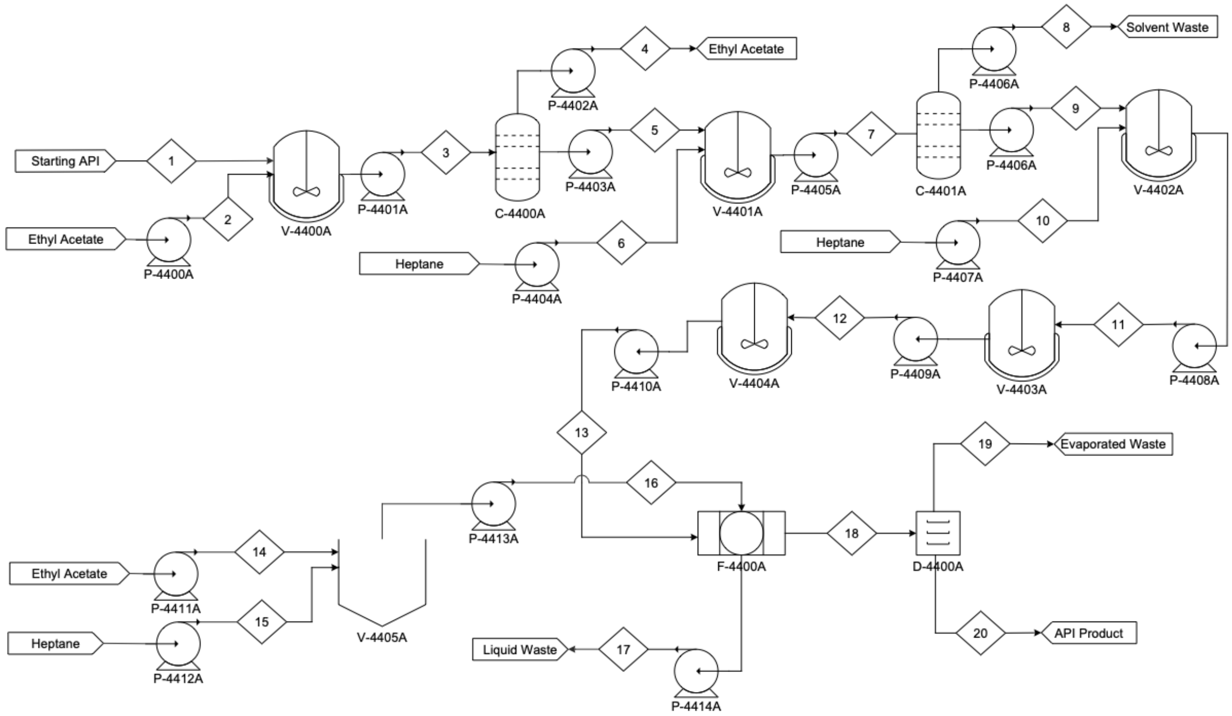

Figure A-46. Process flow diagram of Process 44A – Evaporative Crystallization.

Table A-136. Mass of Each Component in Each Stream of Process 44A (According to Figure A-46). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API (g)	Ethyl Acetate (g)	Heptane (g)
1	1111.11	0.00	0.00
2	0.00	27060.03	0.00
3	1111.11	27060.03	0.00
4	0.00	7015.56	0.00
5	1111.11	20044.46	0.00

6	0.00	0.00	7600.01
7	1111.11	20044.46	7600.01
8	0.00	5011.12	0.00
9	1111.11	15033.35	7600.01
10	0.00	0.00	3800.00
11	1111.11	15033.35	11400.01
12	1111.11	15033.35	11400.01
13	1111.11	15033.35	11400.01
14	0.00	4008.89	0.00
15	0.00	0.00	1520.00
16	0.00	4008.89	1520.00
17	111.11	15233.79	10336.01
18	1000.00	3808.45	2584.00
19	0.00	3808.45	2584.00
20	1000.00	0.00	0.00
Solvent Recovery System	---	---	---
21	0.00	15081.45	75.79
22	111.11	152.34	10260.22
23	11.11	121.87	8208.18
24	100.00	30.47	2052.04
25	0.00	30.47	2052.04
26	100.00	0.00	0.00

Table A-137. Equipment Description for Process 44A and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-4400A	Centrifugal Pump	4.14E-04	
P-4401A	Centrifugal Pump	4.31E-04	
P-4402A	Centrifugal Pump	1.07E-04	
P-4403A	Centrifugal Pump	3.24E-04	
P-4404A	Centrifugal Pump	1.16E-04	
P-4405A	Centrifugal Pump	4.40E-04	

P-4406A	Centrifugal Pump	7.67E-05	
P-4407A	Centrifugal Pump	3.63E-04	
P-4408A	Centrifugal Pump	5.81E-05	
P-4409A	Centrifugal Pump	4.21E-04	
P-4410A	Centrifugal Pump	4.21E-04	
P-4411A	Centrifugal Pump	4.21E-04	
P-4412A	Centrifugal Pump	6.13E-05	
P-4413A	Centrifugal Pump	2.33E-05	
P-4414A	Centrifugal Pump	8.46E-05	
P-4415A	Centrifugal Pump	3.93E-04	
V-4400A	Heating Vessel with Mixing	5.85E-04	Mixing requirement
		9.59E-02	Heating requirement
V-4401A	Heating Vessel with Mixing	3.64E-04	Mixing requirement
		1.26E-01	Heating requirement
V-4402A	Cooling Vessel with Mixing	4.62E-03	Mixing requirement
		-4.67E-01	Cooling requirement
V-4403A	Heating Vessel with Mixing	2.97E-03	Mixing requirement
		2.30E-01	Heating requirement
V-4404A	Cooling Vessel with Mixing	6.49E-03	Mixing requirement
		-2.30E-02	Cooling requirement
V-4405A	Solvent Mixture Vessel	1.35E+00	
C-4400A	Distillation Column	7.23E-01	
C-4401A	Distillation Column	9.39E-01	
F-4400A	Filtration Unit	7.13E-05	
D-4400A	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		9.15E-01	Heating requirement
Solvent Recovery System	---	---	---
SR-P-4400A	Centrifugal Pump	2.32E-04	
SR-P-4401A	Centrifugal Pump	1.61E-04	
SR-P-4402A	Centrifugal Pump	1.28E-04	
SR-C-4400A	Distillation Column	3.79E+00	
SR-F-4400A	Filtration Unit	1.05E-01	

SR-D-4400A	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		2.92E-01	Heating requirement

Table A-138. Recovered Solvent from the Solvent Recovery System Implemented to Process 44A with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Methanol	8786.73	99.85%
Water	4431.11	100.00%
Methyl tert-Butyl Ether	20555.56	100.00%
Heptane	17145.72	99.23%

A.1.47 Process 44B – Evaporative Crystallization

The process flow diagram of Process 44B can be found in Figure A-47. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-139 and Table A-140, respectively. The mass of solvent recovered from Process 44A using solvent recovery techniques are reported in Table A-141.

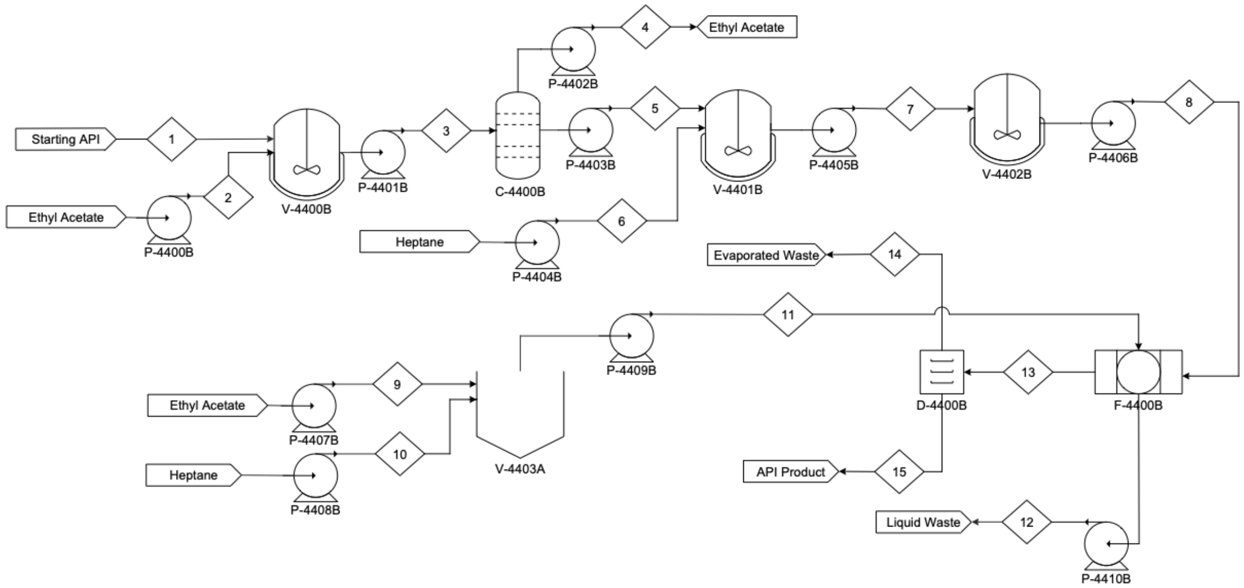

Figure A-47. Process flow diagram of Process 44B – Evaporative Crystallization.

Table A-139. Mass of Each Component in Each Stream of Process 44B (According to Figure A-47). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API (g)	Ethyl Acetate (g)	Heptane (g)
1	1111.11	0.00	0.00
2	0.00	27060.03	0.00
3	1111.11	27060.03	0.00
4	0.00	12026.68	0.00
5	1111.11	15033.35	0.00
6	0.00	0.00	11400.01
7	1111.11	15033.35	11400.01
8	1111.11	15033.35	11400.01
9	0.00	4008.89	0.00
10	0.00	0.00	1520.00
11	0.00	4008.89	1520.00
12	111.11	15233.79	10336.01
13	1000.00	3808.45	2584.00
14	0.00	3808.45	2584.00
15	1000.00	0.00	0.00
Solvent Recovery System	---	---	---
16	0.00	15081.45	75.79
17	111.11	152.34	10260.22
18	11.11	121.87	8208.18
19	100.00	30.47	2052.04
20	0.00	30.47	2052.04
21	100.00	0.00	0.00

Table A-140. Equipment Description for Process 44B and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	Equipment Description	Energy Requirement (kWh)	Note
P-4400B	Centrifugal Pump	4.14E-04	

P-4401B	Centrifugal Pump	4.31E-04	
P-4402B	Centrifugal Pump	1.84E-04	
P-4403B	Centrifugal Pump	2.47E-04	
P-4404B	Centrifugal Pump	1.74E-04	
P-4405B	Centrifugal Pump	4.21E-04	
P-4406B	Centrifugal Pump	4.21E-04	
P-4407B	Centrifugal Pump	6.13E-05	
P-4408B	Centrifugal Pump	2.33E-05	
P-4409B	Centrifugal Pump	8.46E-05	
P-4410B	Centrifugal Pump	3.93E-04	
V-4400B	Heating Vessel with Mixing	5.85E-04	Mixing requirement
		6.81E-01	Heating requirement
V-4401B	Heating Vessel with Mixing	1.19E-02	Mixing requirement
		3.13E-01	Heating requirement
V-4402B	Cooling Vessel with Mixing	4.19E-02	Mixing requirement
		-5.87E-01	Cooling requirement
V-4403B	Solvent Mixture Vessel	0	
C-4400B	Distillation Column	1.24E+00	
F-4400B	Filtration Unit	9.19E-05	
D-4400B	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		9.06E-01	Heating requirement
Solvent Recovery System	---	---	---
SR-P-4400B	Centrifugal Pump	2.32E-04	
SR-P-4401B	Centrifugal Pump	1.61E-04	
SR-P-4402B	Centrifugal Pump	1.28E-04	
SR-C-4400B	Distillation Column	3.79E+00	
SR-F-4400B	Filtration Unit	1.05E-01	
SR-D-4400B	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		2.92E-01	Heating requirement

Table A-141. Recovered Solvent from the Solvent Recovery System Implemented to Process 44B with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Methanol	8786.73	99.85%
Water	4431.11	100.00%
Methyl tert-Butyl Ether	20555.56	100.00%
Heptane	17145.72	99.23%

A.1.48 Process 45 – Reactive Crystallization

The process flow diagram of Process 45 can be found in Figure A-48. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-142 and Table A-143, respectively. The mass of solvent recovered from Process 45 using solvent recovery techniques are reported in Table A-144.

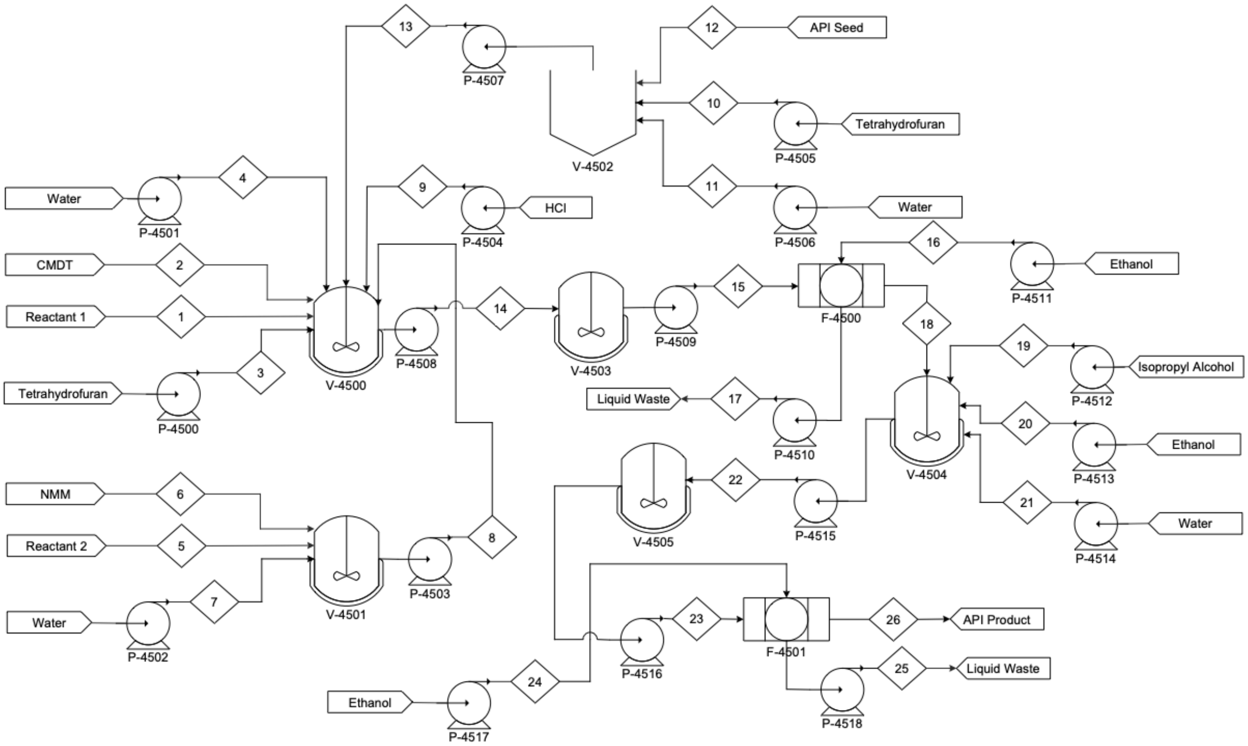

Figure A-48. Process flow diagram of Process 45 – Reactive Crystallization.

Table A-142. Mass of Each Component in Each Stream of Process 45 (According to Figure A-48). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API Reactant 1 (g)	CMDT (g)	Tetrahydrofuran (g)	Water (g)	API Reactant 2 (g)	NMM (g)	Hydrochloric acid	API Product (g)	Ethanol (g)	Isopropyl Alcohol (g)
1	97.53	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	0.00	87.61	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3	0.00	0.00	606.27	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4	0.00	0.00	0.00	97.24	0.00	0.00	0.00	0.00	0.00	0.00
5	0.00	0.00	0.00	0.00	107.29	0.00	0.00	0.00	0.00	0.00
6	0.00	0.00	0.00	0.00	0.00	194.13	0.00	0.00	0.00	0.00
7	0.00	0.00	0.00	680.69	0.00	0.00	0.00	0.00	0.00	0.00
8	0.00	0.00	0.00	777.93	107.29	194.13	0.00	0.00	0.00	0.00
9	0.00	0.00	0.00	0.00	0.00	0.00	217.99	0.00	0.00	0.00
10	0.00	0.00	649.58	0.00	0.00	0.00	0.00	0.00	0.00	0.00
11	0.00	0.00	0.00	729.31	0.00	0.00	0.00	0.00	0.00	0.00
12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.98	0.00	0.00
13	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
14	0.00	0.00	1255.85	1507.24	0.00	0.00	0.00	704.89	0.00	0.00
15	0.00	0.00	1255.85	1507.24	0.00	0.00	0.00	704.89	0.00	0.00
16	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	153.91	0.00
17	0.00	0.00	1004.68	1205.80	0.00	0.00	0.00	70.49	123.13	0.00
18	0.00	0.00	251.17	301.45	0.00	0.00	0.00	634.40	30.78	0.00
19	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	459.97
20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	384.77	0.00
21	0.00	0.00	0.00	486.21	0.00	0.00	0.00	0.00	0.00	0.00
22	0.00	0.00	251.17	787.66	0.00	0.00	0.00	634.40	415.55	459.97
23	0.00	0.00	251.17	787.66	0.00	0.00	0.00	634.40	415.55	459.97
24	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	230.86	0.00
25	0.00	0.00	200.94	630.13	0.00	0.00	0.00	63.44	517.13	367.98
26	0.00	0.00	50.23	157.53	0.00	0.00	0.00	570.96	129.28	91.99
Solvent Recovery System	---	---	---	---	---	---	---	---	---	---
27	0.00	0.00	1193.56	2.00	0.00	0.00	0.00	0.00	2.00	2.00
28	0.00	0.00	12.06	1833.92	0.00	0.00	0.00	133.93	638.26	365.98

29	0.00	0.00	1.06	1.06	0.00	0.00	0.00	0.00	631.88	1.06
30	0.00	0.00	11.00	1832.86	0.00	0.00	0.00	133.93	6.38	364.92
31	0.00	0.00	0.61	0.61	0.00	0.00	0.00	0.00	0.61	361.27
32	0.00	0.00	10.39	1832.26	0.00	0.00	0.00	133.93	5.78	3.65
33	0.00	0.00	8.31	1465.81	0.00	0.00	0.00	13.39	4.62	2.92
34	0.00	0.00	2.08	366.45	0.00	0.00	0.00	120.54	1.16	0.73

Table A-143. Equipment Description for Process 45 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-4500	Centrifugal Pump	9.28E-06	
P-4501	Centrifugal Pump	1.49E-06	
P-4502	Centrifugal Pump	1.04E-05	
P-4503	Centrifugal Pump	1.65E-05	
P-4504	Centrifugal Pump	3.34E-06	
P-4505	Centrifugal Pump	9.94E-06	
P-4506	Centrifugal Pump	1.12E-05	
P-4507	Centrifugal Pump	5.31E-05	
P-4508	Centrifugal Pump	5.31E-05	
P-4509	Centrifugal Pump	2.35E-06	
P-4510	Centrifugal Pump	3.68E-05	
P-4511	Centrifugal Pump	7.04E-06	
P-4512	Centrifugal Pump	5.89E-06	
P-4513	Centrifugal Pump	7.44E-06	
P-4514	Centrifugal Pump	3.90E-05	
P-4515	Centrifugal Pump	3.90E-05	
P-4516	Centrifugal Pump	3.53E-06	
P-4517	Centrifugal Pump	2.72E-05	
V-4500	Cooling Vessel with Mixing	1.40E-02	Mixing requirement
		-1.19E-02	Cooling requirement
V-4501	Heating Vessel with Mixing	1.94E-03	Mixing requirement

		2.37E-03	Heating requirement
V-4502	Solvent Vessel	0.00E+00	
V-4503	Heating Vessel with Mixing	1.04E-02	Mixing requirement
		5.92E-02	Heating requirement
V-4504	Heating Vessel with Mixing	5.99E-03	Mixing requirement
		1.38E-01	Heating requirement
V-4505	Cooling Vessel with Mixing	1.20E-03	Mixing requirement
		-1.51E-01	Cooling requirement
F-4500	Filtration Unit	3.62E-02	
F-4501	Filtration Unit	2.78E-02	
Solvent Recovery System	---	---	---
SR-P-4500	Centrifugal Pump	1.84E-05	
SR-P-4501	Centrifugal Pump	4.57E-05	
SR-P-4502	Centrifugal Pump	9.72E-06	
SR-P-4503	Centrifugal Pump	3.59E-05	
SR-P-4504	Centrifugal Pump	5.56E-06	
SR-P-4505	Centrifugal Pump	3.04E-05	
SR-P-4506	Centrifugal Pump	2.29E-05	
SR-C-4500	Distillation Column	1.95E+00	
SR-C-4501	Distillation Column	4.41E+00	
SR-C-4502	Distillation Column	1.48E+00	
SR-F-4500	Filtration Unit	4.91E-03	

Table A-144. Recovered Solvent from the Solvent Recovery System Implemented to Process 45 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Tetrahydrofuran	1199.56	99.50%
Water	1495.05	98.04%
Ethanol	635.05	99.50%
Isopropyl Alcohol	363.09	99.50%

A.1.49 Process 46 – Reactive Crystallization

The process flow diagram of Process 46 can be found in Figure A-49. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-145 and Table A-146, respectively. Please note that for this process, no solvent recovery system was needed because the purity of the solvents collected were already high enough for reuse. The mass of solvent recovered from Process 46 using solvent recovery techniques are reported in Table A-147.

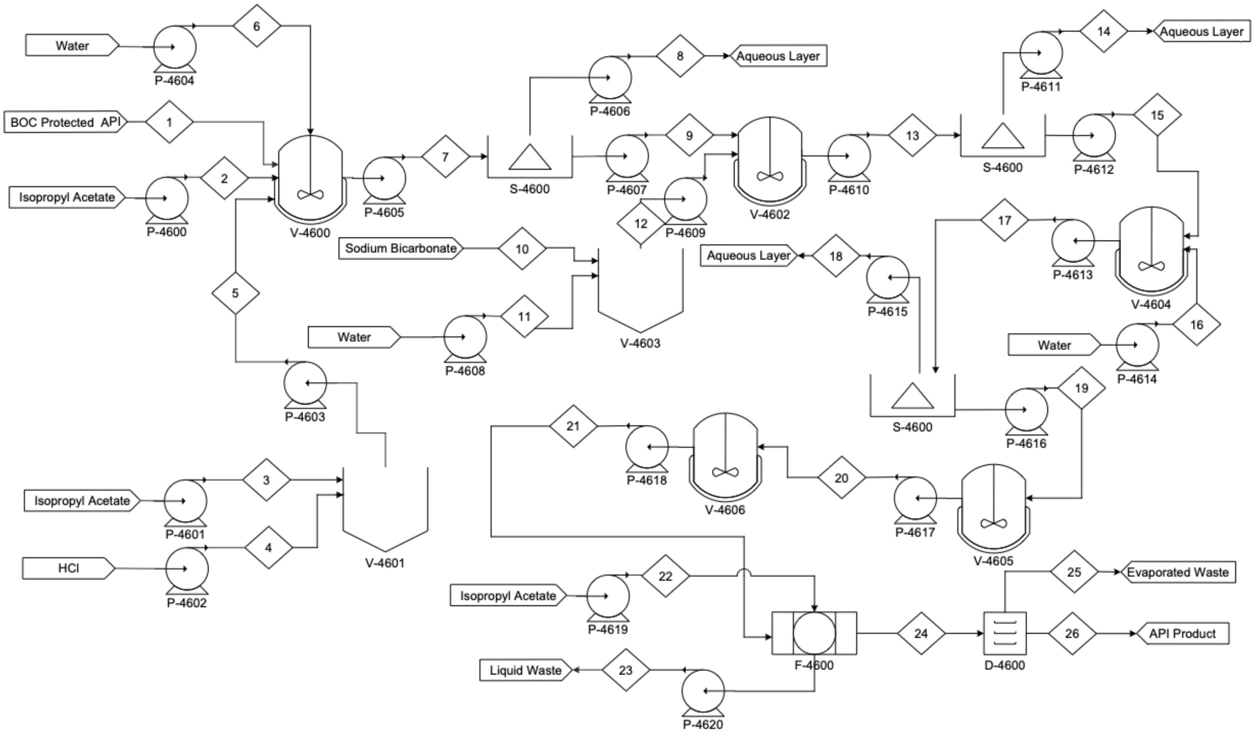

Figure A-49. Process flow diagram of Process 46 – Reactive Crystallization.

Table A-145. Mass of Each Component in Each Stream of Process 46 (According to Figure A-49). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	Boc Protected API (g)	Isopropyl Acetate (g)	Hydrochloric Acid (g)	Water (g)	API Product (g)	Sodium Bicarbonate (g)
1	670.39	0.00	0.00	0.00	0.00	0.00
2	0.00	2916.20	0.00	0.00	0.00	0.00
3	0.00	2627.47	0.00	0.00	0.00	0.00

4	0.00	0.00	275.28	0.00	0.00	0.00
5	0.00	2627.47	275.28	0.00	0.00	0.00
6	0.00	0.00	0.00	3308.81	0.00	0.00
7	0.00	5543.67	0.00	3308.81	1111.11	0.00
8	0.00	0.00	0.00	3308.81	0.00	0.00
9	0.00	5543.67	0.00	0.00	1111.11	0.00
10	0.00	0.00	0.00	0.00	0.00	165.44
11	0.00	0.00	0.00	3308.81	0.00	0.00
12	0.00	0.00	0.00	3308.81	0.00	165.44
13	0.00	5543.67	0.00	3308.81	1111.11	0.00
14	0.00	0.00	0.00	3308.81	0.00	0.00
15	0.00	5543.67	0.00	0.00	1111.11	0.00
16	0.00	0.00	0.00	3308.81	0.00	0.00
17	0.00	5543.67	0.00	3308.81	1111.11	0.00
18	0.00	0.00	0.00	3308.81	0.00	0.00
19	0.00	5543.67	0.00	0.00	1111.11	0.00
20	0.00	5543.67	0.00	0.00	1111.11	0.00
21	0.00	5543.67	0.00	0.00	1111.11	0.00
22	0.00	583.24	0.00	0.00	0.00	0.00
23	0.00	4901.52	0.00	0.00	111.11	0.00
24	0.00	1225.38	0.00	0.00	1000.00	0.00
25	0.00	1225.38	0.00	0.00	0.00	0.00
26	0.00	0.00	0.00	0.00	1000.00	0.00

Table A-146. Equipment Description for Process 46 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-4600	Centrifugal Pump	4.46E-05	
P-4601	Centrifugal Pump	4.02E-05	
P-4602	Centrifugal Pump	4.21E-06	
P-4603	Centrifugal Pump	4.44E-05	
P-4604	Centrifugal Pump	5.06E-05	

P-4605	Centrifugal Pump	1.52E-04	
P-4606	Centrifugal Pump	5.06E-05	
P-4607	Centrifugal Pump	1.02E-04	
P-4608	Centrifugal Pump	5.06E-05	
P-4609	Centrifugal Pump	5.32E-05	
P-4610	Centrifugal Pump	1.52E-04	
P-4611	Centrifugal Pump	5.06E-05	
P-4612	Centrifugal Pump	1.02E-04	
P-4613	Centrifugal Pump	5.06E-05	
P-4614	Centrifugal Pump	1.52E-04	
P-4615	Centrifugal Pump	5.06E-05	
P-4616	Centrifugal Pump	1.02E-04	
P-4617	Centrifugal Pump	1.02E-04	
P-4618	Centrifugal Pump	1.02E-04	
P-4619	Centrifugal Pump	8.92E-06	
P-4620	Centrifugal Pump	7.67E-05	
V-4600	Heating Vessel with Mixing	2.27E-02	Mixing requirement
		1.71E-02	Heating requirement
V-4601	Solvent Vessel	0.00E+00	
V-4602	Mixing Vessel	5.98E-04	Mixing requirement
V-4603	Solvent Vessel	0.00E+00	
V-4604	Mixing Vessel	2.64E-02	Mixing requirement
V-4403A	Heating Vessel with Mixing	3.80E-04	Mixing requirement
		6.90E-02	Heating requirement
V-4404A	Cooling Vessel with Mixing	2.61E-03	Mixing requirement
		-1.21E-01	Cooling requirement
S-4600	Centrifuge	3.40E-02	
S-4601	Centrifuge	3.40E-02	
S-4602	Centrifuge	3.40E-02	
F-4600	Filtration Unit	6.65E-02	
D-4600	Vacuum Dryer	7.72E-01	Vacuum pump requirement

	1.45E-08	Heating requirement

Table A-147. Recovered Solvent from the Solvent Recovery System Implemented to Process 46 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Isopropyl Acetate	5012.64	97.78%
Water	9926.43	100.00%

A.1.50 Process 47A – Cooling Crystallization

The process flow diagram of Process 47A can be found in Figure A-50. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-148 and Table A-149, respectively. The mass of solvent recovered from Process 47A using solvent recovery techniques are reported in Table A-150.

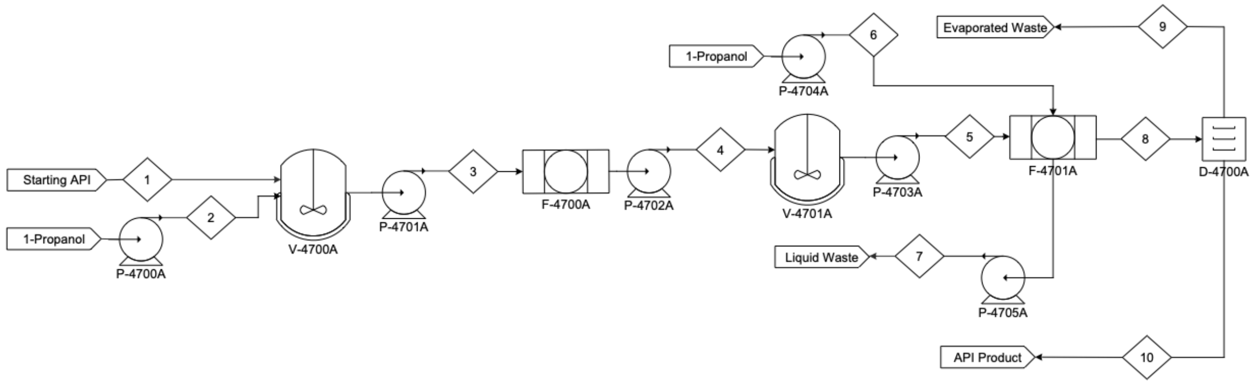

Figure A-50. Process flow diagram of Process 47A – Cooling Crystallization.

Table A-148. Mass of Each Component in Each Stream of Process 47A (According to Figure A-50). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API (g)	1-Propanol (g)
1	1111.11	0.00
2	0.00	9814.45
3	1111.11	9814.45
4	1111.11	9814.45

5	1111.11	9814.45
6	0.00	1784.45
12	111.11	9279.12
13	1000.00	2319.78
14	0.00	2319.78
15	1000.00	0.00
Solvent Recovery System	**---**	**---**
16	0.00	9186.33
17	111.11	92.79
18	11.11	74.23
19	100.00	18.56
20	0.00	18.56
21	100.00	0.00

Table A-149. Equipment Description for Process 47A and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-4700A	Centrifugal Pump	1.50E-04	
P-4701A	Centrifugal Pump	1.67E-04	
P-4702A	Centrifugal Pump	1.67E-04	
P-4703A	Centrifugal Pump	1.67E-04	
P-4704A	Centrifugal Pump	2.73E-05	
P-4705A	Centrifugal Pump	1.44E-04	
V-4700A	Heating Vessel with Mixing	6.02E-04	Mixing requirement
		3.69E-01	Heating requirement
V-4701A	Cooling Vessel with Mixing	6.49E-03	Mixing requirement
		-4.35E-01	Cooling requirement
F-4700A	Filtration Unit	3.03E-05	
F-4701A	Filtration Unit	3.53E-05	
D-4700A	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		6.86E-01	Heating requirement

Solvent Recovery System	---	---	---
SR-P-4700A	Centrifugal Pump	1.41E-04	
SR-P-4701A	Centrifugal Pump	3.12E-06	
SR-P-4702A	Centrifugal Pump	1.31E-06	
SR-C-4700A	Distillation Column	2.20E+00	
SR-F-4700A	Filtration Unit	2.04E-03	
SR-D-4700A	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		5.34E-03	Heating requirement

Table A-150. Recovered Solvent from the Solvent Recovery System Implemented to Process 47A with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
1-Propanol	9271.67	99.88%

A.1.51 Process 47B – Cooling Crystallization

The process flow diagram of Process 47B can be found in Figure A-51. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-151 and Table A-152, respectively. The mass of solvent recovered from Process 47B using solvent recovery techniques are reported in Table A-153.

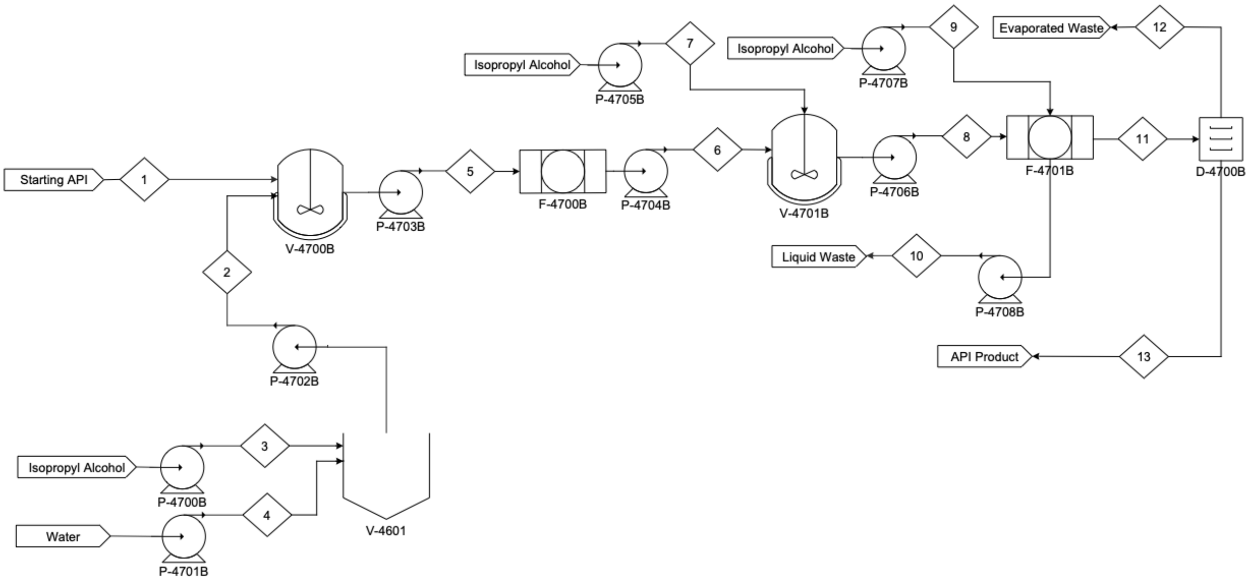

Figure A-51. Process flow diagram of Process 47B – Cooling Crystallization.

Table A-151. Mass of Each Component in Each Stream of Process 47B (According to Figure A-51). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API (g)	Isopropyl Alcohol (g)	Water (g)
1	1111.11	0.00	0.00
2	0.00	4017.34	0.00
3	0.00	0.00	443.11
4	0.00	4017.34	443.11
5	1111.11	4017.34	443.11
6	1111.11	4017.34	443.11
7	0.00	4366.67	0.00
8	1111.11	8384.01	443.11
9	0.00	1746.67	0.00
10	111.11	8104.54	354.49
11	1000.00	2026.14	88.62
12	0.00	2026.14	88.62
13	1000.00	0.00	0.00
Solvent Recovery System	---	---	---
14	0.00	8023.50	40.32
15	111.11	81.05	314.17
16	0.00	80.23	0.40
17	111.11	0.81	313.77
18	11.11	0.65	251.01
19	100.00	80.40	63.16
20	0.00	80.40	63.16
21	100.00	0.00	0.00

Table A-152. Equipment Description for Process 47B and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	Equipment Description	Energy Requirement (kWh)	Note

P-4700B	Centrifugal Pump	6.15E-05	
P-4701B	Centrifugal Pump	6.78E-06	
P-4702B	Centrifugal Pump	6.82E-05	
P-4703B	Centrifugal Pump	8.52E-05	
P-4704B	Centrifugal Pump	8.52E-05	
P-4705A	Centrifugal Pump	6.68E-05	
P-4706B	Centrifugal Pump	1.52E-04	
P-4707B	Centrifugal Pump	2.67E-05	
P-4708B	Centrifugal Pump	1.31E-04	
V-4700B	Heating Vessel with Mixing	2.91E-04	Mixing requirement
		4.57E-01	Heating requirement
V-4701B	Solvent Mixture Vessel	0.00E+00	
V-4702B	Cooling Vessel with Mixing	4.70E-03	Mixing requirement
		-5.62E-01	Cooling requirement
F-4700B	Filtration Unit	1.55E-05	
F-4701B	Filtration Unit	3.25E-05	
D-4700B	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		8.26E-01	Heating requirement
Solvent Recovery System	---	---	---
SR-P-4700B	Centrifugal Pump	1.23E-04	
SR-P-4701B	Centrifugal Pump	7.75E-06	
SR-P-4702B	Centrifugal Pump	1.23E-06	
SR-P-4703B	Centrifugal Pump	6.51E-06	
SR-P-4704B	Centrifugal Pump	4.02E-06	
SR-C-4700B	Distillation Column	3.33E+00	
SR-C-4701B	Distillation Column	2.65E-01	
SR-F-4700B	Filtration Unit	4.26E-03	
SR-D-4700B	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		8.18E-02	Heating requirement

Table A-153. Recovered Solvent from the Solvent Recovery System Implemented to Process 47B with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Isopropyl Alcohol	8144.45	99.50%
Water	262.77	95.52%

A.1.52 Process 48 – Antisolvent Crystallization

The process flow diagram of Process 48 can be found in Figure A-52. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-154 and Table A-155, respectively. The mass of solvent recovered from Process 48 using solvent recovery techniques are reported in Table A-156.

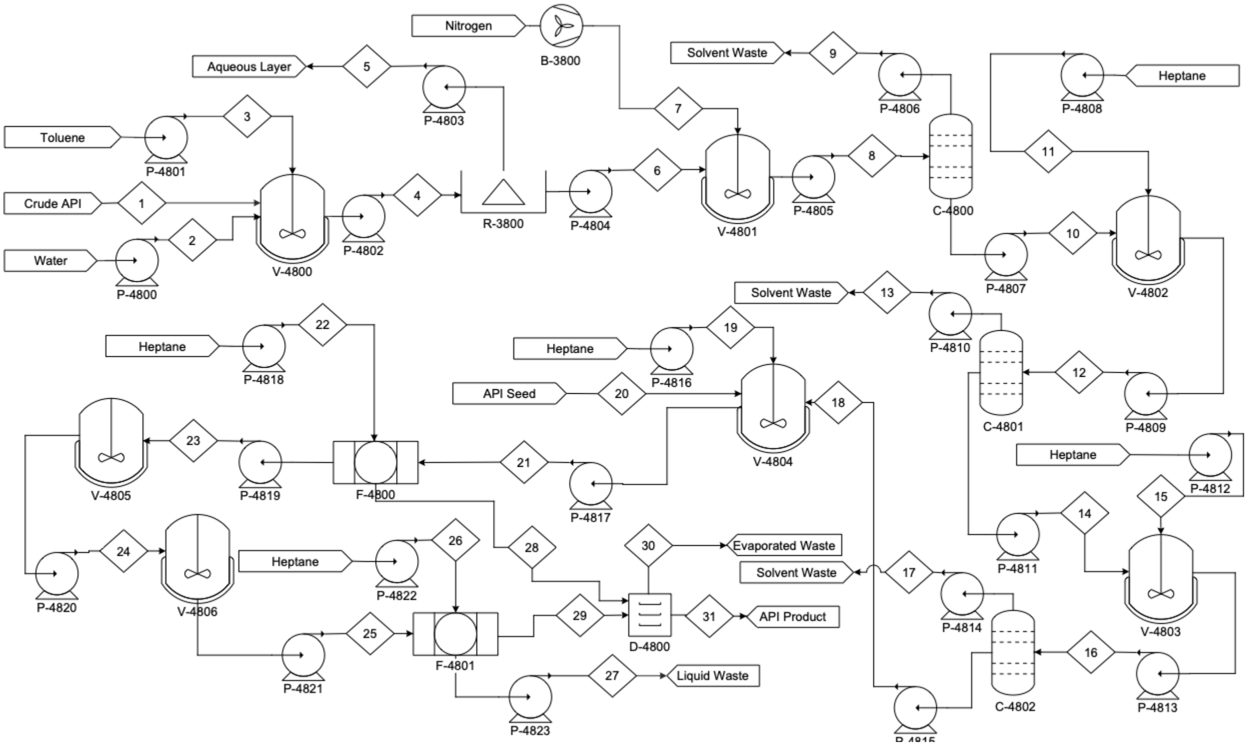

Figure A-52. Process flow diagram of Process 48 – Antisolvent Crystallization.

Table A-154. Mass of Each Component in Each Stream of Process 48 (According to Figure A-52). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	API (g)	Water (g)	Toluene (g)	Heptane (g)

1	944.46	368.34	0.00	0.00
2	0.00	5235.45	0.00	0.00
3	0.00	0.00	6829.19	0.00
4	944.46	5603.79	6829.19	0.00
5	0.00	5603.79	0.00	0.00
6	944.46	0.00	6829.19	0.00
7	0.00	0.00	0.00	0.00
8	944.46	0.00	6829.19	0.00
9	0.00	0.00	3983.69	0.00
10	944.46	0.00	2845.50	0.00
11	0.00	0.00	0.00	3053.05
12	944.46	0.00	2845.50	3053.05
13	0.00	0.00	0.00	3053.05
14	944.46	0.00	2845.50	0.00
15	0.00	0.00	0.00	3053.05
16	944.46	0.00	2845.50	3053.05
17	0.00	0.00	0.00	3053.05
18	944.46	0.00	2845.50	0.00
19	0.00	0.00	0.00	6285.69
20	65.64	0.00	0.00	0.00
21	1010.10	0.00	2845.50	6285.69
22	0.00	0.00	0.00	987.75
23	101.01	0.00	2276.40	5818.75
24	101.01	0.00	2276.40	5818.75
25	101.01	0.00	2276.40	5818.75
26	0.00	0.00	0.00	987.75
27	10.10	0.00	1821.12	5445.20
28	909.09	0.00	569.10	1454.69
29	90.91	0.00	455.28	1361.30
30	0.00	0.00	1024.38	2815.99
31	1000.00	0.00	0.00	0.00
Solvent Recovery System	---	---	---	---
32	0.00	0.00	27.09	32

33	10.10	0.000	1794.028	33
34	1.01	0.00	1435.22	34
35	9.091	0.000	358.806	35
36	0.00	0.00	358.81	36
37	9.09	0.00	0.00	37

Table A-155. Equipment Description for Process 48 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-4800	Centrifugal Pump	8.01E-05	
P-4801	Centrifugal Pump	1.04E-04	
P-4802	Centrifugal Pump	2.05E-04	
P-4803	Centrifugal Pump	8.57E-05	
P-4804	Centrifugal Pump	1.19E-04	
P-4805	Centrifugal Pump	1.19E-04	
P-4806	Centrifugal Pump	6.10E-05	
P-4807	Centrifugal Pump	5.80E-05	
P-4808	Centrifugal Pump	4.67E-05	
P-4809	Centrifugal Pump	1.05E-04	
P-4810	Centrifugal Pump	4.67E-05	
P-4811	Centrifugal Pump	5.80E-05	
P-4812	Centrifugal Pump	4.67E-05	
P-4813	Centrifugal Pump	1.05E-04	
P-4814	Centrifugal Pump	4.67E-05	
P-4815	Centrifugal Pump	5.80E-05	
P-4816	Centrifugal Pump	9.62E-05	
P-4817	Centrifugal Pump	1.55E-04	
P-4818	Centrifugal Pump	1.51E-05	
P-4819	Centrifugal Pump	1.25E-04	
P-4820	Centrifugal Pump	1.25E-04	
P-4821	Centrifugal Pump	1.25E-04	
P-4822	Centrifugal Pump	1.51E-05	

P-4823	Centrifugal Pump	1.11E-04	
V-4800	Mixing Vessel	1.55E-03	Mixing requirement
V-4801	Heating Vessel with Mixing	4.57E-04	Mixing requirement
		1.34E-01	Heating requirement
V-4802	Heating Vessel with Mixing	3.99E-04	Mixing requirement
		7.42E-02	Heating requirement
V-4803	Heating Vessel with Mixing	2.00E-04	Mixing requirement
		8.18E-03	Heating requirement
V-4804	Cooling Vessel with Mixing	4.60E-03	Mixing requirement
		-2.50E-01	Cooling requirement
V-4805	Heating Vessel with Mixing	6.54E-04	Mixing requirement
		1.10E-01	Heating requirement
V-4806	Cooling Vessel with Mixing	2.67E-03	Mixing requirement
		-1.10E-01	Cooling requirement
C-4800	Vacuum Distillation Column	4.30E-01	
C-4801	Vacuum Distillation Column	9.37E-01	
C-4802	Vacuum Distillation Column	6.88E-01	
B-4800	Blower	0	
F-4800	Filtration Unit	2.82E-05	
F-4801	Filtration Unit	2.55E-05	
D-4800	Vacuum Dryer	1.16E+00	Vacuum pump requirement
		5.37E-01	Heating requirement
Solvent Recovery System	---	---	---
SR-P-4800	Centrifugal Pump	8.29E-05	
SR-P-4801	Centrifugal Pump	2.84E-05	
SR-P-4802	Centrifugal Pump	2.26E-05	
SR-C-4800	Distillation Column	2.13E+00	
SR-F-4800	Filtration Unit	3.79E-03	
SR-D-4800	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		5.64E-02	Heating requirement

Table A-156. Recovered Solvent from the Solvent Recovery System Implemented to Process 48 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Heptane	11523.94	99.76%
Toluene	5463.49	99.18%
Water	5603.79	100.00%

A.1.53 Process 49 – Antisolvent Crystallization

The process flow diagram of Process 49 can be found in Figure A-53. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-157 and Table A-158, respectively. The mass of solvent recovered from Process 49 using solvent recovery techniques are reported in Table A-159.

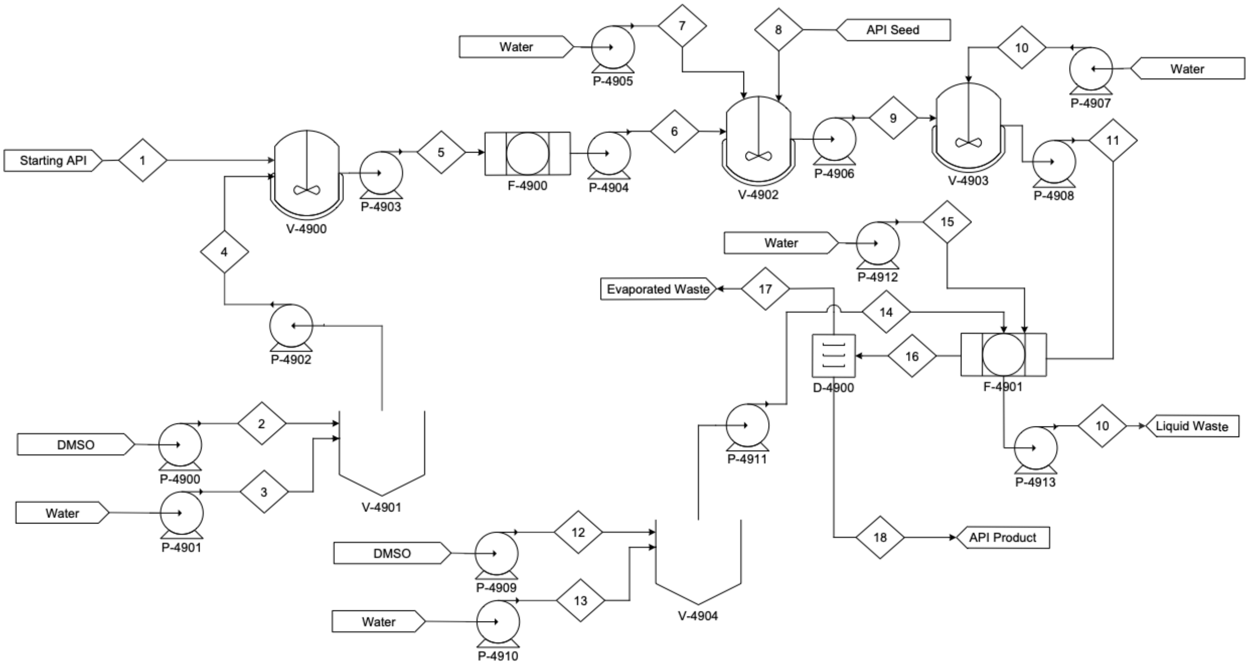

Figure A-53. Process flow diagram of Process 49 – Antisolvent Crystallization.

Table A-157. Mass of Each Component in Each Stream of Process 49 (According to Figure A-53). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	**API (g)**	**DMSO (g)**	**Water (g)**
1	1089.32	0.00	0.00

2	0.00	7549.02	0.00
3	0.00	0.00	760.24
4	0.00	7549.02	760.24
5	1089.32	7549.02	760.24
6	1089.32	7549.02	760.24
7	0.00	0.00	271.51
8	21.79	0.00	0.00
9	1111.11	7549.02	1031.75
10	0.00	0.00	5701.80
11	1111.11	7549.02	6733.55
12	0.00	1198.26	0.00
13	0.00	0.00	1086.06
14	0.00	1198.26	1086.06
15	0.00	0.00	6516.34
16	111.11	6997.82	11468.76
17	1000.00	1749.46	2867.19
18	0.00	1749.46	2867.19
19	1000.00	0.00	0.00
Solvent Recovery System	---	---	---
20	0.00	57.06	11354.07
21	111.11	6940.77	114.69
22	11.11	5552.61	91.75
23	100.00	1388.15	22.94
24	0.00	1388.15	22.94
25	100.00	0.00	0.00

Table A-158. Equipment Description for Process 49 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-4900	Centrifugal Pump	1.16E-04	
P-4901	Centrifugal Pump	1.16E-05	
P-4902	Centrifugal Pump	1.27E-04	

P-4903	Centrifugal Pump	1.44E-04	
P-4904	Centrifugal Pump	1.44E-04	
P-4905	Centrifugal Pump	4.15E-06	
P-4906	Centrifugal Pump	1.48E-04	
P-4907	Centrifugal Pump	8.72E-05	
P-4908	Centrifugal Pump	2.36E-04	
P-4909	Centrifugal Pump	1.83E-05	
P-4910	Centrifugal Pump	1.66E-05	
P-4911	Centrifugal Pump	3.50E-05	
P-4912	Centrifugal Pump	9.97E-05	
P-4913	Centrifugal Pump	2.84E-04	
V-4900	Heating Vessel with Mixing	5.06E-04	Mixing requirement
		1.75E-01	Heating requirement
V-4901	Solvent Vessel	0.00E+00	
V-4902	Cooling Vessel with Mixing	5.06E-04	Mixing requirement
		-2.35E-01	Cooling requirement
V-4903	Mixing Vessel	0.00E+00	Mixing requirement
		0.00E+00	Heating requirement
V-4904	Solvent Mixture Vessel	0.00E+00	
F-4900	Filtration Unit	2.61E-05	
F-4901	Filtration Unit	4.91E-05	
D-4900	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		2.78E+00	Heating requirement
Solvent Recovery System	---	---	---
SR-P-4900	Centrifugal Pump	1.75E-04	
SR-P-4901	Centrifugal Pump	1.10E-04	
SR-P-4902	Centrifugal Pump	8.65E-05	
SR-C-4900	Distillation Column	9.12E+00	
SR-F-4900	Filtration Unit	7.17E-02	
SR-D-4900	Vacuum Dryer	5.79E-01	Vacuum pump requirement
		2.39E-01	Heating requirement

Table A-159. Recovered Solvent from the Solvent Recovery System Implemented to Process 49 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	Mass (g)	Purity
Dimethyl Sulfoxide	5655.47	98.18%
Water	11411.13	99.50%

A.1.54 Process 50 – Reactive Crystallization

The process flow diagram of Process 50 can be found in Figure A-54. The mass stream table and energy requirements with incineration and solvent recovery system can be found in Table A-160 and Table A-161, respectively. Please note that for this process, no solvent recovery system was needed because the purity of the solvents collected were already high enough for reuse. The mass of solvent recovered from Process 50 using solvent recovery techniques are reported in Table A-162.

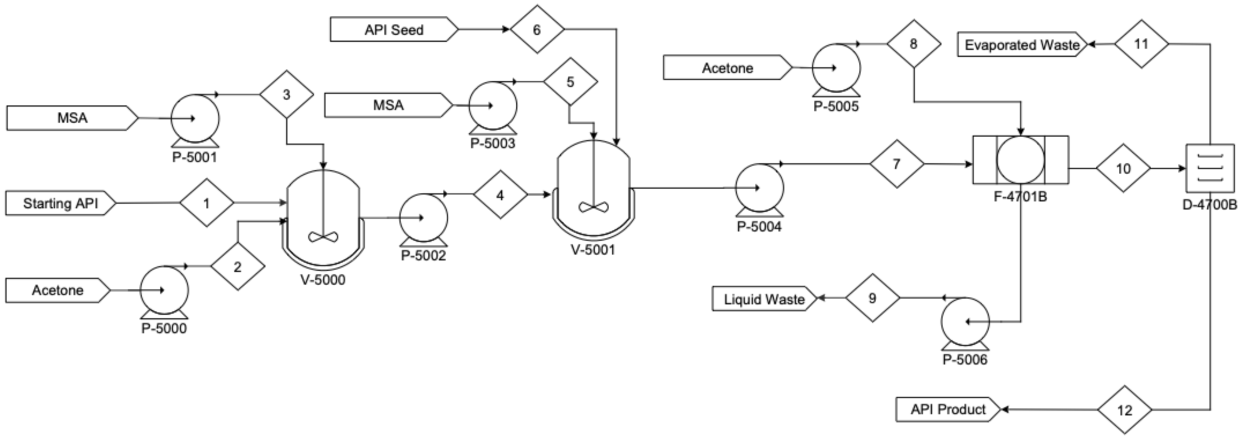

Figure A-54. Process flow diagram of Process 50 – Reactive Crystallization.

Table A-160. Mass of Each Component in Each Stream of Process 50 (According to Figure A-54). Solvent Recovery System Implemented as Alternative Option to Incineration.

Stream	Starting API (g)	Acetone (g)	MSA (g)	API Product (g)
1	904.83	0.00	0.00	0.00
2	0.00	14187.68	0.00	0.00
3	0.00	0.00	52.45	0.00
4	904.83	14187.68	52.45	0.00

5	0.00	0.00	139.85	0.00
6	0.90	0.00	0.00	1.11
7	0.00	14187.68	0.00	1111.11
8	0.00	2128.15	0.00	0.00
9	0.00	13052.67	0.00	111.11
10	0.00	3263.17	0.00	1000.00
11	0.00	3263.17	0.00	0.00
12	0.00	0.00	0.00	1000.00

Table A-161. Equipment Description for Process 50 and According to Energy Requirements. Solvent Recovery System Implemented as Alternative Option to Incineration.

Equipment Label	**Equipment Description**	**Energy Requirement (kWh)**	**Note**
P-5000	Centrifugal Pump	2.17E-04	
P-5001	Centrifugal Pump	8.02E-07	
P-5002	Centrifugal Pump	2.32E-04	
P-5003	Centrifugal Pump	2.14E-06	
P-5004	Centrifugal Pump	2.34E-04	
P-5005	Centrifugal Pump	3.26E-05	
P-5006	Centrifugal Pump	2.01E-04	
V-5000	Heating Vessel with Mixing	6.61E-04	Mixing requirement
		2.64E-01	Heating requirement
V-5001	Cooling Vessel with Mixing	7.09E-05	Mixing requirement
		-3.07E-01	Cooling requirement
F-5000	Filtration Unit	1.32E-01	
D-5000	Vacuum Dryer	7.72E-01	Vacuum pump requirement
		2.01E-01	Heating requirement

Table A-162. Recovered Solvent from the Solvent Recovery System Implemented to Process 50 with Purity Levels of Each Recovered Solvent.

Recovered Solvent	**Mass (g)**	**Purity**
Dimethyl Sulfoxide	5655.47	98.18%

Water	11411.13	99.50%

Appendix B: Sample Calculations

Sample calculations have been provided for equations used throughout the project.

B.1 Energy Calculations

Energy calculations completed using data from P02.

Pump Energy Requirement

$$E_{pump} = 0.01153 \times 10^{-5}\, m_{liq}\ [kWh]$$

$$E_{pump} = \left(0.01153 \times 10^{-5}\ \left[\frac{kWh}{g}\right]\right)(10324.55\ [g])$$

$$\boldsymbol{E_{pump} = 1.58 \times 10^{-4}\ kWh}$$

Filtration Energy Requirement

$$E_{filt} = 0.01\, m_{sol}\ [kWh]$$

$$E_{filt} = \frac{(0.01\ kWh)(1052.63 + 6334.36 + 415.63 + 10{,}398.62 + 1310.68\ [g])}{1000\ \left[\frac{g}{kg}\right]}$$

$$\boldsymbol{E_{filter} = 0.195\ kWh}$$

Heat Capacity Calculation

Going from 25ºC to 50ºC for distilled water where $C_1 = 276{,}370, C_2 = -2090.1, C_3 = 8.125, C_4 = -0.0141116, C_5 = 9.37 \times 10^{-6}$.

$$c_{pL} = C_1(T_2 - T_1) + \frac{C_2(T_2^2 - T_1^2)}{2} + \frac{C_3(T_2^3 - T_1^3)}{3} + \frac{C_4(T_2^4 - T_1^4)}{4} + \frac{C_5(T_2^5 - T_1^5)}{5}$$

$$c_{pL} = 276{,}370(50 - 25) + \frac{-2090.1(50^2 - 25^2)}{2} + \frac{8.125(50^3 - 25^3)}{3} + \frac{-0.0141116(50^4 - 25^4)}{4} + \frac{(9.37 \times 10^{-6})(50^5 - 25^5)}{5}$$

$$\boldsymbol{c_{pL} = 1.882\ kJ/mol}$$

Heat of Vaporization Calculation

Evaporative 50ºC for distilled water where $C_1 = 5.66 \times 10^7, C_2 = 0.6120, C_3 = -0.6257, C_4 = -0.3988, T_c = 647.10℃$.

$$\Delta H_v = (5.66 \times 10^7)(1 - 0.4839)^{(0.6120 + (-0.6257)(0.4839) + (0.3988)(0.4839)^2)}$$

$$\boldsymbol{\Delta H_v = 42.9\ kJ/mol}$$

Dryer Energy Requirement

Using the data provided above for heat of vaporization and heat capacity and mass of water from P02, the dryer energy requirement could be calculated using an efficiency of 85%.

$$E_{dry} = \frac{m_F c_p^F + m_{ES} \Delta H_v^{ES}}{\eta_{heat}}$$

$$E_{dry} = \frac{\left[\frac{(83.13\ g)\left(1.882 \frac{kJ}{mol}\right)}{18.02 \frac{g}{mol}} + \frac{(83.13\ g)\left(42.9 \frac{kJ}{mol}\right)}{18.02 \frac{g}{mol}}\right]}{0.85}\left(2.778 \times 10^{-4} \frac{kWh}{kJ}\right)$$

$$\boldsymbol{E_{dry} = 6.75 \times 10^{-2} kWh}$$

Heating Energy Requirement

The heating requirement for V-200 by raising 415.63 g of water from 22ºC to 80ºC was calculated below.

$$\Delta H = m_F c_p \Delta T$$

$$\Delta H = \left(\frac{\left(4.3695 \frac{kJ}{mol}\right)(415.63\ g)}{18.02 \frac{g}{mol}}\right)\left(2.778 \times 10^{-4} \frac{kWh}{kJ}\right)$$

$$\boldsymbol{\Delta H = 2.80 \ \times 10^{-2}\ kWh}$$

Distillation Energy Requirement

The distillation energy required to separate water and acetonitrile from the solvent recovery system for water and acetonitrile can be found below.

$$\log \alpha = \frac{t_2 - t_1}{T_{boil}}(3.99 + 0.001939 T_{boil})$$

$$\log \alpha = \frac{100 - 84}{86}\big(3.99 + (0.001939)(86)\big)$$

$$\boldsymbol{\log \alpha = 2.167}$$

$$R_{min} = \frac{1}{\alpha - 1}\left(\frac{X_{LD}}{X_{LF}} - \frac{\alpha(1 - X_{LD})}{(1 - X_{LF})}\right)$$

$$R_{min} = \frac{1}{2.167 - 1}\left[\left(\frac{0.9896}{0.9568}\right) - \frac{2.167(1 - 0.9896)}{(1 - 0.9568)}\right]$$

$$\boldsymbol{R_{min} = 0.4388}$$

$$E_{dist} = \frac{m_D \Delta H_v (1.3R_{min} + 1)}{\eta}$$

$$E_{dist} = \left[\frac{\left[\frac{(15{,}996\ g)\left(30.9\frac{kJ}{mol}\right)}{41.05\frac{g}{mol}} + \frac{(72.1\ g)\left(41.4\frac{kJ}{mol}\right)}{18.02\frac{g}{mol}} \right] [(1.3)(0.4388) + 1]}{0.85} \right] \left(2.778 \times 10^{-4}\frac{kWh}{kJ}\right)$$

$$\boldsymbol{E_{dist} = 6.26\ kWh}$$

Stirring Energy Requirement

The stirring requirement for the water component of V-200 has been calculated below.

$$E_{stir(1000L)} = 0.0180\rho_{mix}t$$

$$E_{stir(1000L)} = \left(0.0180\frac{m^5}{s^3}\right)\left(0.998\frac{kg}{m^3}\right)(30\ m)\left(\frac{60\ s}{1\ m}\right)\left(2.778 \times 10^{-7}\frac{kWh}{J}\right)$$

$$\boldsymbol{E_{stir(1000L)} = 8.98 \times 10^{-6} kWh}$$

B.2 Economic Calculations

Economic calculations were determined using data from P02 at the 10,000 kg scale.

Operating Cost without Solvent Recovery Systems

The operating costs for per kilogram of API produced is calculated below.

$$Cost_{operaitng_{inc}} = Cost_{solvent} + Cost_{electricity} + Cost_{incineration}$$

$$Cost_{operating_{inc}} = \frac{\$825.82}{1\ kg\ API} + \frac{\$3.06}{1\ kg\ API} + \frac{\$3.80}{1\ kg\ API}$$

$$\boldsymbol{Cost_{operating_{inc}} = \$832.60/kg\ API}$$

Cost Savings

Cost savings from using solvent recovery systems is calculated below.

$$Savings_{rec} = Cost_{rec,sol} + Cost_{inc,waste} + Cost_{inc,labour} - Cost_{rec,elec} - Cost_{rec,labour}$$

$$Savings_{rec} = \$6{,}091{,}189 + \$38{,}030 + \$79{,}200 - \$30{,}579 - \$237{,}600$$

$$\boldsymbol{Savings_{rec} = \$5{,}940{,}239}$$

Capital Cost

The capital cost of the solvent recovery system for P02 is calculated below.

$$C = \$380{,}000N\left(\frac{Q}{s}\right)^{0.3}$$

$$C = \$380{,}000(2)\left(\frac{0.0222}{0.99}\right)^{0.3}$$

$$\boldsymbol{C = \$3,850,892}$$

Depreciation

The depreciation of solvent recovery system for P02 is calculated below.

$$d = \frac{C_i - C_S}{n}$$

$$d = \frac{\$3{,}850{,}892 - \$0}{25\ years}$$

$$\boldsymbol{d = \$154,036}$$

Payback Period

The payback period for implementing the solvent recovery system for P02 is calculated below.

$$Payback\ Period = \frac{fixed\ capital\ investment}{(annual\ profit + annual\ depreciation)_{avg}}$$

$$Payback\ Period = \frac{\$3{,}850{,}892}{(\$5{,}940{,}239 + \$154{,}036)}$$

$$\boldsymbol{Payback\ Period = 0.6\ years}$$

Return on Investment

The return on investment for the solvent recovery system for P02 is calculated below.

$$ROI = \frac{P}{I} \times 100\%$$

$$ROI = \frac{\$5{,}940{,}239}{\$3{,}850{,}892}$$

$$\boldsymbol{ROI = 154.3\%}$$

Appendix C: Solvent Information

Several solvents were used throughout all the crystallization processes examined in the project. Their general information, including molecular weight, density, boiling point, and cost can be found in Table C-1. All information was gathered from Lab Alley (2024) and Spectrum Chemical, (2024). Costs were estimated assuming all solvents achieved the ACS standard and of volumes of 4-5L. Several chemical constants were also used throughout the analysis (e.g., heats of vaporization, heat capacities, etc.). The values of these constants were determined at various temperatures for the respected compound throughout each process according to the derived equation from *Perry's Chemical Engineers' Handbook* by Green & Southard (2019).

Table C-1. Molecular Weight, Density, and Boiling Point of Solvents Used Throughout Analysis.

Solvent	**Molecular Weight (kg/kmol)**	**Density (kg/m3)**	**Boiling Point (ºC)**	**Cost ($/mL)**	**Reference Volume**
1-Butanol	74.12	0.81	117.7	$ 0.010	55 gal
1-Propanol	60.10	0.803	97.0	$ 0.006	55 gal
1,4-Dioxane	88.11	1.03	101.0	$ 0.015	200 L
2-Methyl Tetrahydrofuran	86.13	0.854	78.0	$ 0.029	200 L
Acetone	58.08	0.784	56.0	$ 0.007	55 gal
Acetonitrile	41.05	0.786	82.0	$ 0.020	55 gal
Dichloromethane	84.93	1.33	39.6	$ 0.012	55 gal
Dimethylacetamide	87.12	0.925	165.0	$ 0.013	200 L
Dimethyl Sulfoxide	78.13	1.1	189.0	$ 0.138	200 L
Ethanol	46.07	0.789	78.4	$ 0.011	55 gal
Ethyl Acetate	88.11	0.902	77.1	$ 0.009	55 gal
Heptane	100.20	0.684	98.4	$ 0.010	55 gal
Isopropyl acetate	102.10	0.87	89.0	$ 0.047	200 L
Isopropyl Alcohol	60.10	0.786	82.3	$ 0.008	55 gal
Methanol	32.04	0.792	64.7	$ 0.003	55 gal
Methyl Tert-Butyl Ether	88.15	0.74	55.2	$ 0.037	200 L
Tetrahydrofuran	72.11	0.888	66.0	$ 0.020	55 gal

Toluene	92.14	0.867	110.6	$ 0.016	55 gal
Water	18.02	0.997	100.0	$ 0.005	200 L
Acetic Acid	60.05	1.05	117.9	$ 0.013	55 gal

The total mass of solvents and cost used in all processes can be found in Table C-2.

Table C-2. Table of solvent mass and cost found in all processes.

Solvent	*Total Mass [kg/kg API]*	Total Cost ($/kg API)
1,4-Dioxane	2.05	$ 30.06
Acetonitrile	18.51	$ 477.29
Dichloromethane	140.21	$ 1,223.92
Methanol	88.44	$ 353.56
Dimethylacetamide	14.34	$ 206.46
Tetrahydrofuran	59.87	$ 1,352.05
Toluene	18.06	$ 340.80
1-Butanol	4.85	$ 62.50
1-Propanol	26.25	$ 181.11
Acetic Acid	10.48	$ 126.37
Acetone	110.49	$ 945.88
Dimethyl Sulfoxide	15.10	$ 1,891.67
Ethanol	82.73	$ 1,106.58
Ethyl Acetate	91.87	$ 952.75
2-Methyl Tetrahydrofuran	12.29	$ 412.62
Heptane	99.20	$ 1,454.13
Isopropyl Alcohol	76.13	$ 798.73
Isopropyl Acetate	54.15	$ 2,901.75
Methyl tert-Butyl Ether	45.96	$ 2,317.02
Ultra Pure Water	279.20	$ 1,287.57