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Methodology for Early-Stage Sustainability Assessment and Efficient Energy by Design

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Foreword

This CEN Workshop Agreement (CWA 18361:2026) has been developed in accordance with the CEN-CENELEC Guide 29 “CEN/CENELEC Workshop Agreements – A rapid way to standardization” and with the relevant provisions of CEN/CENELEC Internal Regulations – Part 2. It was approved by the Workshop CEN “Methodology for Early-Stage Sustainability Assessment for Chemical and Biochemical Manufacturing Processes”, the secretariat of which is held by UNE consisting of representatives of interested parties on 2025-06-19, the constitution of which was supported by CEN following the public call for participation made on 2025-05-06. However, this CEN Workshop Agreement does not necessarily include all relevant stakeholders.

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Introduction

There are some clear drivers indicating a need within the process industries for a simple, non-expert but broadly applicable methodology for comparing options and identifying those most likely to deliver better outcomes in terms of sustainability as early as possible in the product or process development project life cycle. One is increasing corporate and societal demand for more sustainable, safe processes, exemplified by the European Commission's Safe and Sustainable by Design (SSbD) framework. [1] There is also a constant need to develop new products and processes across the chemical and chemical using industries, particularly in pharmaceuticals and fine chemicals, but extending into FMCG, Foundation Industries etc. Finally, there is the societally led drive for the rapid development of new processes to support the transition to a more sustainable economy. These include new processes and technologies for generating biofuels, bio-derived feedstocks, new materials for batteries and other materials underpinning the introduction of sustainable technologies. Such developments are often led by universities and start-ups either publicly funded or by private investors. They often have small projects teams with limited competence in expert skills such as Life Cycle Assessment (LCA) and Techno-Economic Analysis (TEA).

Comparing product and or process development options involves an evaluation and comparison of the risks associated with each option. These can be categorised into process safety, environmental/sustainability risks (which can arise across the whole life cycle not just manufacturing) and the risk of commercial failure. All three categories of risk ultimately fall within the broader compass of sustainability.

The operational safety of any manufacturing process is legally and ethically of paramount importance, and therefore it should be included as part of any methodology for evaluating and comparing alternatives. The recognised standard for process safety assessment in the process industries is to conduct a Hazard and Operability study (HAZOP), however because this technique is exhaustive, it is also time consuming and thus expensive to carry out. Furthermore, it requires a well-developed design to study. This makes the methodology impractical at the early stages of a project where there are multiple options that are only described in outline.

Similarly, LCA is a well-recognised and accepted methodology for assessing environmental impacts, and is in increasing demand from regulators e.g. it is proposed as a requirement for **all new and** existing pharmaceutical licences in Europe (European Commission, 2023) Reform of the EU pharmaceutical legislation. [2] As with HAZOP, LCA is complex, expensive, time consuming, and needs expert input to carry out. It also requires a thoroughly developed quantitative process definition in terms of material inputs and outputs. Application of LCA to the chemical using industries faces an ongoing challenge of inventory data: impact factors are simply not established even for many commonly used, relatively simple chemical species never mind novel substitutes or (for example) novel, complex pharmaceutical APIs. Furthermore the, virtually inevitable, scarcity of, and uncertainty around, data in the early stages of a project will make the results of a full LCA unreliable. All of this makes LCA untenable as a tool for consideration of multiple options at the start of a new process/product development. A project team needs to be able to complete a full LCA only on the option that will eventually be commercialised. A simpler methodology for non-experts is required to enable them to consider the sustainability aspects of proposed alternatives at the early stages of a project.

A product or process cannot be considered sustainable if it fails commercially, so when trying to choose between options at the start of a project and focus development on the more promising alternatives, some consideration of the techno-economics, the business case and technical feasibility is required. However, as in other aspects, financial data is necessarily sparse and uncertain. There will necessarily be limited process understanding and this leads to scale-up and technology transfer risks. A rapid, non-expert assessment can help identify the more robust alternatives from the options available, and to start developing the project programme to mitigate the scale-up risks.

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Taken together, there is a clear need for project teams to be able to quickly and efficiently assess and start to mitigate risks across the board as early as possible in the project life-cycle. Such a methodology needs to cover aspects of: safety, environmental impacts, scale-up/technology transfer risks, the business case, supply chain feasibility and social impacts of the innovation.

Having such a methodology provides a **clear opportunity for businesses and project teams** to focus development on the most promising and sustainable options as early as possible, to change the process early, if necessary, to avoid costly modifications later in development, and to provide a sound basis for formal LCA, TEA, and process safety studies later on in the project's life cycle.

1 Scope

This document specifies a methodology for early-stage assessment of physical, chemical and biochemical manufacturing process development projects enabling project teams to compare options and identify those most likely to deliver better outcomes in terms of sustainability. The methodology is designed to assess a wide range of sustainability impacts. Environmental, energy, process safety and social impacts can be considered. In addition, the economic sustainability of options is also considered, covering technical and supply chain feasibility and the business case for a new process or product.

The methodology is applicable to all sectors in the process industries, including food, drink, formulated products and FMCG. It is expected to be of particular use for the pharmaceuticals, biotechnology and fine chemicals sectors.

Specifically, the methodology is designed to be used very early in the development project life cycle when there is limited and uncertain information about the different options available for selection for more detailed development.

This document has been designed to be used independently, but it can be aligned or integrated with other standards or management systems, such as the European Commission's recommendation for a Safe and Sustainable by Design (SSbD) Framework. [1]

2 Normative references

There are no normative references in this document.

3 Terms and definitions

No terms and definitions are listed in this document.

4 Overview of the methodology

4.1 General

The outline of the methodology is simple (see Figure 1).

- 1) Capture a description of the features of the available alternative process routes to reach the required product for commercialisation.
- 2) Use the five assessment tools to identify benefits, issues, risks and potential for improvement for each of the alternatives in turn.
- 3) Utilise the outputs from (2) to systematic compare and score the available alternatives to identify the option or options to progress to further development.

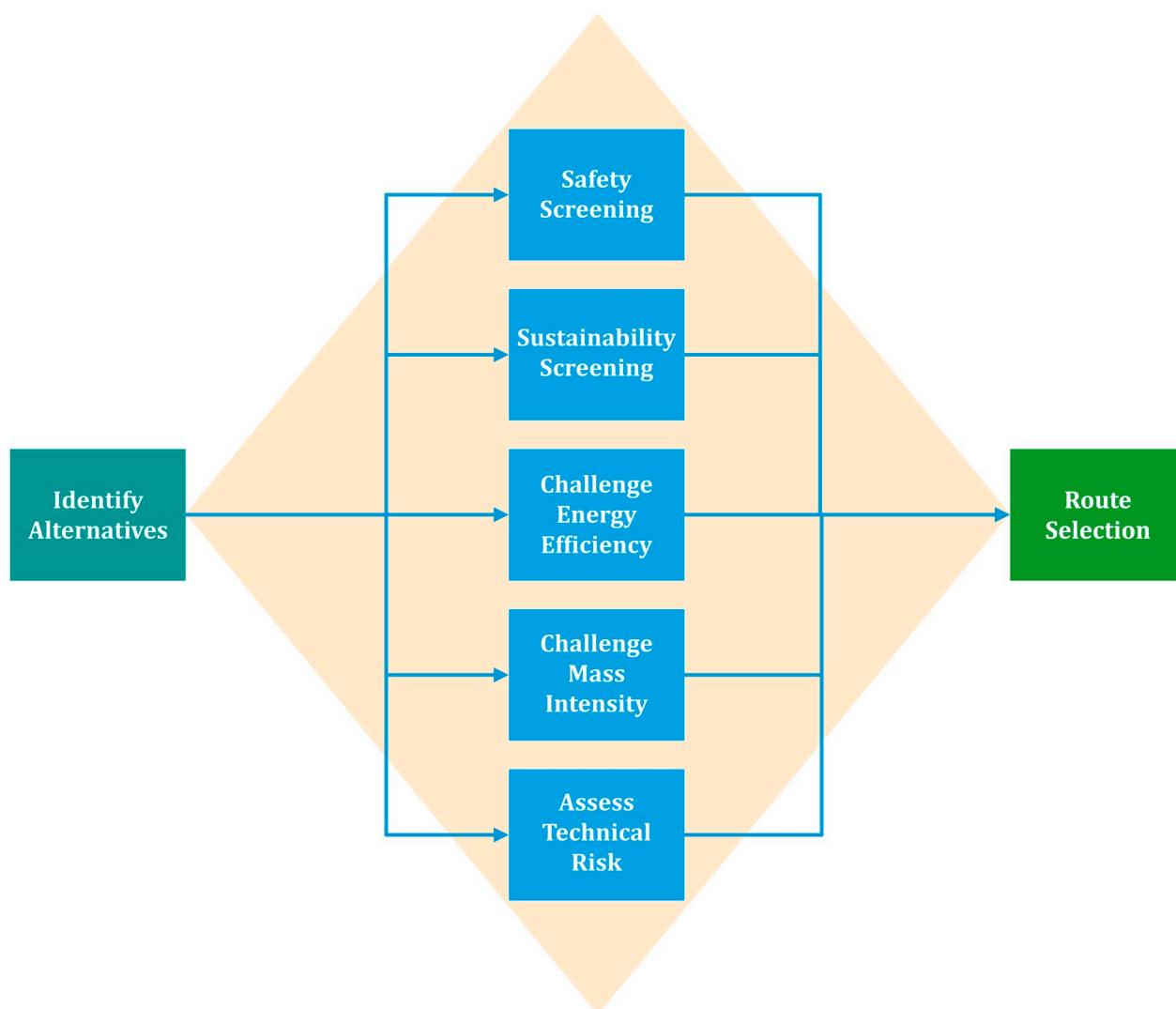


Figure 1 — Overview of Methodology for Early-Stage Sustainability Assessment for Chemical and Biochemical Manufacturing Processes

4.2 Facilitation of the methodology

It is recommended that this methodology is applied by a multi-disciplinary, multi-functional team led by an experienced facilitator in order to obtain the best value from it. This is because people with different backgrounds and responsibilities will contribute different perceptions of the benefits, issues, risks and potential for improvement for the different options leading to a more rigorous assessment.

Preparing the materials for tools employed may be conveniently carried out offline by individuals, in order to make the facilitated discussion more efficient. It is recommended that the whole study team reviews these materials together and any amendments are recorded.

While five separation assessment tools are offered in Figure 1, it may not be necessary or appropriate to use all five in every study. If it is clear that applying a particular assessment is not going to aid differentiation between the alternatives, then it should be omitted.

4.3 Selection and size of the study team

4.3.1 Size of the study team

A study team need to reach conclusions rapidly using the methodology. It should not therefore be too large such that decisions are made by a few dominant members or the discussion becomes open-ended. Equally, too small a team will lose the benefit of diverse viewpoints. A number between 4 to 10 is recommended with 6 or 7 as optimal.

4.3.2 Selection of team members

4.3.2.1 Facilitator

The facilitator should be experienced at leading technical discussions and preferable not part of the project team. This provides a degree of independence and impartiality, enabling critical questioning of the time and another source of experience. It is worth considering having a study scribe to support the facilitator in maintaining a complete record of the discussion. The facilitator is responsible for ensuring that the methodology leads to a clear conclusion.

4.3.2.2 Project leader or manager

This is the immediate leader or manager of the project and their involvement is essential for successful application of the methodology. The project manager should not facilitate the discussion, as their view of the alternatives is unlikely to be impartial. The project leader is responsible for project planning and delivery. They also may be the project owner responsible for the commercial vision, in which this role may be combined with the next.

4.3.2.3 Business/commercial representative

Ideally the project owner whose commercial vision the project is intended to realise. The role of the business/commercial representative is to assist with the business model and supply chain aspects of the project.

4.3.2.4 Scientist/engineer

The technologists most closely associated with the new process/product development need to be represented as part of the study. Ideally both scientific and engineering disciplines should be represented to exploit the different skills and expertise of these disciplines.

4.3.2.5 Subject matter experts

There may be a need to include specific subject matter experts in the study team. These may cover specific technologies involved or key areas such as regulatory, sustainability or process safety as appropriate.

4.4 When to use the methodology

The greatest benefit of application of the methodology comes in the early-stage of a product/process development project. before the programme has focused onto a single technical route to market. This will normally be before significant resources have been committed to commercialisation. This is the point at which changes to the process(es) can be relatively easily made with minimal disruption to resource utilisation, costs or timelines.

5 Identify alternatives

5.1 General

Whenever a new product is devised, there will in most cases be several alternative ways to realise that product and its defined function in a life cycle. The Functional Unit of an LCA according to ISO 14040 and

ISO 14044 is an appropriate measure to identify alternatives. These alternatives can include the different technical means, i.e. process routes consisting of the necessary manufacturing steps from the raw materials to the finished product. End-of-life scenarios may also be included if appropriate.

Identifying the alternatives starts as a brainstorming activity, the provision of a facilitator and the use of some simple tools is recommended to develop and capture the ideas in a somewhat more detailed way to enable subsequent evaluation and the selection of the most promising option or options for further development.

The study team may agree that some alternatives are unfeasible at this stage and this finding should then be recorded together with the reason for rejection but with no further evaluation of that option. Likely reasons to reject alternatives at this stage are likely to include technical impossibility or complexity, non-existent supply for raw materials.

5.2 Product definition

If possible, compile a preliminary product specification. The study team should discuss the specific features required of the product to achieve customer acceptability? These may lead to identification of some constraints on process development. Discussion should cover the whole supply chain to the end user in case this turns up new delivery opportunities that ought to be brought within consideration.

It can also be useful to consider key raw material specifications and particularly different options for obtaining key materials.

5.3 Constraints

The process development project will face constraints limiting freedom of selection of options. Constraints may be identified arising from: business, technical, regulatory, and other practicalities. Not all constraints are necessarily real, some might be perceived rather than absolute and therefore resolvable by negotiation. The real constraints which cannot be resolved need identifying.

5.4 Describing the alternative routes for making the product

5.4.1 General

The innovation process tends to focus on the synthesis step(s) for the new product, but to have a sustainable, and commercially viable process, the whole process from raw material handling to finished product isolation and possible applications, including recycling options, needs to be considered. For assessment of sustainability, it is essential to consider the whole system, ideally from cradle to grave system boundaries. If other boundaries are considered, e.g. cradle-to-gate, the limited scope needs to be acknowledged with a correspondingly limited scope for interpretation. The cradle-to-grave boundaries ensure, that no environmental impacts are excluded and a holistic picture is generated.

For assessment of sustainability, it is essential to consider the whole system, ideally from cradle to grave needs to be considered, although other boundaries such as cradle to gate may be agreed by the study team. This covers the whole supply chain for the product and processes being assessed, thus ensuring that GHP scope 3 and scope 2 emissions to the environment are included in the assessment.

5.4.2 Representation of the process

A graphical representation of the process is preferable to a written description because it is easier for study team members to visualize the whole process and discuss it. A graphical process representation is also used as a basis for the assessment tools used in this methodology.

The most common early-stage process representation that can be used with the methodology is the block flow diagram. A block flow diagram sequential links process operation, e.g. react → filter → dry. The diagram is scale-independent but often assumes the equipment technology to be used. The process can also be represented by a Process Definition Diagram (PDD) which was first described by K. Wall *et al.* in 2001. [3] Here the focus is on the processing experience of the materials rather than the equipment the process is running within. This representation is scale and equipment/technology independent.

Whichever form of process representation is selected, the diagram needs to cover the whole process from raw material preparation through to finished product isolation.

5.4.3 Representation of the supply chain

As for the process, a graphical representation of the supply chains around the process is preferable to a written description. A simple block flow representation is sufficient capturing steps in the chain such as; manufacture, transport, store and unpack. This representation only needs to be at a sufficient level of detail to indicate differences in the upstream and downstream supply chains between process alternatives. The aim is to highlight changes in environmental impacts of alternatives and the identification of improvement potentials along supply chains. The coverage should be all relevant inputs (including energy) and outputs (product(s) and wastes).

6 Process safety screening

6.1 General

The relative risk of using materials is an important starting point to link to safety measures in the next steps of product development. A simplified risk assessment can help in early stages of developments. In later stages, safety measures can be important for further investigation. Risk information concerning the alternative routes provides a good point of comparison as part of a sustainability assessment. In the early stages of a project, a rapid, simple screening method is required (ICI, 1993). [4] As far as possible, and recognising the limited availability of data, such as calorimetry, at this point, the purpose should be to test the understanding of the process and the materials involve, particularly potential for loss of primary containment, in order to establish a preliminary basis for safe operation for all the alternatives. Process safety screening should also identify inherently safe features within a process alternative, these automatically contribute to the basis of safe operation, reducing the process safety risk. (Peeling, 2024) [5].

If no basis for safe operation can be identified, then that option requires no further assessment. An unsafe process cannot be considered a sustainable process.

A rapid method for identifying possible areas of concern for process safety can be implemented using the process representation from 5.4.2 and marking it up in two ways. Firstly, for the material hazards, and then for the potential causes for loss of primary containment. Clusters of tags on the diagram indicate materials and tasks of particular concern, requiring further assessment by the study team. Where the team can identify preventative and mitigation measures to reduce the identified risk, then a basis for safe operation exists. When it is unclear how to prevent or mitigate a risk, then the basis of safe operation is undefined.

Other risk assessments may also be appropriate at this point, especially for some industry sectors e.g. medicines manufacture where an early view on human toxicity would be valuable.

6.2 Material hazards

The most readily available and convenient source of information on many process materials is the material's Safety Data Sheet (SDS) as required by the REACH Regulations. The product and co-products might not have an SDS compiled at this stage, however the study team technical members are likely to be able to provide a likely indication of the material hazards.

On the process representation, add the relevant GHS symbols at each point where a material enters or leaves the process. For mixtures include all the relevant symbols for the materials in the mixture.

6.3 Causes of loss of primary containment

At an early-stage, it is not possible to comprehensively identify all possible process deviations leading to hazardous consequences since the all the process equipment has not yet been designed. It is however readily possible to identify possible causes for loss of primary containment (breaching the equipment containing the activities described in the process representation diagram. The list of possible root causes is quite short, making it convenient to add to the diagram alongside the relevant process activity.

Root causes leading to loss of primary containment:

- Fire and explosion: ignition of process materials;
- Physical overpressure: gas evolution, process blocked in;
- Overfilling: overflow, foaming;
- Structural failure: sudden vacuum, corrosion, erosion;
- Openings: deliberate breaches of primary containment to; add solids, take samples, discharge solids.

When looking at Figure 2 — Example of safety screening using a PDD for a segment of one possible route for production of aspirin, a study team might conclude that task 40 appears to be inherently safe. Since task 10 is a dissolution and task 30 is a chemical reaction, how to complete these tasks safely in a flammable solvent (acetic anhydride) is probably well known and understood and therefore a basis for safe operation is clear, although some further date is needed. It is unclear what the evolved gas in task 20 or how it is generated. At this point in development the basis for safe operation for the task seems unclear.

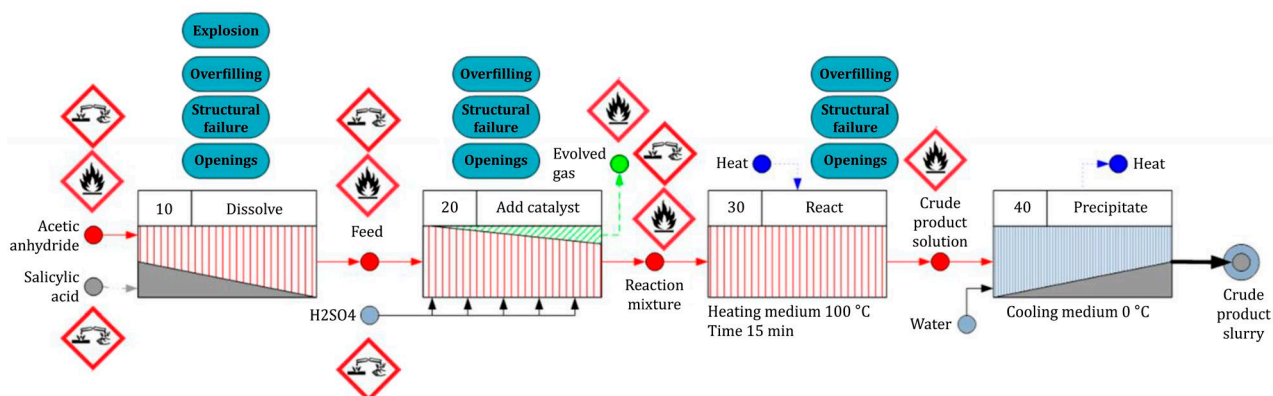


Figure 2 — Example of safety screening using a PDD for a segment of one possible route for production of aspirin

6.4 Inherent safety

Table 1 lists the principles of inherent safety. Employing the table as a guide, a study team can identify and record the features in the steps of a process route that make it more or less safe than its alternatives before the addition of any controls. The team should also record where it finds opportunities to improve an option through application of the principles. It is worth continuing the assessment on the assumption that such improvements will be implemented.

Table 1 — Principles of inherent safety

| Principle | Interpretation | How to Implement |
|---------------------------------|--|---|
| Elimination | Avoid the hazard completely | Change the process design or remove a hazardous activity to eliminate the hazardous event completely, e.g. remove storage tank from design. |
| Substitution | Reduce the hazard severity by changing nature of hazard | Replace a substance with a less hazardous material, or a processing route with one that does not involve a hazardous substance. Replace a procedure with one that presents less of a hazard. |
| Minimisation or Intensification | Reduce the hazard severity by minimising scale of hazard | Use smaller quantities of hazardous materials when the use cannot be avoided. Perform a hazardous procedure as few times as possible if the procedure is unavoidable. |
| Moderation or Attenuate | Reduce the hazard severity by changing the impact of a hazardous event | Use hazardous materials in their least hazardous forms or identify processing options that involve less severe processing conditions. |
| Simplification | Reduce the hazard likelihood by inherent features of the design | Design processes, processing equipment, and procedures to eliminate opportunities for error. Designing equipment that cannot be exposed to extreme pressure or temperature by worst case processing conditions. |

7 Sustainability screening

7.1 General

A rapid method for a study team to compare the general sustainability of the options is to agree a list of sustainability prompts covering the environmental, economic and social aspects of sustainability and apply the prompts to the process representation diagram. Applying the same prompts to the supply chain diagram may also be valuable. An example of a PDD after adding the prompts may be found in Figure 3 — PDD of a proposed process after tagging for sustainability. It is useful to add a measure of impact to the sustainability prompts ranging from positive or tolerable impact to significant negative impact. Colour coding from green to red provides a strong visual reinforcement of the impact of different options when comparing the marked-up process representations for the alternatives.

Table 2 — Specimen list of sustainability prompts

| Sustainability prompts | | |
|------------------------|----------------------------|----------------------------|
| Cost of goods | Pollution | Quality |
| Water usage | Materials usage efficiency | Social |
| Energy usage | Time to process | Globally critical resource |

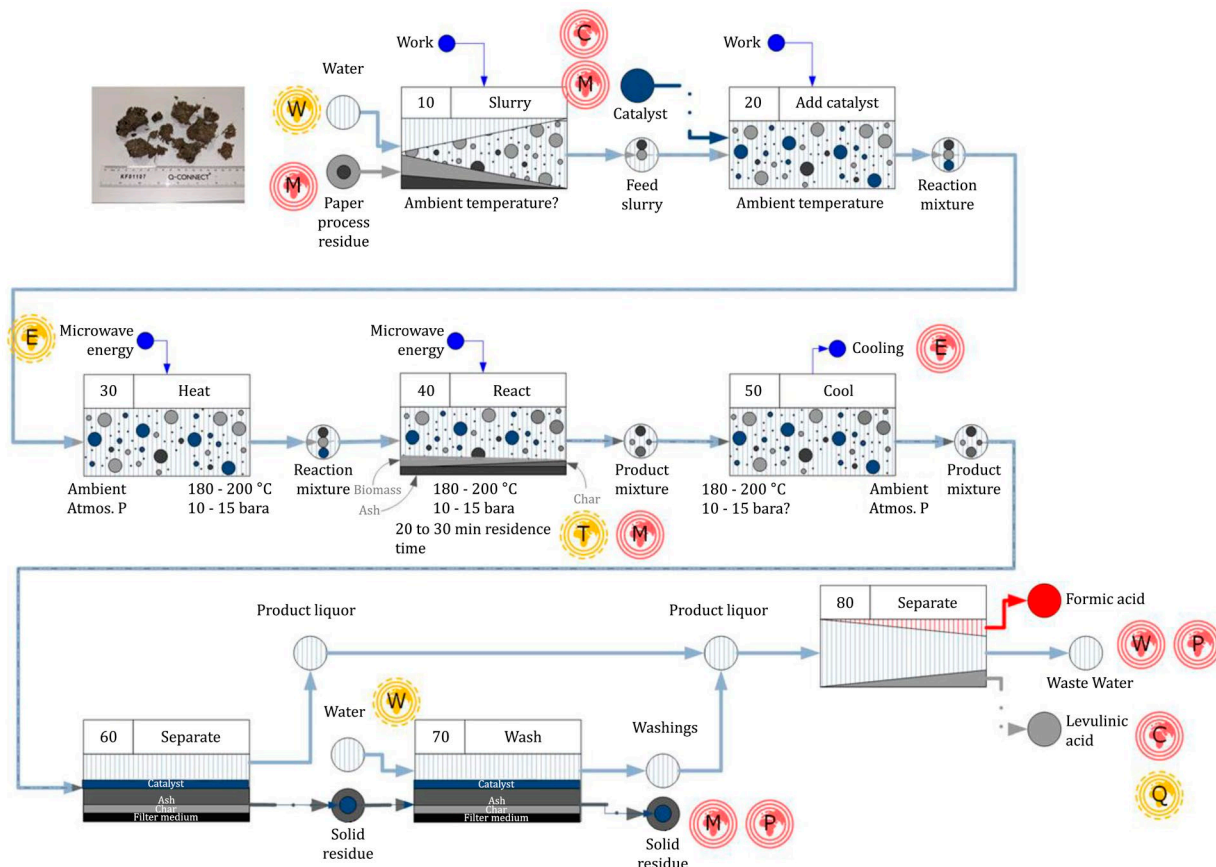


Figure 3 — PDD of a proposed process after tagging for sustainability

The study can review the process alternatives for possible improvements and re-assess as shown in the example in Figure 4 — The PDD of a proposed process in Figure 3 — PDD of a proposed process after tagging for sustainability after making improvements Where a process option has been improved in this way, it is recommended that the improved version is taken forward into the remainder of the evaluation methodology.

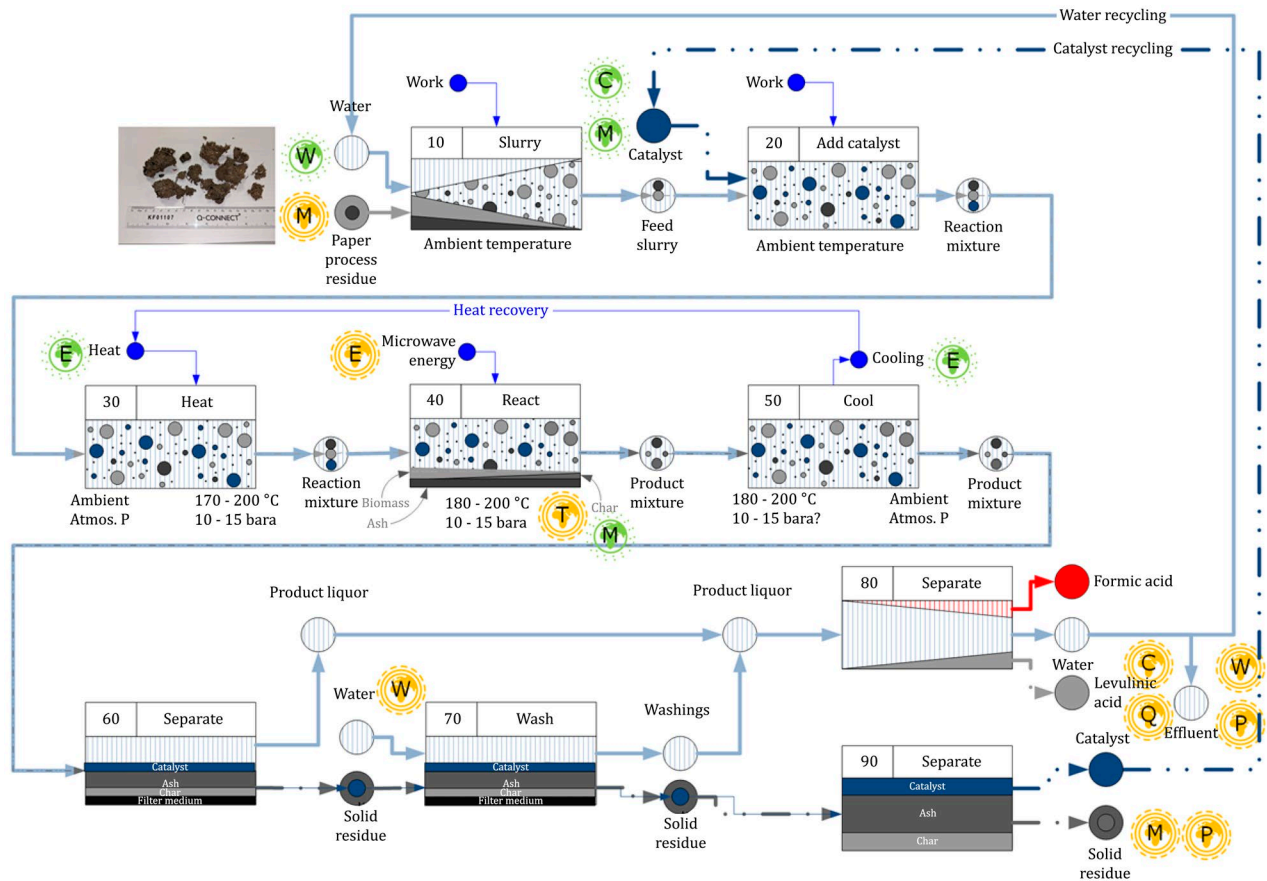


Figure 4 — The PDD of a proposed process in Figure 3 — PDD of a proposed process after tagging for sustainability after making improvements

7.2 Inherent sustainability

The ideas behind the principles of inherent safety can also be extended to sustainability, as shown in Table 3. It is recommended that using the table as a guide with the supply chain representation (see 5.4.3) to identify and capture features that are better (or worse) in one alternative rather than another. The team should also record where it finds opportunities to improve an option through application of the principles. It is worth continuing the assessment on the assumption that such improvements will be implemented.

Table 3 — Principles of inherent safety reapplied to sustainability

| Principle | Interpretation | How to Implement | Examples |
|----------------|--|--|---|
| Elimination | Remove the impact completely | Remove step and associated activities/steps completely from the chain. | Bring successive manufacturing steps together, eliminating the transport steps (incl. packaging, loading / unloading /unpackaging). |
| Substitution | Reduce the impact by changing the resources utilised | Replace globally sourced, primary minerals, and fossil fuels or derived resources with locally sourced, renewable, recycled or re-used alternatives. | |
| Minimisation | Reduce the impact by minimisation of the resources employed | Resource and material efficiency / re-use. Reduce stock. | Just-in-Time systems. Pinch technology for thermal efficiency. Use of grey water. |
| Moderation | Reduce the scale of the impact through use of more sustainable resources | Selection of materials and resources that don't have uses with a societally higher priority. | Use residues from food crops e.g. bagasse but not food crops e.g. grain to fuel alcohol |
| Segregation | Avoid mixing resources to enable more efficient use | Design separation strategies to enable higher value outlets for undesired co-products. | Segregation of drainage systems for black, grey and storm water. |
| Simplification | Reduce the impact through the features of the product. | Design for separation and recycle at end of life. | Use of simple rather than composite materials if possible |

8 Challenge energy efficiency

8.1 General

IS 399 [6] outlines an approach for Energy Efficient Design (EED). The standard advocates the use of an energy Venn diagram. The energy Venn diagram can be adapted to suit assessment at the early-stage of a process development project as shown in Figure 5.

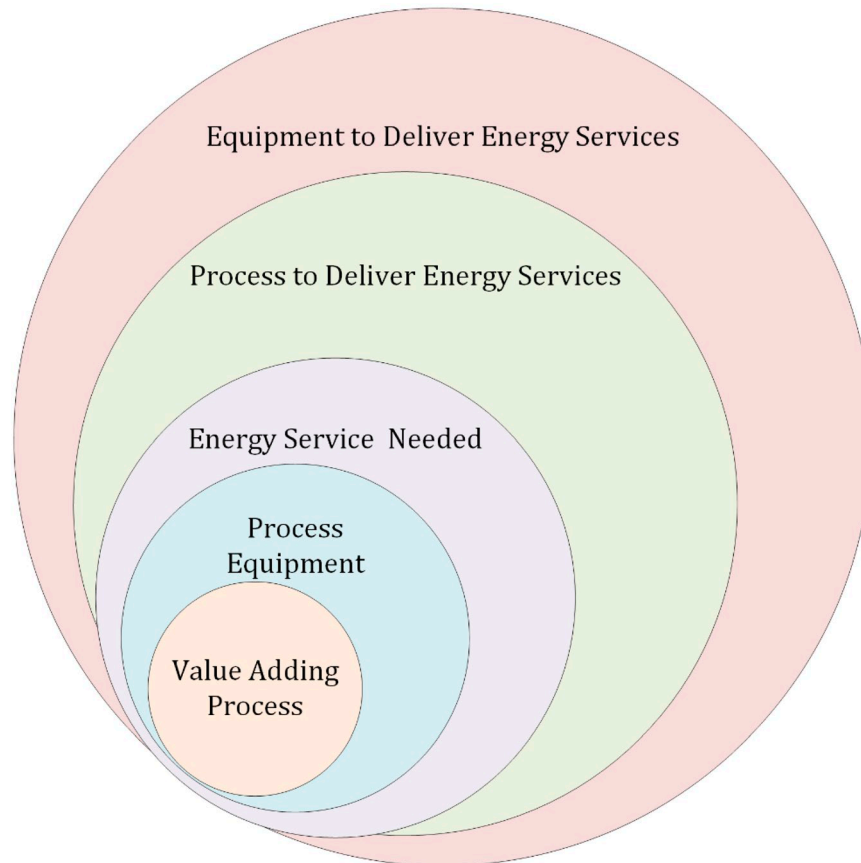


Figure 5 — Modified energy Venn diagram adapted from IS 399

8.2 Challenge and analyse energy efficiency

EED requires a study team to challenge and analyse energy efficiency guided by the energy Venn diagram (i.e. Figure 5 in this methodology). It is recommended that each layer be considered starting from the value adding process and working outwards.

For each layer, discuss the following:

- The current scenario, forming a baseline.
- Challenge the base line. Is there a way to make the process more energy efficient? The inherent principles for sustainability described earlier, have been further adapted in Table 4 for use to guide challenges.
- Analyse the challenges by identifying possible approaches towards improved energy efficiency.
- Conclude which, if any, of the proposed solutions are feasible and should be included within the alternatives taken forwards in development.

The team's responses may conveniently be recorded in tabular form.

Table 4 — Sustainability principles for challenging energy usage

| Principle | Interpretation for EED challenges |
|----------------|--|
| Elimination | Can this service be REMOVED? |
| Minimisation | Can this equipment be REPLACED with more efficient equipment? |
| Moderation | Can this energy service be SUBSTITUTED with something with a lower carbon footprint?" |
| Segregation | Can the energy required to maintain this service be REDUCED ? |
| Simplification | Can the energy rejected by the process be RECOVERED, and REPLACE a process heating service or STORED and REUSED for heating at another time/place? |

9 Challenge mass intensity

9.1 Environmental optimisation factor

The Environmental Optimisation Factor (EOF) is a semi-quantitative metric designed to support early-stage sustainability assessments by providing a structured means of comparing the environmental impact of different process conditions. It enables project teams to go beyond simple mass intensity metrics by incorporating environmental risk and exposure considerations into a single value that can be targeted for reduction during process development.

9.2 Purpose and Context

EOF is particularly valuable in the early stages of process development, where data is often limited and uncertain, but decisions must still be made regarding which process routes to prioritise and which materials to focus on reducing during optimisation. It complements broader sustainability frameworks such as FESSA by offering a focused, material-level assessment that can be embedded into digital twin simulations and used iteratively to guide process optimisation.

9.3 Calculation Method

The EOF is calculated using the following formula:

$$EOF = \frac{\text{weighted inputs and waste}}{\text{weighted product}} \quad (1)$$

$$EOF = \frac{\sum_{n=1}^{\infty} (w_n sm_n + w_n wm_n)}{w_n p} \quad (2)$$

where

EOF is the Environmental Optimisation factor (dimensionless)

w_n is the weighting applied to a process stream (dimensionless)

sm_n is the mass or mass flow of an input stream (e.g. kg or kg/h)

wm_n is the mass or mass flow of a waste stream (e.g. kg or kg/h)

p is the mass or mass flow desired product stream (e.g. kg or kg/h)

n Unique identifier for input and waste streams (dimensionless)

The weighting factor, w_n , is derived from a brief environmental risk assessment that considers the following four categories as a minimum:

- Ecotoxicity severity and likelihood (aquatic, terrestrial, persistence);
- Raw material footprint (e.g., renewability, scarcity, environmental impact of raw material extraction);
- Production footprint (e.g., energy intensity, transport).

Each of these criteria is scored on a scale (typically 1 to 5), and the scores are multiplied by the mass of the material to produce a weighted mass. It is recommended that the study team agree a scoring guide that aligns with readily available data in the early stages of process development enables project teams to rapidly assign weightings in a consistent manner. This approach allows for a more detailed understanding of environmental impact than mass alone, leading to process selection and optimisation that reduces the environmental footprint.

9.4 Application in Process Development

EOF is used to:

- Identify high-impact materials and waste streams;
- Compare alternative synthetic routes;
- Evaluate the benefits of solvent recovery and waste minimisation;
- Model the effect of degradation enzymes on waste treatment;
- The EOF can be recalculated dynamically as process changes are made, making it a powerful tool for real-time optimisation within digital twin environments.

9.5 Benefits and Limitations

As more data becomes available and environmental knowledge improves, the weighting factors used in EOF calculations can be refined, increasing the accuracy and relevance of the metric over time.

EOF provides a pragmatic balance between rigour and usability. It avoids the complexity of full Life Cycle Assessment (LCA) while still offering meaningful insights into environmental performance. However, it is not a substitute for LCA and should be seen as a screening tool to guide early decision-making and digital twin optimisation.

10 Assess technical risk

The technical risk associated with scale-up is the risk that the process option fails to deliver product at the intended rate and or quality when commissioned. A rapid method for a study team to assess the relative scale-up risk of the options is to agree a list of risk factor prompts (see Table 5) and also impacts (see Table 6). The risks and impacts should be marked against each of the process steps in the process representation diagram. An example of a PDD after adding the prompts may be found in Figure 6.

Table 5 — Specimen list of risk factor prompts

| Risk factor | Rationale |
|--|--|
| 1. Moving solids | Solids handling can always cause challenges when changing scale |
| 2. Multiple interacting phases | Rule of thumb: complexity increases with the number of interacting phases. Some physical forms are particularly challenging, especially solids (<i>e.g.</i> sticky or large particles) |
| 3. Human engagement | Any task requiring operator or other human engagement could introduce variability |
| 4. Heat/energy introduction/removal/change | Potential challenges will depend on the magnitude and rate required |
| 5. Sensitive (bio-)chemistry | Are any transformations operating in a tight window with respect to driving forces? |
| 6. Chemical incompatibility/unintended reactions/physical conditions | Impact of unintended (bio-)chemistry can increase on scale-up. Impact of physical conditions |
| 7. Extremes of specification | Is the process sensitive to the grade/source of materials used? Sterile conditions? |
| 8. Time sensitivity | Are any transformations or process materials time sensitive? |

Table 6 — Specimen list of impact factor prompts

| Aspect | Impact on... |
|---------|------------------------|
| Product | Quality |
| | Yield |
| Process | Operability |
| | Safety and environment |

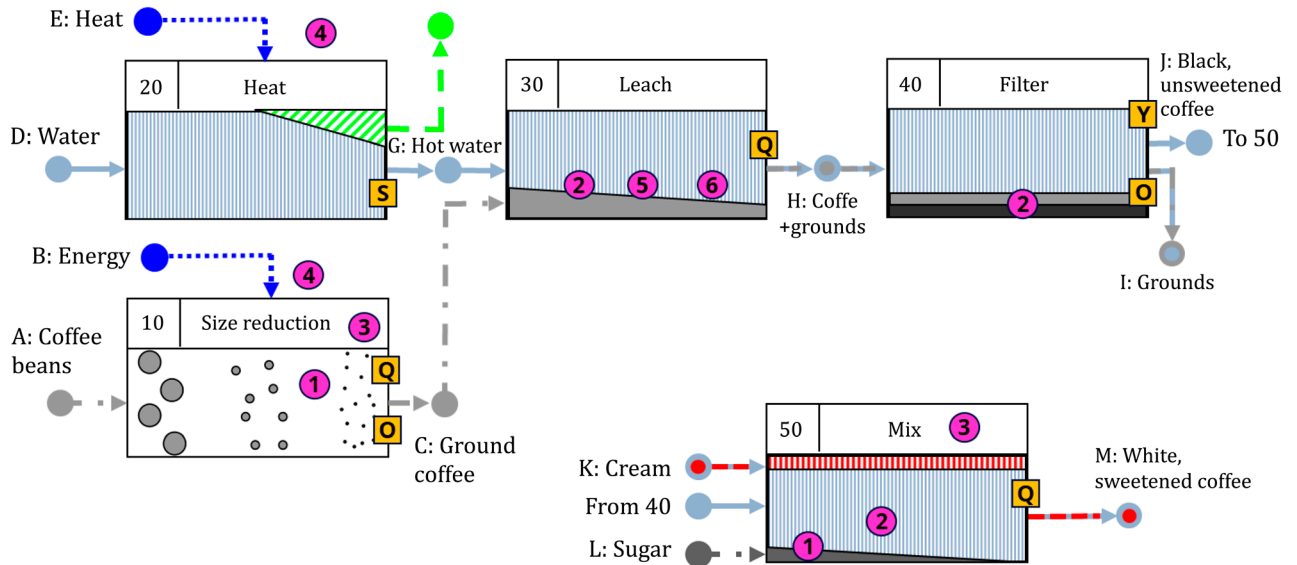


Figure 6 — PDD for making a cup of coffee, marked up with scale-up risks

11 Route selection

11.1 General

Route selection is in one sense the end goal of the Methodology described in this CWA: in practice, decisions must be made to prioritise one route (or routes) over the others. In another sense, it is the means of drawing together the threads of the intervening challenges to the alternative routes presented.

Selecting between manufacturing process options for the best alternative from a sustainability perspective is a suitable problem for Multiple-Criteria Decision Analysis (MCDA). MCDA methods generally involve numerical consideration of:

- Alternatives: the process options to be ranked or selected from (as defined in Section 5);
- Criteria: the qualities against which the alternatives are to be assessed. Sections 6 to 10 will help the project team develop relevant criteria and be prepared to comparatively score the alternatives.

Weighted-sum method MCDA (WSM-MCDA) furthermore introduces suitable weighting factors expressing the relative importance of the criteria in reaching the decision. These are incorporated in the calculation of the outcome score, which sums up the decision-making team's consensus evaluation of the alternative against the suite of criteria used.

11.2 A Framework for Early-Stage Sustainability Assessment

Selecting the best alternative from a sustainability perspective is complicated by the competing issues at play. A guidance framework can help teams to think systematically about the wide range of criteria which go into deciding whether a proposed innovation enhances sustainability or not. Such a framework, which may be readily combined with WSM-MCDA calculations to generate outcome score, has been presented (Ref 4). The two-level hierarchical framework for early-stage sustainability assessment (FESSA) provides at the top-level five main criteria covering the requirement for a sustainable manufacturing process. These are technical feasibility, the business model (including techno-economics), supply chain feasibility, environmental impact, and social impact. Technical and supply chain feasibility are included as prerequisites for a sustainable operation characterised by its economic, environmental, and social impacts. The top-level criteria are helpful for decision analysis, but each is in practice multi-faceted and

too broad in coverage to support a sufficiently focused process of consensus scoring by the decision-making team. Each top-level criterion is therefore split into several contributory sub-criteria, see Table 7.

Table 7 — Framework of Criteria for Early Stage Sustainability Assessment

| C ₁ Technical Feasibility | C ₂ Business Model | C ₃ Environmental Impact | C ₄ Supply Chain Feasibility | C ₅ Social impact |
|--|---|---|--|---|
| C ₁₁ Innovation flexibility | C ₂₁ Improves Net Present Value (NPV) | C ₃₁ Process safety | C ₄₁ Supply lead times | C ₅₁ Satisfies a societal desire, need or necessity |
| C ₁₂ Enabling technology | C ₂₂ Extends existing market share | C ₃₂ Upstream supply chain sustainable | C ₄₂ Supplier stability | C ₅₂ Impact on equality |
| C ₁₃ Will it work? | C ₂₃ Opens access to new markets | C ₃₃ Downstream supply chain sustainable | C ₄₃ Resource flexibility | C ₅₃ How many people will be economically supported? |
| C ₁₄ Does it scale? | C ₂₄ Improves time to commercialisation | C ₃₄ Supply chain for other manufacturing resources is sustainable | C ₄₄ Customer lead times | C ₅₄ Contribution to societal knowledge |
| C ₁₅ Is the product fit for purpose? | C ₂₅ Resilient to existing / new competition | C ₃₅ On-site manufacturing activities sustainable | C ₄₅ Availability of equipment, maintenance, support materials and services | C ₅₅ Job creation |
| C ₁₆ Of required purity? | C ₂₆ Product flexibility | C ₃₆ Fate of assets at end of use | C ₄₆ Routes for disposal of wastes | C ₅₆ Upskilling of workforce |
| C ₁₇ Adequately specified? | C ₂₇ Capacity flexibility | C ₃₇ Circularity | | C ₅₇ Improves working conditions |
| C ₁₈ Acceptable / manageable variability? | C ₂₈ Feedstock flexibility | C ₃₈ Location flexibility | | C ₅₈ Improves economic ecosystem |

It is important to stress the *framework* nature of the standard criteria/sub-criteria set. FESSA is intended to be used as a *guide to thinking* within the context of a facilitated discussion about a complex question at an early stage in the development cycle. Whilst the structure and content of the framework arise from experience and previous literature, and have been tested in multiple case studies, it aspires neither to be exhaustive nor mandatory. It *does* aspire to provide a pragmatic, practical set of prompts which, if followed during Route Selection, those responsible for making and documenting the decision may be reasonably confident of having considered the most encountered ways by which process innovations fail to flourish sustainably. Decisions on inclusion or exclusion of specific criteria (extending to introducing additional sub-criteria if necessary) and the weights applied to criteria, therefore are all permissible within the scope of the framework, *provided a rational justification is provided*. All such justifications

should be documented and recorded as part of the facilitated decision-making process, just as is the case with the scores allocated against each of the criteria for each of the alternatives. In totality, this provides not just a decision as output but a documented record of *the thinking behind the decision*, should it ever need to be revisited and as a basis for the development of more rigorous quantitative assessments later in the development lifecycle.

11.3 Dealing with Uncertainty

Uncertainty is largely an inevitability in early-stage decision making. Early decision making is desirable to avoid sinking time and money into projects that are doomed to fail, and to identify what further work is needed for projects with a future. The earlier one seeks to decide however, the harder it can be to obtain firm evidence (e.g. conclusive experimental data, fully validated costings, or life cycle impacts) upon which the decision is to be based. Such uncertainties can be accommodated within the decision making process and calculations as long as they are acknowledged by the decision makers.

Decisions must be made upon the evidence that is available combined with the *informed judgement* of those with knowledge of the system under consideration. This is best approached as a facilitated, team-based activity where assertions, assumptions and interpolations or extrapolations from the limited data can be tested and challenged. A sound decision-making process needs a suitable computational method for turning this complex qualitative and semi-quantitative assessment into a clear output indicator of potential success or failure for the options under consideration.

11.4 Calculation of decision outcome scores, probabilities, and limits

Many well-established models are available in the MCDA decision making literature for turning input criterion-based preference information into output priority indicators of one kind or another. As well as various WSM-MCDA methods, other approaches employed include multiple pair-wise comparisons, and outranking methods for classification/elimination of alternatives. Provided a method can handle multiple alternatives and criteria, in the context of early decision making the choice of algorithm is not critical provided it can handle the uncertainty in the inputs described in the Section 11.3 and reflect that uncertainty in the output scoring. Suitable WSM-MCDA methods that meet this criterion include Multi-Attribute Range Evaluations (MARE) (Hodgett et al., 2014) [7], Simulated Uncertainty Range Evaluations (SURE) (Hodgett & Siraj, 2019) [8], and Computed Uncertainty Range Evaluations (CURE) (Henderson & Peeling 2024). [9]

All of these last three methods use the same input model of three consensus-based estimates per alternative for each criterion evaluated: the minimum (a), the maximum (b), and the most likely (c) scores. All criteria should be expressed in terms where a maximum is desirable, or if a minimizing criterion is used the corresponding decision variable is inverted before use in calculations. If there is no uncertainty about a given score, this can be handled readily by inputting identical values for a, b, and c. The scores comprise a triangular distribution where a and b have a probability density of zero and c has probability density $\frac{2}{b-a}$. The scores are then normalised for each criterion relative to the maximum

value across all the alternatives, by max scale normalisation (Chakraborty and Yeh). [10] A useful consequence of normalisation is that decision makers can mix objective, quantified scores with numerically expressed but qualitative, subjective judgements within the overall decision structure.

The MARE algorithm simply applies the criterion weights to the normalised values and sums $w_j a_j^*$, $w_j b_j^*$ and $w_j c_j^*$ for the j criteria to produce the minima, maxima and most likely outcome values for each of the i alternatives. SURE utilises simulations based upon triangular distributions to create a plot which visualises the preferences and overlapping uncertainties of decision alternatives. Instead of independently calculating single values for the minimum, most likely and maximum for each alternative, random deviates are generated based upon triangular distributions and the results presented using a kernel density plot. CURE uses a computationally lighter approximation method (based upon the

application of Central-Limit Theorem) to generate Gaussian (Normal) output probability density plots. The standard properties of the Normal distribution can be used to define both likely boundaries upon outcome scores for a given alternative, and to detect whether differences in the outcomes are significant or not given the uncertainty in the inputs. Full details may be found in (Henderson & Peeling, 2024). Figure 7 and Figure 8 show examples of equivalent MARE / CURE outcome score limits and CURE probability distribution outputs for the same decision-making scenario.

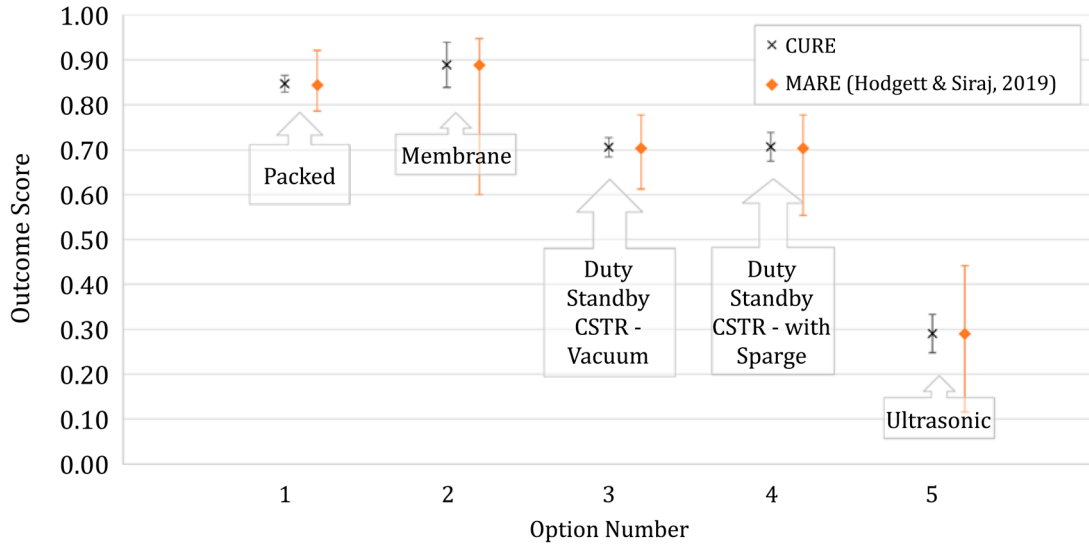


Figure 7 — Equivalent MARE and CURE output (Equipment Selection example described in Hodgett and Siraj (2019))

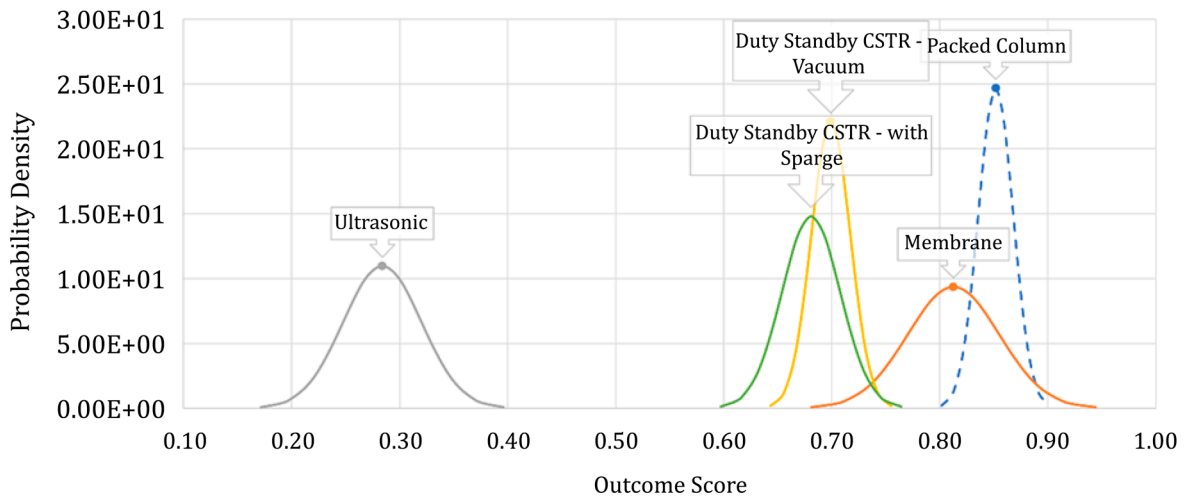


Figure 8 — CURE probability density distributions (Equipment Selection - example described in Hodgett and Siraj (2019))

Figure 9 illustrates how the additive contributions of the top level FESSA framework criteria to the outcome decision scores may be usefully graphically represented along with the uncertainty in the outcomes (computed using CURE) for a different decision-making scenario.

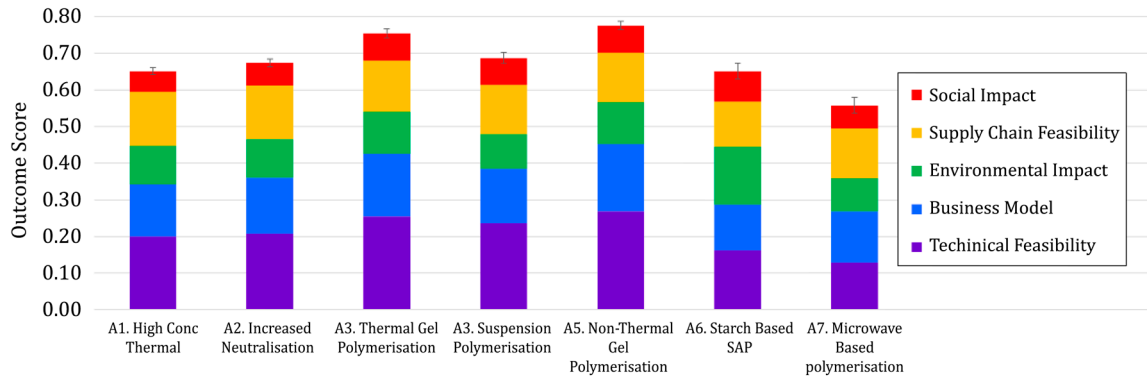


Figure 9 — Contributions to FESSA-based outcome scores (Superabsorbent polymerisation example described in Henderson & Peeling 2024)

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