Conceptual and practical approaches to improve the utility of SSbD assessments

Preliminary insights from SETAC-EC online Consultations and an on-site Workshop in Seville, May 6, 2024

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Executive summary

This report summarizes the priority insights gained from the three-step consultation process on *Safe and Sustainable by Design* (SSbD) resulting from a collaboration between SETAC Europe and the European Commission's Directorate-General for Research & Innovation (DG RTD). The overall consultation was undertaken to mobilize the membership of SETAC to contribute scientifically to the development, implementation, and optimal utility of the *Safe and Sustainable by Design* (SSbD) concept and framework, to advance the goals of the European Green Deal *Chemicals Strategy for Sustainability* (CSS).

The first consultation step collated science-based ideas for improving SSbD in an online event formatted as a SETAC-Café. A second consultation step expanded on that with a provisional roadmapping activity, using the same format, the third and final step in this consultation series was an on-site workshop, held on May 6, 2024 during the 34th SETAC Europe Annual Meeting in Seville, Spain.

This report provides a preliminary overview of priority ideas and points of attention, extracted from the three events (with emphasis on the on-site workshop).

Disclaimer

As a disclaimer, we emphasize that the present report is a preliminary summary of results and impressions, which may be refined in the final report. Furthermore, the final report will also provide a detailed compilation of the findings.

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1 Introduction

1.1 Societal problem definition

The use of chemicals and the relevance of the chemical sector for our society is of key importance, but it also poses challenges concerning safety and sustainability as does any human activity (eg deep sea mining). In 2020, the European Union published the *Chemicals Strategy for Sustainability* (CSS), which sets out to address these challenges. One of the key advances of the CSS is the idea of applying a *"Safe and Sustainable by Design"* (SSbD) approach in Research and Innovation – such that new chemicals and products are intrinsically designed to be safe and sustainable.

1.2 Scientific challenge

The concept of SSbD is highly innovative in general. The chemical sector is taking the lead in this development. As is commonly the case for innovative concepts, strong efforts are needed to operationalize it. Specifically, the approach asks for science-based, valid concepts, models and data that allow characterization of the aforementioned safety and sustainability aspects, preferably in a quantitative manner and even under the data-poor conditions that are typical for early-stage innovation steps. This presents a wide array of challenges to science and practice. SETAC uses the slogan "Environmental Quality through Science" to convey its vision and there is a plethora of relevant expertise within the society's membership to address this challenge.

As organizers of the SETAC-EC consultation process, we (originally the SETAC Sounding Board for the European Commission High Level Roundtable for the Implementation for the CSS), in consultation with the policy experts from the European Commission (DG Research and Innovation [DG RTD] and Joint Research Centre [JRC]), set out to consider, which conceptual methods, practical tools and datasets could be developed and made available for use in SSbD assessments to improve the scientific basis for, and utility of, that concept.

1.3 Aims

The report aims to provide a preliminary overview of priority ideas and suggestions that may help to enhance the scientific basis and efficacy of methods in the SSbD context. Following on from this preliminary report, a more detailed final report will be generated that will compile all the ideas and suggestions generated during the two online consultation events and the on-site workshop.

1.4 Reading guide

The various Chapters described the following results:

- Chapter 2, entitled "Overarching ideas and suggestions for improvements" describes the preliminary overview of results from the SSbD consultation series.
- Chapter 3, entitled "Roadmapping of ideas" presents a preliminary roadmap example, as an illustration of the preferred approach to summarizing the consultation results. The roadmap-approach has been used to generate scientific inputs during the consultation process, starting from aspirational goals that would optimize the scientific basis and utility of SSbD, and is useful for prioritizing the research needs and planning research phases and steps.
- Chapter 4, titled "Discussion, Outlook and Recommendations" describes, in a concise manner, the discussion of the results, with an outlook to future steps and associated recommendations.
- Appendix 2 describes the impressions that were summarized by the Organizing Committee, as basis for Chapters 2 and 3.
- Appendix 3 describes the preliminary roadmaps as they were created during the workshop in Seville.

2 Overarching ideas and suggestions for improvements

2.1 Contents of this section

This section presents a narrative overview of the priority ideas and suggestions, based on inputs collected by the Organizing Committee. The original notes on which this Chapter is based are collated in Appendix 2 and 3 of this report and in the two preliminary reports from the online consultation events. This overview is preliminary, as extensive analysis of the inputs of both on-line consultations and the on-site workshop may provide further insights and details.

2.2 SSbD in a wider context

Ideas proposed in the consultation process show that there is latitude to transfer the SSbD concept and framework to a wider array of opportunities. That would improve the effective use of available scientific insights, as well as the efficacy of eventual policies and practices.

As an example of the initial stages of an innovation process, the consultation yielded the input by utilizing Nature-Based Solution (NBS) approaches as a basis to consider specific functions in the innovation process when searching for novel molecules. NBS embodies an array of theoretical and practical approaches and case studies, based on which initial SSbD-oriented innovations may be started. Nevertheless, while NBS and SSbD have many things in common, they are formally separated entities that are, so far, not logically tied together.

As an example of how the consultation process could impact the outcomes of SSbD, it was suggested to design SSbD approaches, models, data, and output parameters such that they can be further interpreted in metrics that are relevant e.g. Environment, Social, and Governance (ESG)-reporting of companies in the framework of the *Corporate Sustainability Reporting Directive*.

As a further outlook, related to the idea of potential Green Swan trajectories (Elkington, 2020 and Posthuma et al, 2024) that were also generated in the context of the consultations the final output of SSbD-assessment could be designed such that they can also be used in an approach that embodies a drive towards continuous improvement (such as e.g. *x%* improvement on SSbD-metrics in *y* years), which can translate into *ambition goals* for separate companies, for product categories, or for the economy as a whole.

The consultations have shown here that there is latitude to consider how development of the SSbD-framework, and development of its necessary approaches, models, data, tools, and output metrics, can be linked to other contexts. It is recommended to explore such opportunities further, both in regulation and science. The final report will provide some examples for further consideration.

2.3 Considering aspirational goals as a method to improve SSbD

The Cambridge University method of roadmapping defined by (Phaal et al. 2011) starts with an initial question, being: "*What is the aspired goal to be reached?*". With SSbD itself being an aspirational goal within the CSS, the key question is whether there are specified goals that – if solved – would solve specific practical problems for implementing SSbD.

The general impression of using this roadmapping approach is that it has previously been shown to uncover good ideas and initiatives. These principles have resulted in three formats and types of results:

1. Oriented towards useful outputs that relate to the next regulatory phase: It is considered key to start with defining a user-oriented dashboard, with e.g. 'traffic-light' summary-

result outputs, in which the outcomes of an SSbD-assessment are summarized, for the end-results as well as intermediate results for earlier stages of innovation. By contemplating key outputs, one can start formulating, (i) which outcomes are to be presented and how, and (ii) how end-results of an SSbD process would relate to and provide information for the regulatory context that will apply when a novel chemical is to be evaluated for market entry.

2. Oriented at steering SSbD-relevant research and SSbD parameters: Common research programs often progress from the current situation to deliver novel scientific insights – but those may not be relevant for or applicable in SSbD assessments. *Vice versa*, by considering what is exactly meant e.g. biodiversity impacts of chemicals, and defining key impact types to be prevented, one can define and steer SSbD-relevant research. Or: accounting for the insights from the Planetary Boundaries framework, and how that framework needs to be translated into boundaries for safety and sustainability in the SSbD context. Application-oriented research can be planned to be both relevant (for SSbD impact categories being most relevant and valued) and operational, in various stages of innovation (tools and tiers).

3. The priority aims derived under point 2 would help to drive the development, operationalization and organization of pertinent approaches, models, and data (collection, harmonization, FAIR re-use, etc.), and at the same time avoid collating approaches, models and data that are less relevant for operational SSbD.

2.4 Innovation stages, tiering and weighting

The application of scientific principles in safety assessment has, so far, resulted in (amongst other things) the development and adoption of a principle of tiering (Figure 2). Tiering is a very common principle in the assessment of chemical risks, where simpler and more conservative techniques are used in earlier stages of assessments to e.g. deselect the worst compounds from an array of compounds.

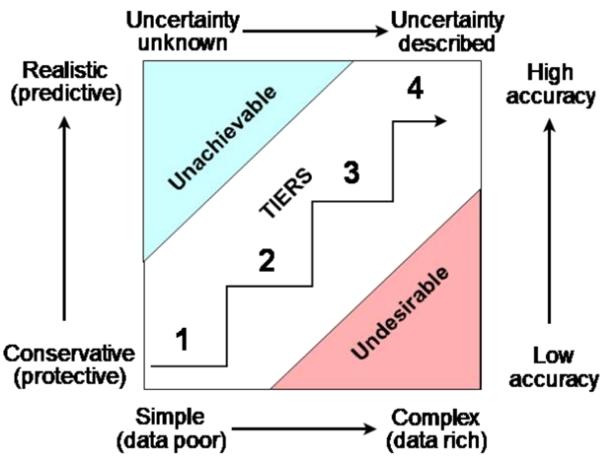

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Figure 1. Principle of tiering in the applied environmental sciences. Adapted from Solomon et al. (2005).

The principles of tiering relate closely to the SSbD-practice, where innovation processes follow a stepwise stage-gate approach across the various technological readiness levels (TRLs). In turn, the tiering and innovation-TRLs represent some typical problems, recognized during the consultations. The following main subjects were identified:

1. Bridging data-poor conditions:
Early-stage innovation steps are commonly data poor, and science can deliver approaches to bridge data gaps – consider, for example, specific suggestions about new

approach methodologies (NAMs) and machine learning/ artificial intelligence (ML/AI) methods. See Appendix 1 for the role that NAMs can play in the prediction of complex endpoints. In addition a non-comprehensive, illustrative list of well-developed *in silico* NAM models is provided, for use in hazard assessment, risk assessment and LCA with associated software currently available either as freeware or commercially. It should be noted that the amount of commercial software available vastly outweighs the freeware. This indicates that recommendation of commercial software by the Regulatory Authorities should not be dismissed. While the use of commercial software implies proprietary information and may hamper the ability to externally validate it, this challenge could be overcome by the application of a mandated third party overseeing software in a similar way to that of laboratory accreditation for Good Laboratory Practice.

2. Early-stage identification of dominant impact categories:
   SSbD can cover many safety and sustainability metrics, related to the two major safety considerations (human and environmental health) and the various impact categories that are scored regarding sustainability (e.g., 16 potential categories of the Product Environmental Footprint). It was mentioned that a relatively low number of impact categories dominate the set of footprints that can be derived and that there is (thus) a need to develop and implement scientific methods by which one can recognize dominant impact categories relevant for the SSbD-assessment at hand.

3. Tier-related simplification of available models and approaches:
   In various cases, methods for relatively precise approaches to make a safety or sustainability assessment are available, but they can be too expensive or complicated or data-demanding for the early stages of innovation. For such cases, it is recommended to identify those approaches and carry out the necessary research to define a responsible simplification, that is: a simplification that is in line with the principles of tiering. In turn, that means that truly worst-performing compounds are de-selected first, even when employing the simplified, lower-tier approaches for their judgment.

4. Absolute versus relative interpretations:
   In various ways, contributors suggested ideas that boil down to an incremental process, in which (apart from optional reasons relating to assessments defined by planetary boundary considerations) outcomes are used incrementally, instead of an ‘all or nothing’ type of approach.

5. Weighting, per stage and final:
   The consultations put specific emphasis on weighting as a key subject to be developed further, given the multi-dimensionality of interim- and final outputs. Given the principles of tiering, one must be able to evaluate stage-gate-specific outcomes of multiple candidate chemicals for a function, to select the one(s) that proceed(s) to the next TRL stage. The field of Life Cycle Assessment (LCA) has developed and implemented various methodologies of weighting, to move from mid- to endpoint-level outcomes. However, there are more weighting techniques, such as swing weighting. In combination with one of the earlier mentioned points, it may be feasible to develop weighting such that outcomes can serve in designing a Green Swan trajectory of improvement.

At the end of the day, the aspired goal here would be, that available science–and when needed: novel science–are formatted as a series of logically tiered tools, that can be employed onwards from early-stage innovation to selecting the potential final SSbD candidate molecule for a function (which is then further evaluated in the pertinent regulatory framework, if applicable).

Earlier stages can likely profit most from e.g. NAMs and ML/AI, even if the final (regulatory) stage is not (yet) ready to implement those.

2.5 Data, missing data and bridging data gaps

During the entire consultation process, the scientists who contributed to the process highlighted problems relating to data:

1. Data lack, especially in early stages of innovation,
2. Data are difficult to obtain, collate and analyze,
3. Data re-use is not facilitated,
4. Data-poor chemicals, however much potential they have, are at risk of being penalized for being data-poor.

Across the board, the solutions to these problems are process-related (organizing that data are FAIR-ly available, and that they can be easily combined and re-used), which is not further addressed here, beyond the need for an open database allowing all access to peruse for acquisition of data which has already been generated. Opportunities to bridge data gaps via ML/AI methods were numerously mentioned.

Another useful tool proposed was an inventory methodically maintained up-to-date by an objective, scientific third party (e.g., JRC) of the latest methods, NAMs (*in vitro* and *in silico*) and tools, together with their applicability domains such that all stakeholders can verify the current options available when they generate new data.

Attendees also suggested ideas on how ML/AI applications could be used to bridge data gaps and were partially found to be under development, such as for safety assessments and ecotoxicological impacts. Those ideas were far less developed for sustainability assessment practices, but this was not seen as unfeasible but as a stimulus for development.

2.6 Process aspects

The consultation provided not only conceptual ideas, but also experience and practice related ideas on process optimization. The ideas originate from experiences gained in e.g. ring-testing novel test protocols for chemical safety assessment, in that such ring tests help to evaluate whether one approach can be consistently implemented in different laboratories and by different stakeholders. Ideally, ring-tests yield similar insights for the same problem across the ring test, or it shows where the methodology can and needs to be improved.

The consultation provided some ideas, such as:

1. Organizing an ecosystem in which co-creation can thrive, and in which data can be shared, SSbD-practices can be improved, and communication and education are key elements.
2. The need to develop a common language and principles for safety and sustainability assessments and teach/train those from a novice-student to an experienced-practitioner levels.
3. The need for simplification, which can be embodied (upon practice-oriented research) into tiering, tools-per-tier, clear weighting, dashboard-presentation of summary results (and suggested next steps).

2.7 Educational skills and training aspects

A topic frequently highlighted in the consultation process was the need for further integration of safety and risk assessment expertise with LCA expertise. It was even suggested to develop Master and PhD programs across Europe to ensure that there are enough people trained as experts in these integrated fields.

It was further proposed that these new programs should incorporate training on general principles, skills, and best practices for informed decision-making within their syllabuses. The aspirational goal here is to achieve the application of SSbD principles in the innovation process with informed decision-making and clear trade-off evaluations, ensuring that socio-economic considerations are included in SSbD assessments as well. Training should be provided at all levels and special attention should be made to training courses for SMEs which are often lacking the regulatory staff and are only partially aware of their obligations.

More generally, the consultation process recognized that there is a need for more clarity on terminology in the SSbD space. Roundtables and interactive workshops can help to improve the understanding of these terminologies. Terms have different meanings in different disciplines, which is a key issue for interdisciplinary working, which will be required to fully address the challenges of SSbD. For example, there is no common understanding of the term sustainability (the term is used in an economic, a social and environmental context and means different things in different disciplines). SSbD thinking needs to become integrated and mainstream not only for chemistry, material sciences, and environmental and human health studies but also among current professionals, so that it becomes a 'natural approach' for the next generation of environmental science professionals in the broadest sense.

2.8 Equity, Diversity and Inclusion considerations

During the on-site workshop, it was inferred that equity, diversity, and inclusion (EDI) should be an integral criterion for the SSbD framework. Chemicals should be equally safe for everyone, irrespective of ancestry or sex-gender identity, and irrespective of socio-economic and/or culturally different exposures.

2.9 Longer-term considerations

The consultation process showed that scientists were willing to engage in the process, to support and help drive SSbD forward, and they also had a desire to continue that engagement. Various ideas were suggested, including establishing a SETAC SSbD Affinity Group (a forum for engagement), which might explore improving the SSbD framework, its elements and/or its utility.

Despite the involvement of many scientists in the consultation process, participation at the 34th SETAC Europe Annual Meeting highlighted that there are other methods to evaluate how science can improve SSbD. During the Annual Meeting, it was clear that many platform presentations and posters embodied research that could fit the three SSbD research tracks, but these researchers were not present at the SETAC-EC SSbD consultations, and thus could be unaware of the potential utility of their work for improving SSbD. For example, it was mentioned by one of the participants that quantitative studies in green chemistry generated results that may be translated into 'rules of thumb' for safe chemical design, by providing limit-values beyond which a chemical can cause some specific type of harm. Rather than a calculation tool, 'rules of thumb'-type approaches may embody a method for early innovation stages. By evaluating the Annual Meeting abstracts book it is very likely that many more examples could be identified with an eye towards identification of potential candidate methodologies for SSbD improvement.

3 Roadmapping of ideas

The three-step consultation process has generated many ideas, highly different in nature, categorization and completeness. That is, some ideas have been voiced as an aspirational goal, and an associated (current) problem, but not (yet) with concrete ideas to make research- or practical steps to solve those.

The body of ideas can – for practical planning purposes – be formatted as roadmaps, after identification of the following implementation-related categories:

1. Category 1 includes ideas for which both the concepts and the tools exist, but that are not (yet) linked to the SSbD framework. The task here is to make that link, which could lead to their swift adoption and use for SSbD assessments.

2. Category 2 includes ideas for which either the concepts or the tools exist, so that linkage to and use in the context of the SSbD framework asks for scientific or practical development (of concept or tool) and then linking to the SSbD framework.

3. Category 3 includes ideas for which novel developments of both scientific and practical aspects are needed, followed by a link to the SSbD framework.

In this preliminary report, the results of all three consultation events have not yet undergone a detailed evaluation. Therefore, this is just an impression, and without further explanation, the results of one breakout group have been collated as provisional roadmap-steps, which include the aforementioned categorization. The results shown in Figure 2 are only an illustration.

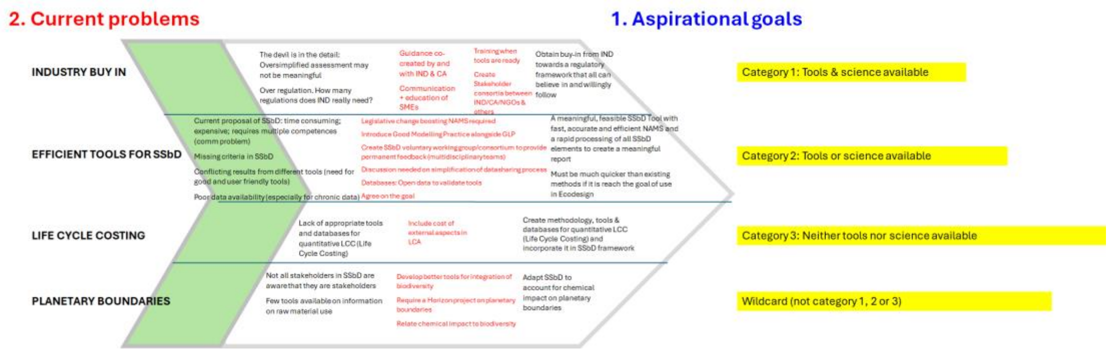

Figure 2. Illustration of an early-stage summary of the proposed science-based ideas to improve SSbD, from one of the breakout groups at the Seville workshop to illustrate how ideas on SSbDs can be put in a roadmapping context.

4 Discussion, Outlook and Recommendations

This preliminary report provides a first-look at the workshop data to identify potential priority ideas to improve SSbD. The Organizing Committee fully appreciates that an in-depth analysis and a detailed report exploring all the generated data will provide a more robust synthesis. However, we are also aware of the SSbD evaluation timeframe, and we hope that the data in this timely preliminary report will feed into the gap analysis for the 2025 Horizon Europe Work Programmes. Further data synthesis will be undertaken and a final report, which collates the entire consultation series, will be produced in due course.

Within SETAC, establishing an SSbD Affinity Group will allow for continued engagement with the membership on these topics. Similarly, for the past 5 years, Special Sessions have been held at the SETAC Europe Annual Meetings on topics related to CSS and SSbD, and these sessions will continue to engage the membership in discussions on these important topics. This would also provide and opportunity for different Horizon projects related to SSbD to become aware of eachother and be introduced to eachother.

We recommend that the scientific community is continuously challenged and encouraged to contribute to SSbD-improvements, as SSbD is a concept that has ample latitude to develop into a Green Swan trajectory (*sensu* Elkington, 2020) – if implemented with optimal methods, tools, data and associated policies and practices.

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Appendices

Appendix 1

Prediction of complex endpoints *via* New Approach Methodologies (NAMs):

SSbD is designed to evaluate chemical safety by employing ‘gold-standard’ hazard data. However, SSbD cannot make use of such data in early-stage innovation processes, if the following points are not taken into account:

1) The only way to assess relative safety of multiple substances effectively in SSbD assessments will be to use NAMs rather than the standard experimental *in vivo* methodologies classically recommended in the REACH Annexes VII to X;

2) Basing the comparison on the acute effects of these substances only does not take into account the potential for long- term effects. This may lead to unfortunate substitution choices being made. Thus, there is a specific need to develop and validate (and eventually achieve regulatory acceptance) of high-performance NAMs that enable the identification of chronic (long- term exposure) hazards;

3) Owing to the high accuracy of QSAR methodological approaches, it has become possible to determine QSAR-based quantitative endpoint effect values that are the same as would be expected in experimental studies. In some cases, QSAR approaches can even predict effects that cannot be assessed in experimental procedures due to the difficult-to-test properties of the test substance;

4) Thanks to *in vitro* technologies (including both the ones for Human and Environmental health assessment), NAMs can be used to inform on potential effects and even completely replace studies run on animal models;

5) Due to developments being made in the *in silico* and *in vitro* fields, it is now possible to use NAMs to indicate mechanistic impacts of substances based on structural alerts at different cellular levels;

6) Good Modeling Practice needs to be developed in addition to Good Laboratory Practice.

For all the above reasons, provision of appropriate research funding opportunities will be essential to accelerate the development of new NAMs to evaluate long-term effects, being key for SSbD practices. See the table below for an overview of NAM models currently available as freeware or commercially for hazard assessment, risk assessment, and life cycle assessment.

Table with non-comprehensive, illustrative list of well-developed *in silico* NAMs for hazard assessment, risk assessment and LCA and software currently available either as freeware or commercially.

Software name	Main endpoints covered (SARs, QSARs, 3D etc)	Commercial/ freeware	Link
HAZARD ASSESSMENT			
ACD/Labs	***Structural*** **HH : Acute toxicity (LD50), ED, Mutagenicity, Eye & Skin irritation ENV: LogP, acute toxicity to fish and daphnids**	**Commercial**	**https://www.acdlabs.com/products/percepta-platform/tox-suite/**
AMBIT	***DB*** **& models HH: repeated dose, DART ENV: BCF/Bioaccumulation**	**Freeware**	**https://cefic-lri.org/toolbox/ambit/**
CASE Ultra	***Statistical*** **HH : Mutagenicity, Genotoxicity, Carcinogenicity, Skin sensitisation, Acute toxicity, ED, DART…**	**Commercial**	**https://multicase.com/case-ultra**
ChemTunes	***Structural*** **HH: DART, Genetic toxicity, Carcinogenicity, dermal toxicity, bioavailability etc**	**Commercial**	**https://mn-am.com/products/chemtunestoxgps/**

Danish QSAR Toolbox	***Structural*** **SARs & QSARs for hazard assessment**	**Freeware**	**https://qsar.food.dtu.dk/**
DEREK NEXUS	***Mechanistic*** **HH : Mutagenicity, Carcinogenicity, Skin sensitisation**	**Commercial**	**https://www.lhasalimited.org/solutions/skin-sensitisation-assessment/**
ECOSAR	***Structural*** **ENV : acute & chronic toxicity to fish, daphnids and algae**	**Freeware**	**https://www.epa.gov/tsca-screening-tools/download-epi-suitetm-estimation-program-interface-v411**
EPIWIN	***Structural*** **ENV : logP, Water solubility, VP, Biodegradation, aborption…**	**Freeware**	**https://www.epa.gov/tsca-screening-tools/download-epi-suitetm-estimation-program-interface-v411**
iSafeRat® Desktop	***Mechanistic*** **(MechoA SAR): ENV: water solubility, VP, logP, Acute & chronic ecotoxicity (fish, daphnids, algae, ASRIT (Activated Sludge Respiration Inhibition Test)), BCF, Biodegradation HH: Skin & eye irritation, skin sensitisation**	**Commercial**	**https://www.kreatis.eu/isaferat_page**
iSafeRat® ED	***Mechanistic*** **ED EATS QSAR and 3D models**	**Commercial**	**http://www.kreatis.eu/**

KATE	***Structural*** **ENV : acute & chronic fish, daphnids and algae**	**Freeware**	**KAshinhou Tool for Ecotoxicity, Ecotoxicity prediction system (nies.go.jp)**
Leadscope	***Statistical*** **HH: Genetic toxicity, Rodent carcinogenicity, DART, neurotoxicity, acute toxicity, skin sensitisation…**	**Commercial**	**Instem - Computational Toxicology**
META Ultra	***Statistical*** **HH : Metabolite formation**	**Commercial**	**META Ultra - MultiCASE**
Meteor Nexus	***Structural*** **Metabolite ID**	**Commercial**	**Metabolite Identification And Analysis | Lhasa Limited**
OASIS Catalogic	***Structural*** **ENV: Biodegradation, BCF, metabolism, acute fish, (cerio)daphnid, algae, microtox**	**Commercial**	**Software (oasis-lmc.org)**
OASIS Times	***Structural*** **HH: AMES mutagenicity, metabolic similarity**	**Commercial**	**Software (oasis-lmc.org)**
OECD Toolbox	***DB*** **containing multiple HH and ENV endpoints (also includes other models e.g. Danish TB & Toxtree)**	**Freeware**	**About ⬣ QSAR Toolbox**

OPERA	***Structural/atomic/KNN*** **HH: PBK parameters ENV : BCF, Biodegradation, soil adsorption**	**Freeware**	**OPERA (nih.gov)**
Sarah Nexus	***Structural*** **HH : Statistical : Mutagenicity**	**Commercial**	**In Silico Mutagenicity Assessment | Lhasa Limited**
TEST	***4 models (statistical/mechanistic)*** **HH : Acute oral rat, Developmental, Mutagenicity ENV : Acute fish and daphnids + protozoa**	**Freeware**	**Toxicity Estimation Software Tool (TEST) | US EPA**
Toxtree	***Structural/Mechanistic*** **SARs for environment and HH Cramer classifications**	**Freeware**	**Toxtree – Toxtree - Toxic Hazard Estimation by decision tree approach (sourceforge.net)**
VEGA	***Structural/ Statistical/AI*** **ENV : Biodegradation, BCF, acute & chronic fish, daphnids & algae**	**Freeware**	**VEGA QSAR – VEGA HUB…**
RISK ASSESSMENT			
CHESAR	**-**	**Freeware**	**Included in IUCLID**
ECETOC TRA	**-**		**Targeted Risk Assessment (TRA) - ECETOC**

LCA Models			
Simapro		**Commercial**	**https://simapro.com/**
GaBi		**Commercial**	**https://www.thinkstep.com/products/gabi-software**
One Click LCA		**Commercial**	**https://www.oneclicklca.com/**
Open LCA		**Free**	**https://www.openlca.org/openlca/**
Ecochain Mobius	**PEF/LCA**	**Commercial**	**https://ecochain.com/mobius/**
Umberto	**LCA/LCC**	**Commercial**	**https://www.ifu.com/umberto/lca-software/**
SolidWorks Sustainability	**LCA/LCC**	**Commercial**	**https://www.solidworks.com/product/sustainability**
Sphera Gabi	**LCA/LCC**	**Commercial**	**Life Cycle Assessment Software and Data | Sphera (GaBi)**
LCA Databases			
Ecoinvent	**Database**	**Commercial**	**Database - ecoinvent**
openLCA Nexus	**Database list**	**Free/ Commercial**	**openLCA Nexus: The source for LCA data sets**
GaBi	**Database**	**Partly free/ Commercial**	**GaBi Databases | GHG Protocol**
PEF	**Database**	**Free**	**European Platform on LCA | EPLCA (europa.eu)**
National Mileudatabase (NMD)	**Database**		**National Mileudatabase (NMD)**

Appendix 2: Notes from Organizing Committee members

The Appendix lists the summary texts provided by the members of the Organizing Committee, without substantial editing. The main text (Chapter 2) has been derived as a narrative summary of these inputs, categorizing the different ideas on the chosen paragraph structure (of related items), which has implied some editing and sorting of subjects in categories (and alike) for clarity.

Summary Comments of the Chair of Group 1

In order of popularity, the first recognized problem was that the current proposal of SSbD is time-consuming, expensive, and requires multiple competencies (with related communication problems). Criteria are recognized as missing from the SSbD methodology. There are currently conflicting results from different tools (there is a need for robust and user-friendly tools), and poor data availability (especially for chronic data). The aspirational goal is to achieve a meaningful, feasible SSbD tool with fast, accurate, and efficient NAMs and rapid processing of all SSbD elements to create a meaningful dossier. To reach this goal there is a need to make legislative changes, that boost NAMs; the introduction of Good Modelling Practice alongside Good Laboratory Practice; creation of SSbD voluntary working group/consortium to provide permanent feedback (multidisciplinary teams); databases with open data to validate tools and simplification of the data-sharing process.

Secondly, it was recognized that industry needs to be included rather than isolating and regulating. The goal would be to co-create with all stakeholders (perhaps via a consortium) a regulatory framework that industry can believe in and willingly follow. Guidance should be co-created by and with IND and Competent Authorities in an open framework like the RIP process prior to REACH. Communication and education of SMEs is essential.

The third issue was around the lack of appropriate tools and databases for quantitative Life Cycle Costing (LCC). There is a need to create methodology, tools, and databases for quantitative LCC and incorporate into the SSbD framework.

The fourth issue involved recognition of the impact of chemicals on the planetary boundaries and information availability on the subject: Not all stakeholders in SSbD are aware that they are stakeholders! Few tools are available that can inform on raw material use. There is a need to develop better tools for integration of biodiversity and to relate chemical impact to biodiversity as well as harmonized approaches to analyze biodiversity impact.

Summary Comments of the Chair of Group 2.

The group (as well as the earlier consultations) showed that the inverse-planning that is typical of the Cambridge University roadmapping is inspirational and effective. That is, various ideas were proposed that seem far-fetched at first sight, but that show up as useful ideas that trigger the experts to define realistic pathways to materialize the ideas.

In line with this, to start the group results, it was concluded that SSbD-outputs should have the characteristic of being easy to understand and communicate, which suggested the need for, e.g., a well-designed dashboard in which priority signals of good or bad safety- and sustainability outcomes are summarized. Or that SSbD studies should be driven by major considerations on specified definitions of how non-safety or non-sustainability would be defined when considering (other) concepts such as Planetary Boundaries, or when defining more specifically what “bending the curve on biodiversity loss” would mean for key SSbD-metrics to be collected. The most-valued outputs should thus be discussed, to drive the SSbD needs, not *vice versa* (where available science defines next steps – as end results of that strategy may not be relevant for final SSbD evaluations).

With contributing expertise ranging from safety to sustainability experts, the general impression was that data gaps hinder safety assessments as well as assessment of impact categories for sustainability assessments and that this can in part be addressed by developing, implementing and validating artificial intelligence-based methods. As early-stage innovation implies data-poor conditions almost by definition, the use of AI-based approaches could be highest in early stages of the innovation. The same holds for NAMs. The application of these approaches asks for effective data collection and sharing.

Experiences from the realm of chemical safety assessments and associated testing resulted in process-related ideas such as organizing ring-testing (whereby one SSbD case would be evaluated by multiple actors), developing standardized and available sources that can be reused, and other assessment efficacy-improving approaches.

Various suggestions imply a look beyond SSbD *sensu stricto*, as attendees mentioned to consider alignment of data and models between SSbD and other approaches. As example, liaising SSbDs to a wide field of associated expertise, the goals of SSbD may intertwine with those of Nature-Based Solutions (NBS), whereby the link to that field might inspire safe and sustainable ideas at the phase of initiating innovation with NBS-principles. At the other end, considering outputs of SSbD assessments, it is clever to anticipate multi-use of SSbD-(intermediate) outcomes for matters such as indicator development for the *Corporate Sustainability Reporting Directive* (SSbD-results could effectively feed into that, and should relate) when considering multi-use of assessment outputs.

The SSbD framework can result in multiple assessment tiers (related to TRL's and thus innovation stages) and 18 (or more) safety- and sustainability metrics (2 for safety [for humans and the environment], and 16 from e.g. the Product Environmental Footprint approach for sustainability). To reduce complexity, improve cost-effectivity, and given scientific insights that often some impact categories dominate in the 18 footprints that could result from a 'complete SSbD', and given the request for a final dashboard-summary information, there is a need for upfront science-based methods to identify the dominant impact categories upfront (to have those in focus in an SSbD assessment) and to weigh multi-dimensional results for the selected SSbD-impacts in the end (for each tier).

Summary Comments of the Chair of Group 3.
One of the most common themes mentioned in connection to SSbD framework implementation was related to data needed to inform SSbD assessments.

Participants highlighted various challenges related to data gaps and the need to generate more data, especially for *data-poor compounds* but also for *specific novel endpoints and metrics* introduced within the SSbD framework, such as various sustainability parameters. Of note, the majority of novel substances generated at the design stage—which forms the gist of the SSbD approach—can be expected to fall exactly into the "data-poor" category. Hence, these concerns are not trivial and the various solutions proposed by the SETAC membership deserve the fullest attention of the community of SSbD practitioners and visionaries, as well as proper investments from the government and interested industry alike.

Further concerning challenges that need to be overcome, the lack of suitable tools and approaches has been highlighted frequently, e.g., the need to develop high-throughput NAMs for prediction of chronic toxicity effects, or the approaches for numerically weighting safety and sustainability scores against each other.

Another crucial concern expressed throughout the SSbD consultations related to low feasibility due to the (perceived) high complexity of the proposed SSbD framework and assessment processes, which require intensive contributions from interdisciplinary experts and might necessitate high investment of resources upfront. The latter might be difficult to justify particularly at the design stage, where the final application of the developed chemical or material (and hence any potential return on investments) are not even clear yet. In this regard, the suggested solutions included, e.g., increasing the regulatory requirements associated with the SSbD framework in order to ensure a level-playing field for all industries concerned; developing dedicated expertise centers that offer SSbD assessment services; greatly simplifying the framework in general; developing a digitalized, simplified tool for SSbD assessment that should include multiple aspects required; and developing specific SSbD guidelines to vary the breadth of assessment requirements in relation to different TRLs.

The high degree of interdisciplinarity associated with SSbD assessments also results in the problem of the involved experts frequently speaking “different languages”. This necessitates the development of common vocabularies as well as implementation of global strategies for educating people about the SSbD framework, approaches, and related tools in general. The need to reach out to different communities of practitioners has also been highlighted, for example, how to increase the acceptance and implementation of the SSbD principles by chemists working at the early stages of molecular design.

Lastly, with regard to framework simplification, interesting suggestions for potential future developments have in fact stemmed from the initial realization that the framework *misses certain elements yet*. For example, it was highlighted that the SSbD assessments do not yet integrate the concept of planetary boundaries. Similarly, it is currently not clear how the promotion of the SSbD approach could contribute to protecting biodiversity from potentially harmful effects of chemicals. In this regard, it was suggested that the community of experts should try to agree on the most important (hazardous) properties of chemicals that we are most concerned about about potential negative effects on biodiversity. The example provided in Group 3 was persistence [1]. If there were to be consensus on an undesirable property of a chemical this could be communicated to chemists and material developers. With regards to hazard properties, which ones are the ones we are concerned about the most? For example, with regards to human health, this could be the CMR properties. What are the “CMRs” for environmental concerns and which ones are the most important with regards to biodiversity protection? Identifying and focusing on these few properties first could help reduce the scope of required SSbD assessments and simultaneously make them more efficient in achieving the highest benefits for reducing chemical pressure on the environment in relation to the invested resources.

Summary Comments of the Chair of Group 4

The expertise in breakout group 4 had a strong affinity with LCA, which resulted in a cluster of priority ideas related to LCA.

LCA was unanimously considered to be the missing link to measure and ensure the sustainability of a product. However, the linkage of the theoretical framework of LCA to the SSbD concept in a way that allows for large-scale screening of candidate compounds/products is currently hindered by several challenges that the LCA community is grappling with internally. First, significant data gaps prevent the application of LCA tools on a large scale across product categories and applications. This can only be accounted for with high uncertainties with regards to the relevance and contribution of individual environmental impact categories on a product’s sustainability. These uncertainties are particularly high at low technology readiness levels. This calls for systematically filling data gaps that provide the highest leverage.

Additionally, there was a strong call for simplification of the hazard assessment framework. Rather than requiring (and thus investing time and resources into) one-to-one replacements of current test systems (that are already flawed), we should rethink the hazard assessment

[1] It is noted by the editors, however, that there is no societal or regulatory consensus that all persistent chemicals are undesirable.

framework. This should be approached from the point of identifying mechanistic protection targets and then finding methods that sensitively and reproducibly represent those protection targets. An example here could be a NAM (or an array of NAMs) that specifically cover neurotoxic modes of action instead of relying on that being a part of assessing acute fish mortality. These protection targets need to be prioritized (i.e., hard cutoffs for certain properties) and integrated with each other.

This directly feeds into the need for better education of researchers and engineers tasked with creating new compounds and materials. They need better guidance on what properties are undesirable within the SSbD mindset. At the current level this could easily be implemented through a decision-tree, particularly for SMEs, while on a broader level this needs to become an integral part of the education within chemistry and material science curricula. Here, it is integral to foster ownership of this new aspect of product development and to not let the need for consideration of safety/toxicological aspects become only an additional burden on the chemists/material scientists. Rather motivate them to see it as a challenge and provide them with concrete tools to foster agency.

Summary Comments of the Chair of Group 5

An educational theme that was prioritized in one of the breakout groups during the workshop in Seville related to bringing the science of risk assessment and LCA together, thereby creating a pool of scientists that are knowledgeable both in safety assessment and in environmental sustainability (LCA) in the context of SSbD. It was proposed to create Master and PhD programs to establish this, not only once the SSbD framework has been established, but also in the process of developing it.

Another theme that was prioritized, related to ensuring EDI is an integral criterion for the SSbD framework. Chemicals should be equally safe for people, irrespective of ancestry, sex-gender identity, and irrespective of socioeconomic and /or culturally different exposures.

It was commonly recognized that there is a need for absolute safety and sustainability concepts that are developed through tiered approaches, considering tradeoffs between different criteria. A need for guidance on which tools and methods to use of the many that are available in each SSbD step, and in each case, was brought up as well.

Having better tools to assess impact categories (e.g., biodiversity and toxicity) for certain materials, considering the use phase, was identified as an aspirational goal. It was proposed by some research how the e-DNA tool might be used to quantify impact on biodiversity in certain cases.

The SSbD framework should apply to both data-rich and data poor substances so that there is penalization on data availability. Also, it is essential to make the SSbD framework truly applicable throughout the research and innovation process, not just after scale up. Problems are encountered with scaling up for certain compounds in the design stage. Currently, comparing different substances to each in the development phases does not work, exactly because they are data poor.

Summary Comments of Steering Committee Member who attended Group 5

- NAMs to be developed and used to inform the process, but especially the early innovation process, in a way that is separate from CLP (which is currently step 1 of the framework).
- Consider tradeoffs by bringing in weighted processes instead of absolute decisions as it is now, instead of a reductive scoring approach (development need).
- Consider chemical management processes with the framework, moving it away from absolute hazard characterizations, as demonstrated from phase 1 case studies

(development need).
- SSbD should be anchored in stepwise, incremental improvement process, instead of being “all or nothing” (development need).

Summary Comments of the Chair of Group 6
The group included ten people with LCA expertise and the group generated ten suggestions:
1) Better development and harmonization of LCA approaches
2) Expansion of the S-LCA procedures
3) Innovation level (TRL) specific data tools are needed
4) Tools for SMEs and low TRL/innovation level – e.g. via a dash-board
5) Multi-disciplinary and improved communication and cross-fertilization are needed
6) Capitalization of AI possibilities
7) Same as 6)
8) We need to better define criteria for sustainability and the assessment of this
9) SSbD screening tools for SMEs and low on the innovation ladder
10) Tiered SSbD approach

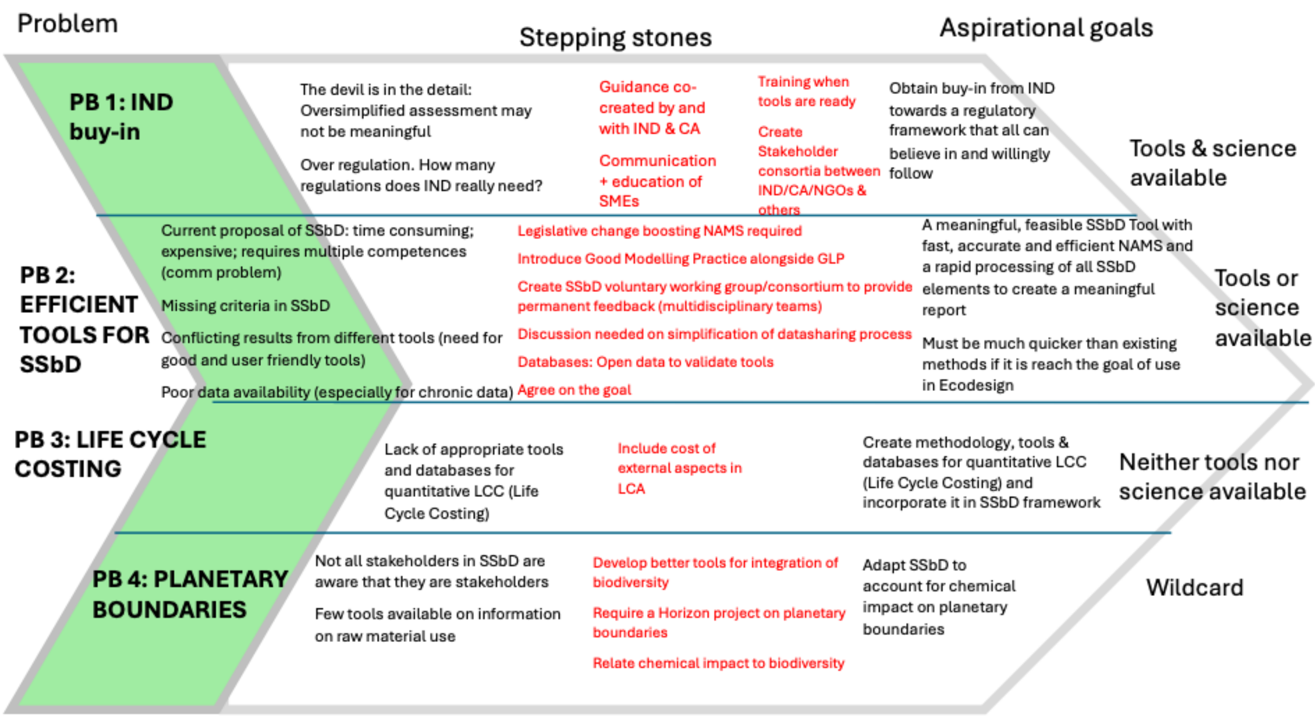
The input falls in three categories and we concluded the following:
1) Regarding data (#1;6;7):
We discussed the need to fund FAIR AI projects as a stepping stone towards capitalization of the potential and reaching the aspirational goal.
2) Regarding tools (#3;4;9;10):
A need to further develop the SSbD terminology and language and bring more harmonization and common understanding across disciplines.
3) On tiers (#2;5;8):
We need to better understand the needs and limitations of SMEs.

So, in terms of synthesis. We have a lot of data and tools that we can currently use. We also have tiers we can adapt. We can use the PEF steps and develop intermediate steps for each of these 16 endpoints from low TRL/innovation level for deselection based on binary decision-tree models.
For the next step, the use of simple models was suggested (e.g. for GWP – just A1-A3 – cradle-to-gate) – so for each endpoint we can make a series of TRL specific tools – starting with the simplest and moving up. For toxicity, we need to include all compartments, not only freshwater. We need to develop more of the S-LCA – and also consider a biodiversity-LCA. And prioritize the most important challenges facing the planet and hence the industry in the PEF – and right now it is climate change related, and biodiversity related. Moreover, to consider the linkage of the endpoint to the ongoing reporting standards and requirements – multi-purpose assessments in support of sustainability assessment of the whole company as well.

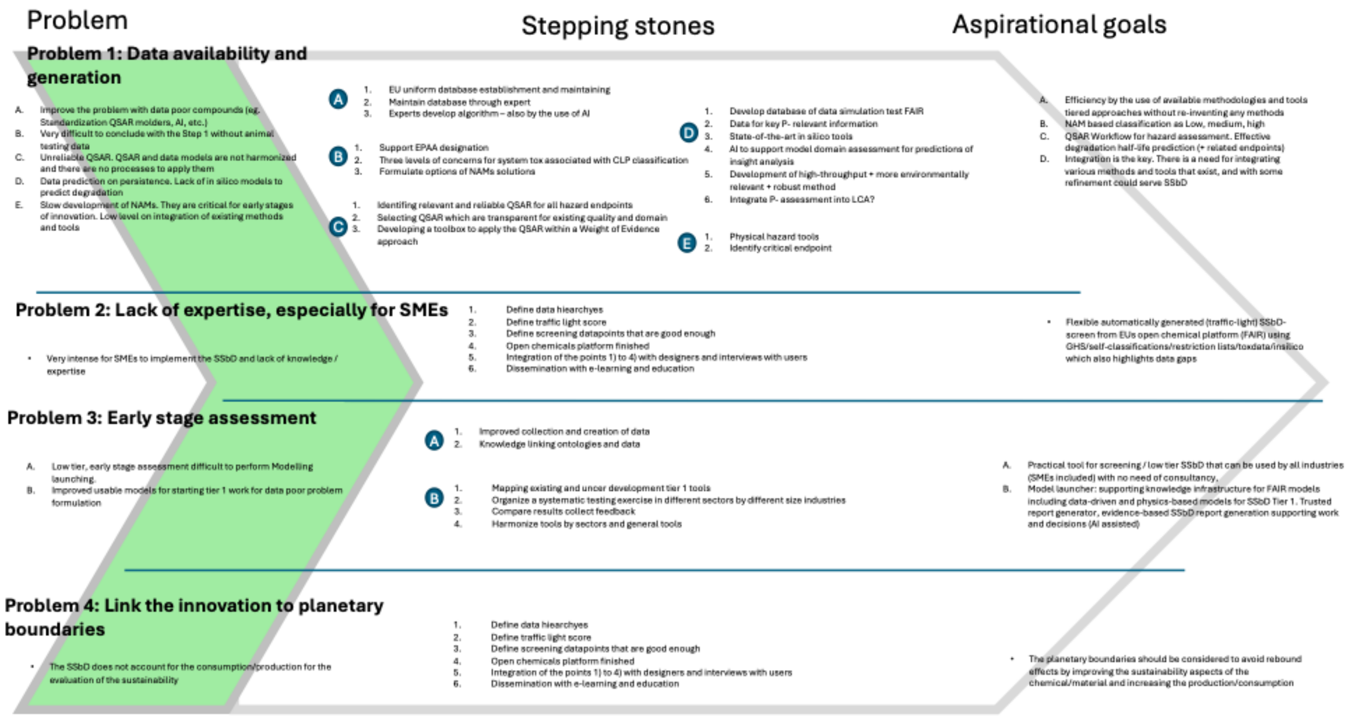
Appendix 3: Roadmaps as created by the breakout groups in the Seville workshop

Below the raw results of the roadmaps created during the Seville workshop on the 6th of May, by each of the breakout groups 1, 2, 3, 4, 5 and 6 are presented, without further explanation. The categorization referred to on page 10 of the main body of this report (category #1 science and tools available; #2 either science or tools available # 3 neither science nor tools available) has not always been captured in the graphics below.

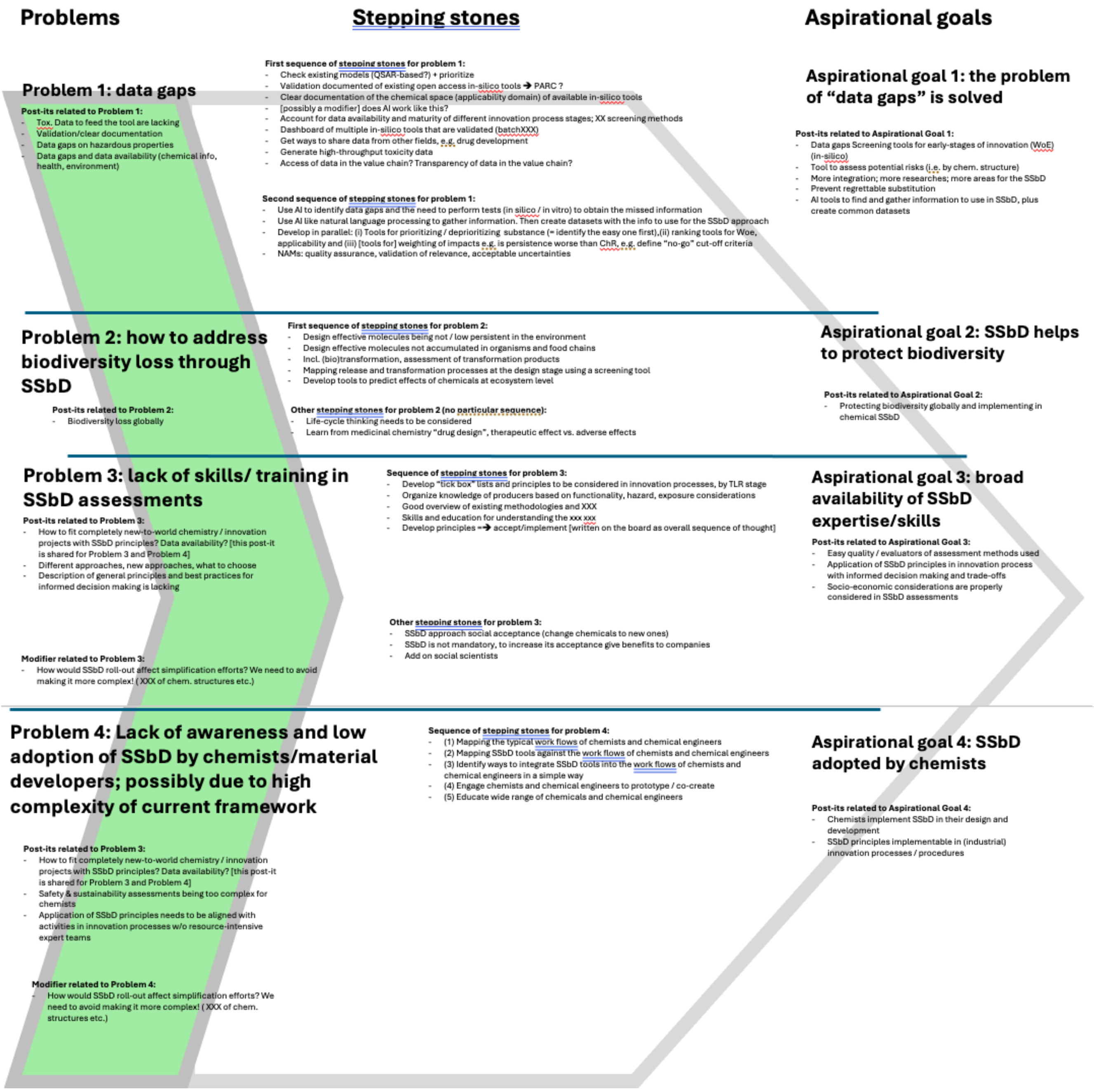
Group 1



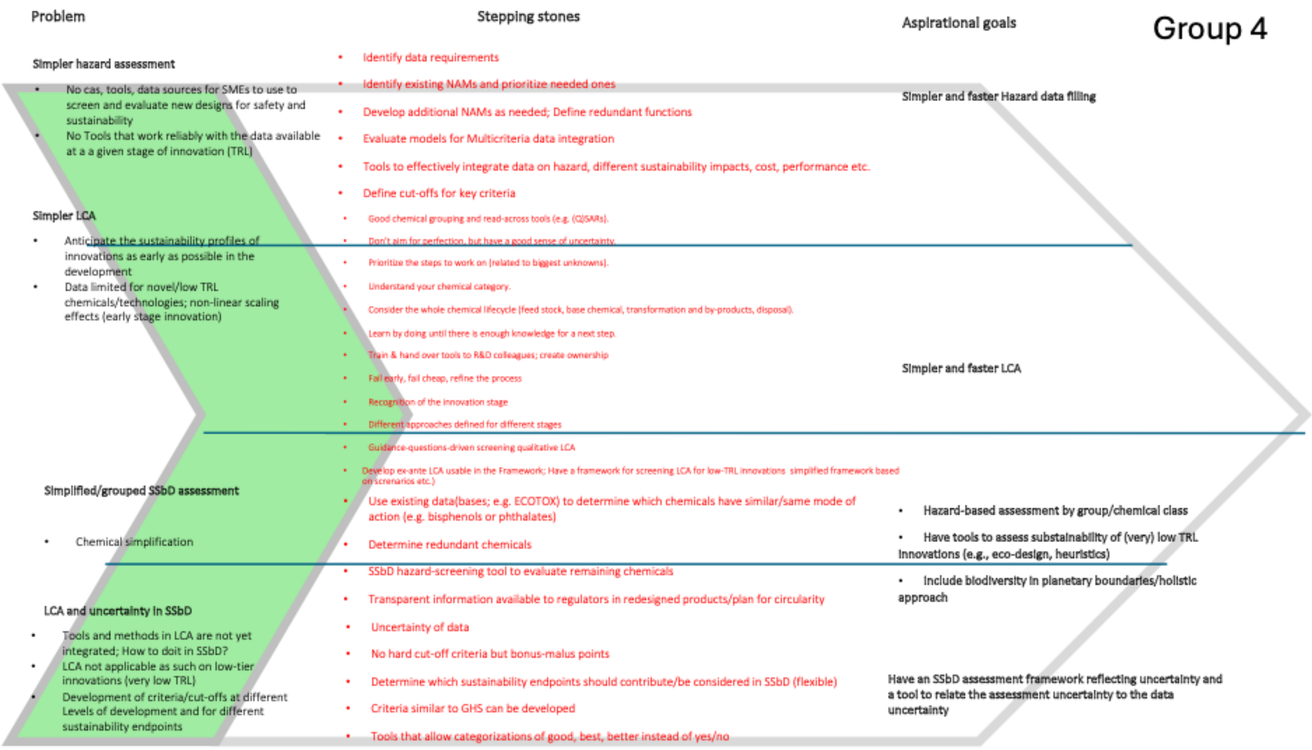
Group 2


Problem
Stepping stones
Aspirational goals
Problem 1: Data availability and generation
A. Improve the problem with data poor compounds (eg. Standardization QSAR molders, AI, etc.)
B. Very difficult to conclude with the Step 1 without animal testing data
C. Unreliable QSAR. QSAR and data models are not harmonized and there are no processes to apply them
D. Data prediction on persistence. Lack of in silico models to predict degradation
E. Slow development of NAMs. They are critical for early stages of innovation. Low level on integration of existing methods and tools
A
1. EU uniform database establishment and maintaining
2. Maintain database through expert
3. Experts develop algorithm – also by the use of AI
B
1. Support EPAA designation
2. Three levels of concerns for system tox associated with CLP classification
3. Formulate options of NAMs solutions
C
1. Identifing relevant and reliable QSAR for all hazard endpoints
2. Selecting QSAR which are transparent for existing quality and domain
3. Developing a toolbox to apply the QSAR within a Weight of Evidence approach
D
1. Develop database of data simulation test FAIR
2. Data for key P- relevant information
3. State-of-the-art in silico tools
4. AI to support model domain assessment for predictions of insight analysis
5. Development of high-throughput + more environmentally relevant + robust method
6. Integrate P- assessment into LCA?
E
1. Physical hazard tools
2. Identify critical endpoint
A. Efficiency by the use of available methodologies and tools tiered approaches without re-inventing any methods
B. NAM based classification as Low, medium, high
C. QSAR Workflow for hazard assessment. Effective degradation half-life prediction (+ related endpoints)
D. Integration is the key. There is a need for integrating various methods and tools that exist, and with some refinement could serve SSbD
Problem 2: Lack of expertise, especially for SMEs
• Very intense for SMEs to implement the SSbD and lack of knowledge / expertise
1. Define data hiearchyes
2. Define traffic light score
3. Define screening datapoints that are good enough
4. Open chemicals platform finished
5. Integration of the points 1) to 4) with designers and interviews with users
6. Dissemination with e-learning and education
• Flexible automatically generated (traffic-light) SSbD-screen from EUs open chemical platform (FAIR) using GHS/self-classifications/restriction lists/toxdata/insilico which also highlights data gaps
Problem 3: Early stage assessment
A. Low tier, early stage assessment difficult to perform Modelling launching.
B. Improved usable models for starting tier 1 work for data poor problem formulation
A
1. Improved collection and creation of data
2. Knowledge linking ontologies and data
B
1. Mapping existing and uncer development tier 1 tools
2. Organize a systematic testing exercise in different sectors by different size industries
3. Compare results collect feedback
4. Harmonize tools by sectors and general tools
A. Practical tool for screening / low tier SSbD that can be used by all industries (SMEs included) with no need of consultancy.
B. Model launcher: supporting knowledge infrastructure for FAIR models including data-driven and physics-based models for SSbD Tier 1. Trusted report generator, evidence-based SSbD report generation supporting work and decisions (AI assisted)
Problem 4: Link the innovation to planetary boundaries
• The SSbD does not account for the consumption/production for the evaluation of the sustainability
1. Define data hiearchyes
2. Define traffic light score
3. Define screening datapoints that are good enough
4. Open chemicals platform finished
5. Integration of the points 1) to 4) with designers and interviews with users
6. Dissemination with e-learning and education
• The planetary boundaries should be considered to avoid rebound effects by improving the sustainability aspects of the chemical/material and increasing the production/consumption

Group 3


Problems
Stepping stones
Aspirational goals
Problem 1: data gaps
Post-its related to Problem 1:
- Tox. Data to feed the tool are lacking
- Validation/clear documentation
- Data gaps on hazardous properties
- Data gaps and data availability (chemical info, health, environment)
First sequence of stepping stones for problem 1:
- Check existing models (QSAR-based?) + prioritize
- Validation documented of existing open access in-silico tools → PARC ?
- Clear documentation of the chemical space (applicability domain) of available in-silico tools
- [possibly a modifier] does AI work like this?
- Account for data availability and maturity of different innovation process stages; XX screening methods
- Dashboard of multiple in-silico tools that are validated (batchXXX)
- Get ways to share data from other fields, e.g. drug development
- Generate high-throughput toxicity data
- Access of data in the value chain? Transparency of data in the value chain?
Second sequence of stepping stones for problem 1:
- Use AI to identify data gaps and the need to perform tests (in silico / in vitro) to obtain the missed information
- Use AI like natural language processing to gather information. Then create datasets with the info to use for the SSbD approach
- Develop in parallel: (i) Tools for prioritizing / deprioritizing substance (= identify the easy one first),(ii) ranking tools for Woe, applicability and (iii) [tools for] weighting of impacts e.g. is persistence worse than ChR, e.g. define "no-go" cut-off criteria
- NAMs: quality assurance, validation of relevance, acceptable uncertainties
Aspirational goal 1: the problem of "data gaps" is solved
Post-its related to Aspirational Goal 1:
- Data gaps Screening tools for early-stages of innovation (WoE) (in-silico)
- Tool to assess potential risks (i.e. by chem. structure)
- More integration; more researches; more areas for the SSbD
- Prevent regrettable substitution
- AI tools to find and gather information to use in SSbD, plus create common datasets
Problem 2: how to address biodiversity loss through SSbD
Post-its related to Problem 2:
- Biodiversity loss globally
First sequence of stepping stones for problem 2:
- Design effective molecules being not / low persistent in the environment
- Design effective molecules not accumulated in organisms and food chains
- Incl. (bio)transformation, assessment of transformation products
- Mapping release and transformation processes at the design stage using a screening tool
- Develop tools to predict effects of chemicals at ecosystem level
Other stepping stones for problem 2 (no particular sequence):
- Life-cycle thinking needs to be considered
- Learn from medicinal chemistry "drug design", therapeutic effect vs. adverse effects
Aspirational goal 2: SSbD helps to protect biodiversity
Post-its related to Aspirational Goal 2:
- Protecting biodiversity globally and implementing in chemical SSbD
Problem 3: lack of skills/ training in SSbD assessments
Post-its related to Problem 3:
- How to fit completely new-to-world chemistry / innovation projects with SSbD principles? Data availability? [this post-it is shared for Problem 3 and Problem 4]
- Different approaches, new approaches, what to choose
- Description of general principles and best practices for informed decision making is lacking
Modifier related to Problem 3:
- How would SSbD roll-out affect simplification efforts? We need to avoid making it more complex! (XXX of chem. structures etc.)
Sequence of stepping stones for problem 3:
- Develop "tick box" lists and principles to be considered in innovation processes, by TLR stage
- Organize knowledge of producers based on functionality, hazard, exposure considerations
- Good overview of existing methodologies and XXX
- Skills and education for understanding the xxx xxx
- Develop principles → accept/implement [written on the board as overall sequence of thought]
Other stepping stones for problem 3:
- SSbD approach social acceptance (change chemicals to new ones)
- SSbD is not mandatory, to increase its acceptance give benefits to companies
- Add on social scientists
Aspirational goal 3: broad availability of SSbD expertise/skills
Post-its related to Aspirational Goal 3:
- Easy quality / evaluators of assessment methods used
- Application of SSbD principles in innovation process with informed decision making and trade-offs
- Socio-economic considerations are properly considered in SSbD assessments
Problem 4: Lack of awareness and low adoption of SSbD by chemists/material developers; possibly due to high complexity of current framework
Post-its related to Problem 3:
- How to fit completely new-to-world chemistry / innovation projects with SSbD principles? Data availability? [this post-it is shared for Problem 3 and Problem 4]
- Safety & sustainability assessments being too complex for chemists
- Application of SSbD principles needs to be aligned with activities in innovation processes w/o resource-intensive expert teams
Modifier related to Problem 4:
- How would SSbD roll-out affect simplification efforts? We need to avoid making it more complex! (XXX of chem. structures etc.)
Sequence of stepping stones for problem 4:
- (1) Mapping the typical work flows of chemists and chemical engineers
- (2) Mapping SSbD tools against the work flows of chemists and chemical engineers
- (3) Identify ways to integrate SSbD tools into the work flows of chemists and chemical engineers in a simple way
- (4) Engage chemists and chemical engineers to prototype / co-create
- (5) Educate wide range of chemicals and chemical engineers
Aspirational goal 4: SSbD adopted by chemists
Post-its related to Aspirational Goal 4:
- Chemists implement SSbD in their design and development
- SSbD principles implementable in (industrial) innovation processes / procedures

Group 4


Group 4
Problem
Stepping stones
Aspirational goals
Simpler hazard assessment
No cas, tools, data sources for SMEs to use to screen and evaluate new designs for safety and sustainability
No Tools that work reliably with the data available at a given stage of innovation (TRL)
Simpler LCA
Anticipate the sustainability profiles of innovations as early as possible in the development
Data limited for novel/low TRL chemicals/technologies; non-linear scaling effects (early stage innovation)
Simplified/grouped SSbD assessment
Chemical simplification
LCA and uncertainty in SSbD
Tools and methods in LCA are not yet integrated; How to doit in SSbD?
LCA not applicable as such on low-tier innovations (very low TRL)
Development of criteria/cut-offs at different Levels of development and for different sustainability endpoints
Identify data requirements
Identify existing NAMs and prioritize needed ones
Develop additional NAMs as needed; Define redundant functions
Evaluate models for Multicriteria data integration
Tools to effectively integrate data on hazard, different sustainability impacts, cost, performance etc.
Define cut-offs for key criteria
Good chemical grouping and read-across tools (e.g. (Q)SARs).
Don't aim for perfection, but have a good sense of uncertainty.
Prioritize the steps to work on (related to biggest unknowns).
Understand your chemical category.
Consider the whole chemical lifecycle (feed stock, base chemical, transformation and by-products, disposal).
Learn by doing until there is enough knowledge for a next step.
Train & hand over tools to R&D colleagues; create ownership
Fail early, fail cheap, refine the process
Recognition of the innovation stage
Different approaches defined for different stages
Guidance-questions-driven screening qualitative LCA
Develop ex-ante LCA usable in the Framework; Have a framework for screening LCA for low-TRL innovations simplified framework based on screnarios etc.)
Use existing data(bases; e.g. ECOTOX) to determine which chemicals have similar/same mode of action (e.g. bisphenols or phthalates)
Determine redundant chemicals
SSbD hazard-screening tool to evaluate remaining chemicals
Transparent information available to regulators in redesigned products/plan for circularity
Uncertainty of data
No hard cut-off criteria but bonus-malus points
Determine which sustainability endpoints should contribute/be considered in SSbD (flexible)
Criteria similar to GHS can be developed
Tools that allow categorizations of good, best, better instead of yes/no
Simpler and faster Hazard data filling
Simpler and faster LCA
Hazard-based assessment by group/chemical class
Have tools to assess sustainability of (very) low TRL innovations (e.g., eco-design, heuristics)
Include biodiversity in planetary boundaries/holistic approach
Have an SSbD assessment framework reflecting uncertainty and a tool to relate the assessment uncertainty to the data uncertainty

Group 5

Problem | **Stepping stones** | **Aspirational goals**

Category 1: science and tools available

Problem

A. Very few people know about both CSA and LCA.
B. Need for absolute safety and sustainability concepts by through tiered approaches and considering trade offs.)
C. There is there is a wide number of tools and methods available for SSbD but there are no clear criteria to determine whith ones to use/ apply in each SSbD step/case.

Stepping stones

A
1. Define multidisciplinary teams to develop SSbD with experts from sustainability and safety domains from industry / government, etc. .
2. Set up EU-wide PhD schools and Masters programmes

B
1. Develop screening tool to support R&I
2. Develop and check weighing methodologies throughout the process.I

C
1. Ask PARC to create an inventory as part of their '' Toolbox''.
2. Prioritisation and guidance about tools/methods to develop the different steps of SSbD

Aspirational goals

A. Fit for purposed SSbD
B. Definition of clear and homogenized tools and methods to address the different steps of SSbD.
C. Sufficient number of people that are knowledgeable in both Safety (CSA) and environmental sustainability.

Category 2: science or tools available

Problem

A. There is a lack of reliable tools to assess certain impact categories for certain materials (eg toxicity) There is a disregarding of the use phase.
B. There are limited socio-economic data which provide information at the company / regional / country scale.
C. There is a lack of data bases containing the results of SSbD and data required for SSbD hazard scenarios.

Stepping stones

A
1. Populate commercial and public data bases wirh reliable data (primary if possible)
2. Improve existing tools to evaluate (ecot) toxicity impacts in LCA.
3. Develop harmonised metrics to evaluate bioversity impacts (and tools)
4. Evaluate impacts throughout full life cycle (including use) and end of life.

B
- No stepping stones identified

C
1. Structure a database
2. Build a data base for required data for (early) screening phases of SSbD
3. Build a data base of the results of SSbD.

Aspirational goals

A. There will be reliable sustainability assessment outcomes
B. Cradle to grave socio-economic data are available which can allow comparison of chemicals at the early stages of innovation.
C. Minimise the resources and efforts to perform SSbD

Category 3: neither science nor tools (fully) developed

Problem

A. How to measure / quantify / assess impact of materials on biodiversity – considering the use phase in particular
B. The SSbD framework does not sufficiently apply to the upstream scale of production (prior to scale up)
C. Chemicals that are data-poor are being penalised
D. How to establish a limit and the relevant criteria when you want to assess a material containing a lot of substances (eg UVCB)
E. pre-screening of product / project material to see if its eligible to apply for the SSbD framework. Eg where are the initial hotspots? There is a lack of information and knowledge of your product at the beginning of the project.

Stepping stones

A
1. Study how e-DNA has been used to date in other disciplines.
2. Determine what would be a representative range of DNA's to collect.
3. Determine whether this tool can be linked to an individual (or group of) chemical(s)
4. Develop an e-DNA map for reference.
5. Develop harmonized metric to evaluate biodiversity impacts (and tools).

B, C
. No stepping stones identified

D
1. Establish a multi-criteria model to prioritise substances.
2. Establish clear criteria about SSbD scope (substances prioritization).

E
1. Define a list of main criteria or ''hot spots'' in each step.

Aspirational goals

A. Methods and tools (eg e-DNA) have been developed to measure and quantify biodiversity.
B. The SSbD framework is truly applicable throughout the R&I process (not just after scale-up)
C. The SSbD framework works / is applicable for both data-rich and data-poort subtances (no penalizing on account of data availability).
D. Tools and a set of criteria are available to assess products containing several chemical substances (eg UVCBs).
E. A predictive SSbD tool will be available or an SSbD fast-track tool or a preliminary SSbD tool will be available.

Category 4: not yet considered in SSbD framework

Problem

- EDI is not an integral criterion in the SSbD framework

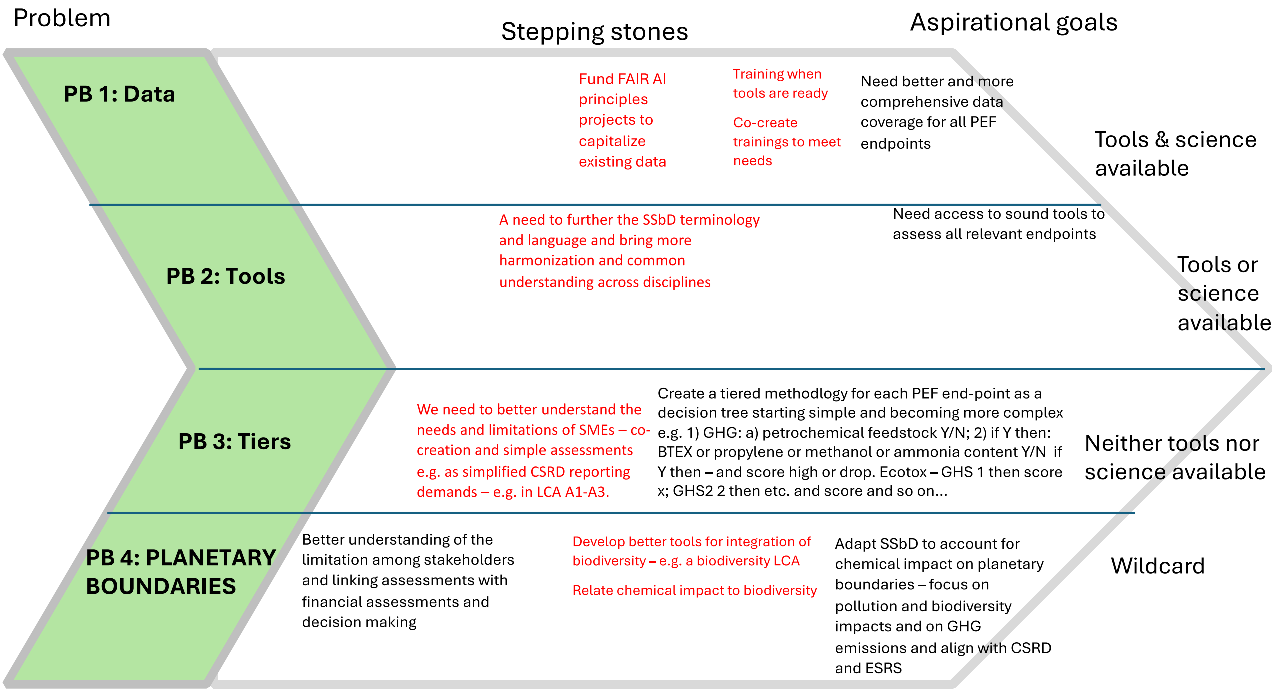
Stepping stones

1. Build QSAS and AI tool and toolbox (for S.F.)
2. Research how chemicals affect different people depending ancestries, sex-gender identities and life stories = socio-economic differential exposure.

Aspirational goals

- EDI is an integral criterion in the SSbD framework, so that chemicals are equally safe for people irrespective of ancestry, sex-gener ID; life studies and / or culturally different exposure potential.

Group 6


Problem
Stepping stones
Aspirational goals
PB 1: Data
Fund FAIR AI principles projects to capitalize existing data
Training when tools are ready
Co-create trainings to meet needs
Need better and more comprehensive data coverage for all PEF endpoints
Tools & science available
PB 2: Tools
A need to further the SSbD terminology and language and bring more harmonization and common understanding across disciplines
Need access to sound tools to assess all relevant endpoints
Tools or science available
PB 3: Tiers
We need to better understand the needs and limitations of SMEs – co-creation and simple assessments e.g. as simplified CSRD reporting demands – e.g. in LCA A1-A3.
Create a tiered methodlogy for each PEF end-point as a decision tree starting simple and becoming more complex e.g. 1) GHG: a) petrochemical feedstock Y/N; 2) if Y then: BTEX or propylene or methanol or ammonia content Y/N if Y then – and score high or drop. Ecotox – GHS 1 then score x; GHS2 2 then etc. and score and so on…
Neither tools nor science available
PB 4: PLANETARY BOUNDARIES
Better understanding of the limitation among stakeholders and linking assessments with financial assessments and decision making
Develop better tools for integration of biodiversity – e.g. a biodiversity LCA
Relate chemical impact to biodiversity
Adapt SSbD to account for chemical impact on planetary boundaries – focus on pollution and biodiversity impacts and on GHG emissions and align with CSRD and ESRS
Wildcard