2024 ANNUAL REPORT MISTRA SAFECHEM

MISTRA

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This is the annual report for 2024 from Mistra SafeChem,
a reseach programme funded by Mistra,
The Swedish Foundation for Strategic Environmental Research.

MISTRA

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MISTRA SAFECHEM

ANNUAL REPORT FOR 2024

The Swedish research programme Mistra SafeChem has a vision: **To enable and promote the expansion of a safe, sustainable and green chemical industry.**

Its first phase ran from 2020 until the summer of 2024. The second phase started on 1 July 2024 and will run for another four years, until 2028.

This is the fifth annual report from Mistra SafeChem. It is both a summary of the results of phase 1 and a presentation of the work to be done during phase 2.

PARTNERS IN PHASE 1

AC2T research, AstraZeneca, BASF We create chemistry, chemsec, cytiva, DTU, enginzyme, H&M, HOLMEN, ivl Swedish Environmental Research Institute, IKEM, KRAHNEN WIR SAUGEN MIT SICHERHEIT, KTH Vetenskap och Konst, Perstorp, RENFUEL, RI.SE, Stockholm University, Stockholm Vatten och Avfall, WARGÖN INNOVATION, VOLVO

PARTNERS IN PHASE 2

AstraZeneca, BASF We create chemistry, Cambrex, DTU, enginzyme, ivl Swedish Environmental Research Institute, KTH Vetenskap och Konst, LigniCore, MERCK, Nouryon, Perstorp, RI.SE, Stockholm University, Stockholm Vatten och Avfall, Uppsala Universitet

Programme director John Munthe was moderator when Mistra SafeChem phase 2 had its kick-off at RISE in Stockholm in October 2024.

ABOUT MISTRA SAFECHEM 2024:

An intense period of final reporting and start of work in the new phase

This annual report covers the year 2024 and includes both the end of phase 1 and the start of phase 2.

It has been an intense period with both final reporting and dissemination of all the results of the first four and a half years and, in parallel, a major effort to build the team (with both new and old partners) for the next four years.

The last six months of the first phase generated several publications and reports but also included ambitious communication activities with seminars hosted by our industry partners and a final all-day webinar. Scientific highlights at the end of phase 1 include several publications reporting the results of multidisciplinary research that combined results from novel catalysis and biocatalysis research with toxicity/ecotoxicity and life cycle sustainability assessment using Mistra SafeChem tools.

The proposal for phase 2 was approved by the Mistra board on March 26, 2024, followed by intensive preparations for the formal launch on July 1.

Even broader cooperation in phase 2

The consortium in phase 2 is to some extent the same as in phase 1 although a few partners unfortunately have decided to leave. On the other hand, we were pleased to gain new industry partners, such as Nouryon, Merck, and Cambrex, indicating the strong relevance of the programme to the chemical industry in Europe. In addition, we invited new research partners from KTH and Uppsala University to join and further strengthen and broaden our competence in the programme.

The external evaluation of the results of phase 1 and the proposal for phase 2 was very positive and the international panel recommended a continuation.

The panel acknowledged both the basic science results, the applicability and relevance of the research and the potential for a broader cooperation with other academic and industry partners focusing on green and sustainable chemistry. The panel specifically highlighted the research efforts made by the PhD students and the ambition of the programme to promote and facilitate interactions between PhD students working on specific topics to enable future cooperation and leadership in the field.

Focus: Safe and Sustainable by Design

The new industry partners joined the programme with a focus on safe and green catalysis/biocatalysis processes for the generation of building blocks for the chemical and pharmaceutical industry, valorisation of waste and by-product resources and application of Safe and Sustainable by Design (SSbD) assessment methods to existing products.

The multidisciplinary approach of the programme, combining basic and applied research, relevant case studies and strong links to the ongoing development towards a safe, green and sustainable chemicals industry in the EU, as described in the EU Chemicals Strategy for Sustainability, proved to be an attractive environment for national and international industry.

By focusing on SSbD and processes and products that minimise chemical risks throughout the value chain, Mistra SafeChem will also enable the implementation of material circularity and a circular economy.

With the launch of phase 2, many of the partners also started to recruit new experts, post-docs, and PhD students. This also included the leadership of Mistra SafeChem where a new programme management team was formed to ensure a long-term commitment in both scientific leadership and programme management.

John Munthe,
IVL Swedish Environmental Research Institute,
Programme Director
(until December 2024)

Patrik Andersson,
IVL Swedish Environmental Research Institute,
Programme Director
(from January 2025)

2024 in numbers

This list can in part summarize Mistra SafeChem in 2024:

103
researchers and industry representatives active in the programme

39
tools in the Mistra SafeChem toolbox

20
scientific articles published

16
news articles published on the website

10+
presentations at external seminars and conferences

6
external reports published

1
final webinar, phase 1

1
final tour, phase 1

1
kick-off, phase 2 of the programme

CHAIRMAN
OF THE BOARD:

New partner collaborations a positive step

It was very satisfying for the board to read the positive assessment by the evaluation panel of Mistra SafeChem's achievements during phase 1. Mistra's decision to continue the funding in phase 2 seemed logical.

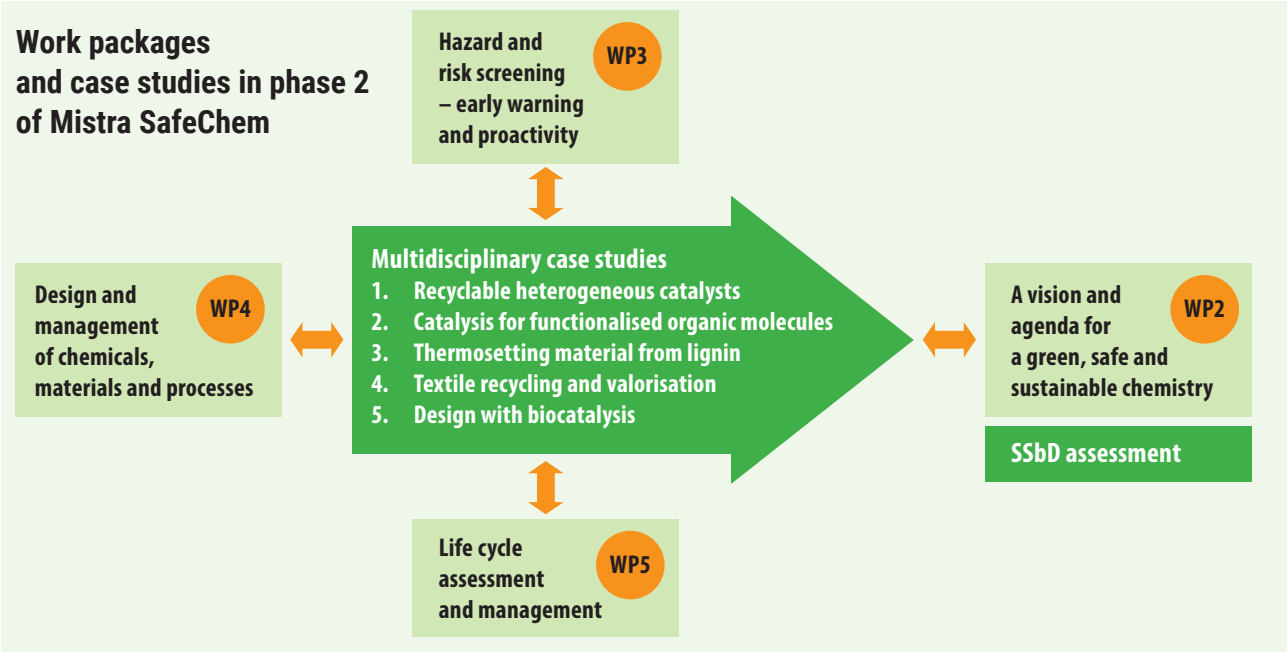
The transition from phase 1 to phase 2 has been quite seamless for most of the researchers involved. The senior scientists are rather much the same, which means that the direction of research has not changed dramatically.

However, there have been considerable changes among the industries involved in the programme and the character of the interactions between the academic and industrial partners is different in phase 2.

During phase 1 end-users of chemicals, such as H&M and Volvo Cars, were partners and initiated work related to issues of specific relevance to these companies. In phase 2 several major chemical companies have joined the program and much of the research is now conducted in close contact with more than one company.

The board is very pleased with this development.

Krister Holmberg
Professor Emeritus, Chalmers, Chairman of the Mistra SafeChem board



PLANS FOR PHASE 2:

Focus on multidisciplinary case studies

Phase 2 of the Mistra SafeChem programme formally launched in July 2024 with a new partnership and a new programme plan for the next four years.

The work continues with the vision ”To enable and promote the expansion of a safe, sustainable and green chemical industry”. However, an important revision from phase 1 is that ”in Sweden” has been removed to emphasise the global nature of the chemical industry and value chains in general, and of the industry partners in the second phase in particular.

The research in phase 2 will continue to focus on the development of novel synthesis processes for chemicals and materials, hazard screening tools and methods for assessing chemical risks in a life cycle perspective. In this way, Mistra SafeChem is expected to contribute both to the implementation of SSbD and to enabling a future circular economy.

A major difference is an increased focus on multidisciplinary case studies where novel synthesis processes will be developed and assessed for chemical safety and sustainability using *in silico* tools, advanced analytical methods and life cycle assessment.

The case studies will provide an opportunity to gain experience on assessment of safety and sustainability in an early stage of the innovation process. They focus on catalytic and biocatalytic syntheses of building blocks for the chemical and pharmaceutical industry, production of thermoset materials from lignin and valorisation of textile residues into nanocellulose.

Basic development of methods and preparatory work for the case studies will be performed in separate work packages.

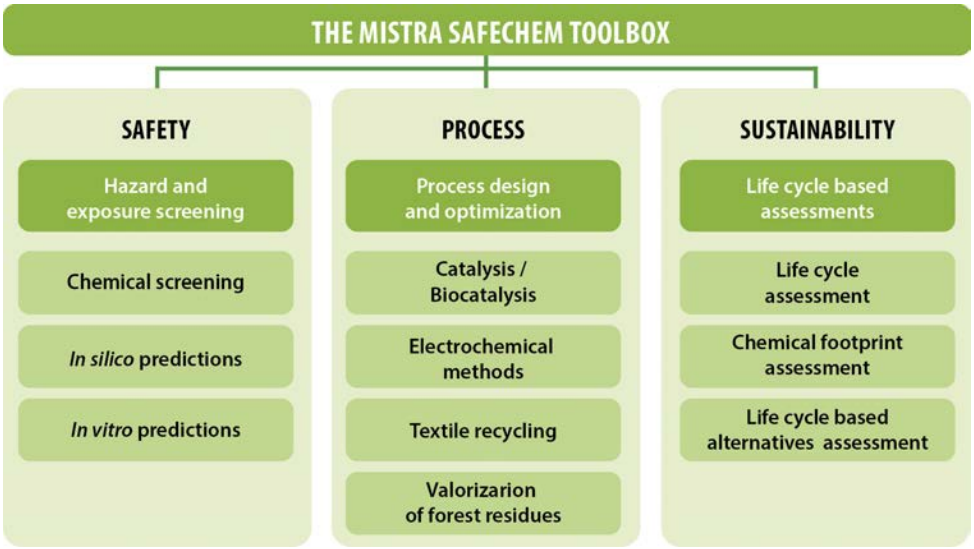
One specific work package includes method development and activities to assess SSbD (Safe and Sustainable by Design) for existing chemicals and products according to the framework and guidelines presented by the EU's Joint Research Centre (JRC). Through active participation in EU activities and dialogue with industry and authorities, the work package is also expected to contribute to the finalisation of the SSbD concept and methodology currently underway at the JRC. Another key objective is to form the basis for a platform for research and innovation on safe and sustainable chemistry.

All research activities will be performed in close collaboration with the industry partners who will also contribute with their own expertise and engagement.

In phase 2, the partnership has been strengthened by adding new partners from the chemical industry, reflecting the relevance and importance of research and innovation with a strong emphasis on safety and sustainability for this sector. With the addition of new international industry partners, and with the strong EU focus on both safety and sustainability including innovative materials and industrial competitiveness, Mistra SafeChem will be well placed to contribute to these challenges in the coming years.

The Mistra SafeChem toolbox keeps growing

A central part of Mistra SafeChem's work is to develop and disseminate tools that facilitate the transition to a safe, sustainable, circular and green chemical industry. In phase 2, the aim is to add new tools and refine the existing ones.



The Mistra SafeChem toolbox is a compilation of major outcomes from the programme and is intended to guide the reader to scientific publications, reports, and expertise in the field. It includes results describing new green chemical processes, analytical chemical processes, methods for predicting and testing human toxicity and ecotoxicity, and methods for life cycle assessment including process safety and chemical footprint.

In phase 2, the intention is to explore possibilities to present a user-friendly interface to access and apply the in silico tools developed in the programme.

By the end of 2024, 39 tools and processes had been added to the toolbox. Most of them have a reference to an article describing the tool or its application, either already published or as a manuscript in progress that will be available later. Some of them are for the time being fully available only for internal use in the programme.

You can find the entire toolbox on the website MistraSafeChem.se, subpage Toolbox.

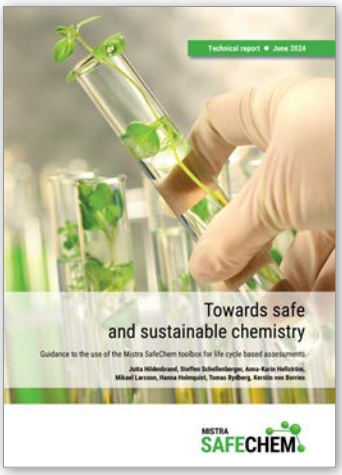
A guide to life cycle based assessment tools

A report, published in 2024, gives guidance to the use of the Mistra SafeChem toolbox for life cycle based assessments.

This report provides information on life cycle based assessments to be used to develop safe and sustainable chemistry, as they have been used in the Mistra SafeChem research programme.

– The requirement to consider various aspects anchored in different research communities is rather novel and it is therefore expected that adjustments and iterations will be necessary based on the results of research programmes such as Mistra SafeChem, comments Jutta Hildenbrand, RISE, one of the authors.

The report provides background on established assessment contexts for chemical alternatives assessment, life cycle assessment and integrated chemical footprint assessment. It includes a synthetic case study to showcase the application of tools and current challenges, providing data, modelling and interpretation of results.



The report is written by Jutta Hildenbrand, Steffen Schellenberger, Anna-Karin Hellström and Mikael Larsson, all from RISE, Hanna Holmquist and Tomas Rydberg, IVL, and Kerstin von Borries, DTU.

Read the report: Towards safe and sustainable chemistry – Guidance to the use of the Mistra SafeChem toolbox for life cycle based assessments.

HIGHLIGHTS FROM 2024:

ProScale – a rewarded and further developed tool

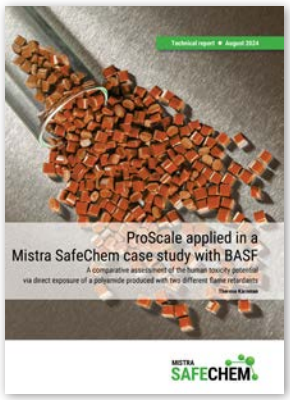
The ProScale tool was in the spotlight in 2024. It won an award and was the subject of two external reports by Mistra SafeChem.

ProScale, which is used to assess the chemical risks of products in a life cycle perspective, is one of the tools used within Mistra SafeChem and also further developed in the programme.

Cefic, the European Chemical Industry Council, rewarded ProScale with the Responsible Care Award in 2024, recognising its contribution to the development of safe and sustainable chemicals.

– The tool combines three aspects: a life-cycle approach, a risk- and exposure-based assessment of products, and the ability to aggregate from a chemical to a complete product. ProScale can provide what we call a "chemical footprint" as it quantifies chemical risks in a similar way to how the carbon footprint quantifies climate-impacting emissions, says Tomas Rydberg, IVL Swedish Environmental Research Institute.

The ProScale scoring system assesses chemical risks to humans, but there is a need to also focus on environmental impacts. Maja Halling, IVL, has carried out an interview study that provides the basis for a sibling, ProScaleE, by gathering user needs.



Another ProScale case study, conducted with the industry partner BASF, has compared the human toxicity potential of a polyamide produced with two different flame retardants.

– The results indicate that a nitrogen-based, halogen-free flame retardant has a lower toxicity potential than a brominated in terms of human toxicity via direct exposure in the defined cradle-to-gate systems, says the author Therese Kärnman, IVL.

Read the reports:
ProScaleE – user needs and perspectives
ProScale applied in a Mistra SafeChem case study with BASF

Successful publishing of multidisciplinary research

A key aim of the Mistra SafeChem programme is to perform multidisciplinary research where innovative synthesis methods for specific chemical products and materials can be tested and assessed for safety and sustainability during the development process.

This multidisciplinary approach is expected to provide decision support for selection of input materials, catalysts and reactants in the process of developing novel synthesis processes and to ensure that the choices made contribute to increased safety and sustainability in the final results. The successful performance of multidisciplinary research requires dialogues and training for an increased understanding of the disciplines involved by all participating researchers.

Large efforts were made in the programme to facilitate and enable this and towards the end of the programme, several examples of successful multidisciplinary research were published.

Notable examples include studies of biocatalytic amide bond formation (Söderberg et al., 2024); electrochemical hydrogenation (Tortajada et al, 2024) and several studies of the use and fate of chemicals in textile upcycling (Ruiz-Caldas et al., 2022, Åström et al. 2024).

Belén Martín-Matute, Stockholm University, **Per-Olof Syrén**, KTH, and **Aji Mathew**, Stockholm University, have all led research groups within Mistra SafeChem that have published multidisciplinary research in phase 1.

The experiences from these studies have formed the basis for the design of the programme in phase 2, i.e. with a strengthened focus on multidisciplinary case studies.

Tour and illustrations used to disseminate results

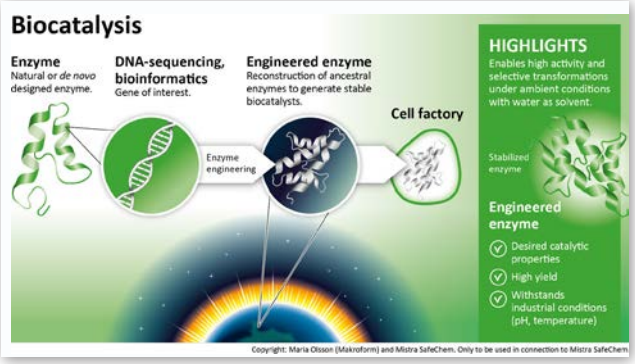
At the end of Mistra SafeChem's first phase, it was time to find clever ways to disseminate the results of the programme. Some unusual methods were chosen: a tour and ten illustrations.

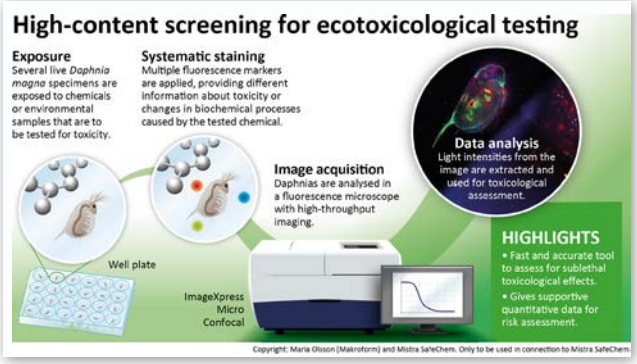
The aim of Mistra SafeChem is to enable and promote the expansion of a safe, sustainable and green chemical industry. Phase 1 therefore ended with a tour, visiting chemical companies and organisations, where the programme's researchers were able to give an insider's view of the particular research areas of interest to those attending each meeting. The tour included visits to AstraZeneca and Perstorp, among others.

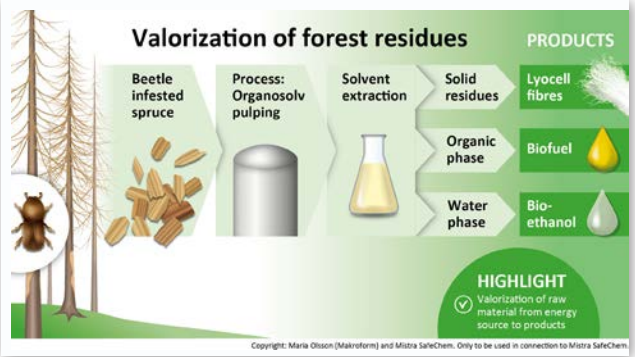
– The visits gave us the opportunity to present and discuss our results to larger audiences at the partner industries which was beneficial for us and, we hope, the participants. We also presented to the West Swedish Chemistry and Materials Cluster, which provided an opportunity to reach companies outside the programme, says John Munthe.

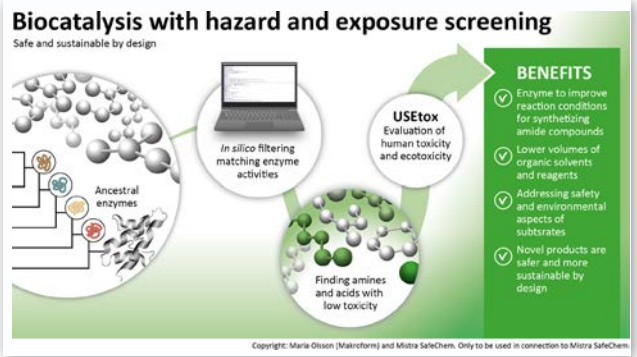
To visualise some of Mistra SafeChem's main conclusions, the programme management decided to produce illustrations that summarise and to some extent simplify the results. Some of them are shown below, the others on the pages about the work package achievements (pages 12-15). Illustrator Maria Olsson produced them in close collaboration with the researchers. They were used both during the tour and in the final webinar (more on this on the next page).

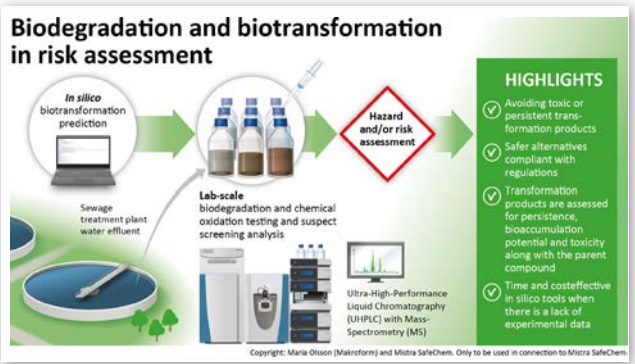
A new communication channel was opened in 2024 when Mistra SafeChem left X (formerly Twitter) and instead started a LinkedIn account, where the number of followers grew steadily during the year.

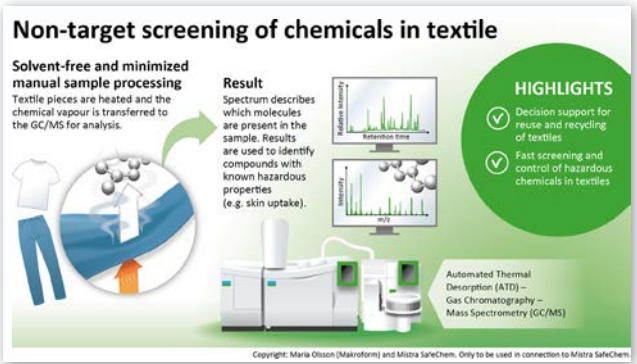












RESULTS FROM PHASE 1:

Findings presented at the Mistra SafeChem final webinar

In June 2024, Mistra SafeChem organised a final webinar to present the results, insights and highlights of phase 1. The researchers presented their findings after four years of intensive work.

The whole day was recorded and you can now watch the final webinar via links on the startpage of the website MistraSafeChem.se.

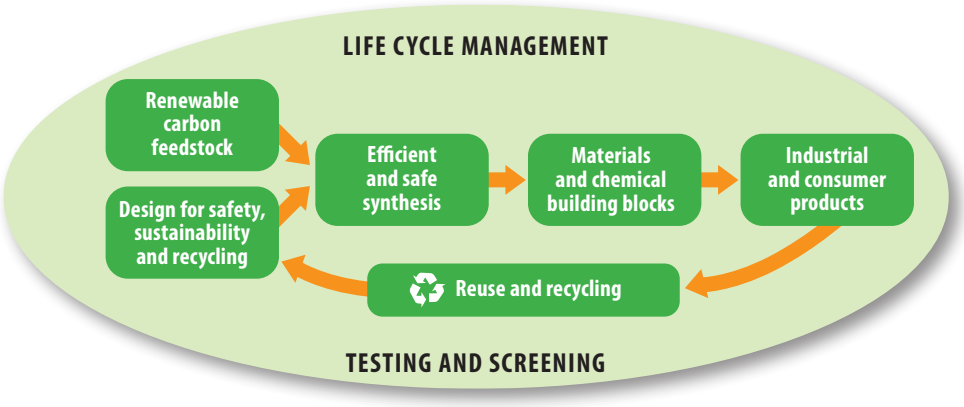
Read more about the phase 1 results
In the following pages we summarise the key acheivements of the five research work packages in phase 1 of Mistra SafeChem.

KEY ACHIEVEMENTS IN PHASE 1: WORK PACKAGE 2

A vision and agenda for green and sustainable chemistry

● A main activity in the final year of WP 2 was to summarise and synthesize the results of the programme's first phase. Results and achievements of WP 3-6 are presented in the respective section of this report and can be summarised to over 100 scientific publications and external reports. Results were also disseminated at external conferences and at 8-10 events (digital and physical) arranged by the programme. A key feature for the excellent scientific production was also the creation of a network of scientists and practitioners from the fields of chemistry, (eco)toxicology and life cycle assessment – the number of individuals engaged in the programme was close to 100.

● A second task was to continue the formulation of an agenda for the future development of a safe, sustainable and green chemical industry. The formulation was to a large extent driven by external factors such as the on-going work to implement the EU Chemical Strategy for Sustainability (CSS) with an increased focus on safety and sustainability but also on increasing the global competitiveness of the EU industry. Specifically, the concept of Safe and Sustainable by Design (SSbD) continued to receive large attention from the Mistra SafeChem researchers and provided a framework for the continued development of hazard screening tools (WP 3), novel synthesis processes for chemicals and materials (WP 4) and methods for chemical risk assessment in a life cycle perspective (WP 5).



A simplified concept for visualising and communicating the Mistra SafeChem version of safe, green and sustainable chemistry.

● Based on experiences from the programme and dialogues with actors in Sweden and the EU, a set of general conclusions and recommendations related to the future development of a safe, sustainable and green chemistry were formulated:

• The SSbD framework can provide a structured approach to assessing and communicating chemical risks and sustainability of chemicals, materials, products and processes. The concept and methodological guidance are under development at the EU Joint Research Centre and tools for the practical implementation are under development in Mistra SafeChem and other research initiatives.

• Challenges to overcome for a successful implementation of SSbD include:

◦ Increased transparency and availability of data and information on chemical use and properties in complex industrial value chains (while securing commercially important and confidential information).

◦ Availability of simple-to-use tools that promote innovation.

◦ Integration of chemical safety and sustainability in terms of expertise, mandate and management of conflicting goals.

◦ Directed funds for multidisciplinary research and innovation are needed to foster cooperation and generation of new safe, green and sustainable chemistry.

Participants in WP2

AstraZeneca, IKEM, IVL Swedish Environmental Research Institute, KTH, Perstorp, RISE, Stockholm University and Volvo Cars.

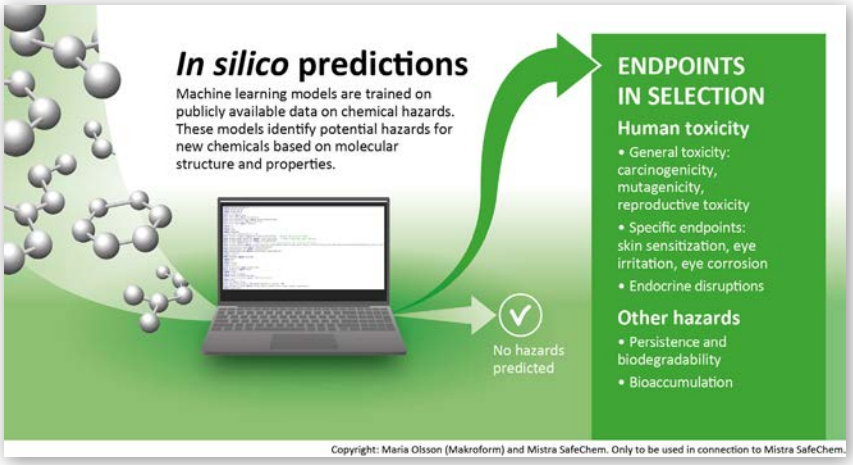
WP leaders

John Munthe, IVL

Lennart Bergström, Stockholm University

KEY ACHIEVEMENTS IN PHASE 1: WORK PACKAGE 3

Hazard and risk screening – early warning and proactivity



● We have developed an *in silico* toolbox for early hazard screening, using machine learning and AI-based approaches, so far mainly available within the programme. This has resulted in state-of-the-art tools for a variety of hazards such as skin sensitization, carcinogenicity, mutagenicity and hormone disruption, with accompanying uncertainty prediction.

● The *in silico* toolbox has been supplemented with a tool for prediction of the EU's H-phrases for health and environmental hazards, as well as a tool for prediction of environmental fate and biodegradability.

● We have developed a simplified interface for the entire *in silico* toolbox, with definitions of how individual tools were validated, and how to make decisions based on output from the various models.

● We have developed cell-based assays to fill in hazard data gaps and *in vitro* methods to determine biodegradability in ecologically relevant media, allowing measures of persistence in the ecosphere to be vectored into decision-making in process development.

● Chemical processes often contain complex mixtures of both desired and undesired products. We have developed a machine learning model, MS2Tox, that predicts ecotoxicity (LC predictions in Fish) and acute toxicity of unknown substances in high throughput from their mass spectra revealed by non-target analysis.

● Our novel, non-target ATD-GC/MS analysis tools have provided input to the identification of potential ”bad actor” chemicals produced in chemical processes, particularly in the textile processing for cotton and cotton blend garments, and potentially other types of materials

● Clusters of *in silico* and *in vitro* tests covering regulatorily relevant hazards such as skin sensitization, mutagenesis and hormone disruption have laid the foundations for several important so-called Defined Approaches which can be used to screen for potential hazards.

● The mutagenesis and skin sensitization (Micro-AMES, hCLAT and peptide bioreactivity) and skin permeation (Strat-M membrane) bioassays have been applied in concert with *in silico* tools in the textile processing case study, discovering novel toxicity profiles for identified compounds, supporting decision making via application of quantitative risk assessment and paving the way for further deployment of Defined Approaches in a tiered approach to hazard assessment within the continuing programme.

● Case study research using *in silico* predictions to characterize non-estrogenic bisphenols suitable for synthesizing polyesters with attractive mechanical and thermal properties, as well as in predictions of non-toxic starting materials and products, in combination with the application of USEtox, enabling biocatalytic amide-bond formation of safer substrates and products in the pharmaceutical sphere, have direct relevance to ongoing efforts to establish Safe and Sustainable by Design (SSbD) approaches within the programme.

Participants in WP3

AstraZeneca, ChemSec, Cytiva, IVL Swedish Environmental Research Institute, RISE, Stockholm University. Four PhD students and one postdoc.

WP leaders

Ian A Cotgreave, RISE

Jonathan Martin, Stockholm University

KEY ACHIEVEMENTS IN PHASE 1: WORK PACKAGE 4

Design and management of chemicals, materials and processes

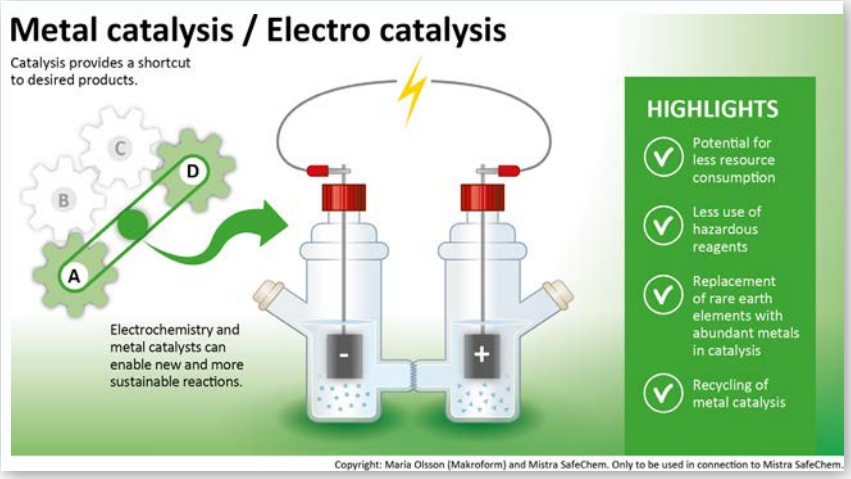
● A a sequence-based protein engineering pipeline to generate biocatalysts with enhanced robustness was developed. Its safety and sustainability in biocatalytic amide bond synthesis by applying all tools developed in the programme (*Green Chem.* **24**) were explored. Benefitting from the high stability of our enzymes, three families of starting enzyme scaffolds for cross-coupling reactions under LED illumination were generated.

● We have developed new recyclable homogeneous and heterogeneous metal catalysts to construct (chiral) organic compounds, including important natural products and biologically active compounds (*Chem. Commun.* **2025**, *Cell Rep. Phys. Sci.* **2024**, *Org. Lett.* **2024**).

● A biomimetic electrochemical oxidation in an undivided cell was developed, where anodic oxidation leads to an efficient palladium-catalyzed carbonylation-carbocyclization.

● Hydrogenation reactions are industrially performed with H2 as reductant, and catalysts based on scarce metals (Pd). An electrochemical method using H_2O instead of H_2 and a Ni foam catalyst was developed, taking into account life cycle, safety and toxicological aspects. The screening LCA showed lower environmental performance due to the Pt counter electrode, which was improved by replacing Pt with graphite (*Green Chem.* **2024**).

● New heterogeneous catalysts were developed to convert CO_2 into diverse chemicals, including carbonates and carboxylic acids. The method is being extended to the synthesis of ^{13}C and ^{14}C isotope-labelled compounds, key molecules for establishing



safety profile of drugs, and used in quantitative autoradiography, human adsorption, distribution, metabolism, and excretion studies (*ChemSusChem* **2024**, *Green Chem.* **2025**).

● A new milder processing route for upcycling postconsumer textiles into nanocellulose using citric acid instead of H_2SO_4 was developed. The cotton fraction was upcycled into cellulose nanocrystals (CNC) while the polyester or acrylics were recovered without decrease in molecular weight. Various grades of nanocellulose derived from textile waste were produced and used in the fabrication of lightweight materials, foams, and films.

● A screening LCA showed that producing CNC from textiles has a significant environmental benefit compared to using wood as the source. However, the environmental burden is high when using citric acid hydrolysis. We developed a method to recover ~60% of the acid with >90% purity, leading to a pending patent and to the spin-off Cellucircle AB (*Cell Rep. Phys. Sci.* **2024**, *J Mater. Chem. A.* **2023**, *ChemSusChem* **2024**).

● A method to regenerate and spin viscose fibres from forestry tops and branches was developed. An LCA shows beneficial results on the footprint categories.

● A method to convert bark beetle infested spruce to a dissolving grade pulp, which can be converted to the man-made natural fibre Lyocell, was developed. The lignin has also been upgraded to a biofuel. An LCA has been performed showing advantages in the footprint categories.

Participants in WP3

AstraZeneca, Holmen, Krahnen, KTH, Perstorp, RenFuel, Stockholm University, Wargön Innovation.
Six PhD students and four postdocs.

WP leaders

Belén Martín-Matute, Stockholm University

Per-Olof Syrén, KTH

KEY ACHIEVEMENTS IN PHASE 1: WORK PACKAGE 5

Life cycle assessment and management

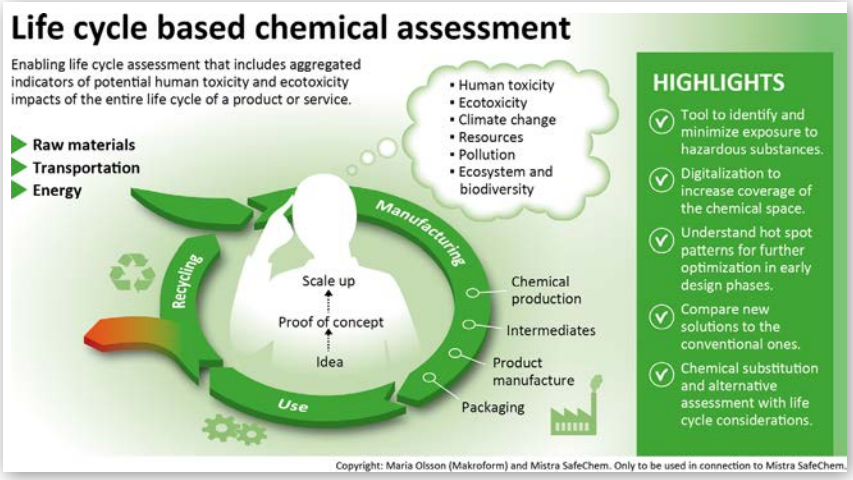
● A toolbox for life cycle based chemicals assessment has been developed and included in the Mistra SafeChem toolbox, available on the page Toolbox on the programme's website.

● A guidance document on how to use the life cycle-based assessment toolbox has been published. It provides background information on established assessment contexts for chemical alternatives assessment, life cycle assessment, and integrated chemical footprint assessment. The document includes a fictive case study to demonstrate the application of tools and current challenges, covering data, modeling, and result interpretation.

● The life cycle based chemicals assessment toolbox has been explored as decision support in process optimization in early design stages and chemical alternatives assessment. Early screening LCA studies including ”chemical footprint” was shown to be useful for understanding and improving the environmental performance and life cycle toxicological potentials.

● USEtox and ProScale life cycle impact assessment (LCIA) models for ecotoxicity and human toxicity are key tools in the toolbox. These tools have been further developed as part of Mistra SafeChem, improving possibilities to include indicators for ecotoxicity and toxicity (i.e., ”chemical footprint”) in life cycle assessment (LCA) and chemical alternatives assessment (CAA) with life cycle considerations.

● USEtox's methodological advancements have been reported in several scientific articles. Based on a methodological framework



for advancing near-field/far-field exposure and human toxicity characterization USEtox was made available as beta-stage version 3, at usetox.org.

● A case study describing the applicability of ProScale in product environmental footprint (PEF) has been published in a brief technical report. The work is based on the PEF pilot study but is limited to selected components of the life cycle. The results show that ProScale can be used in a PEF context but that more work is needed to include all life cycle stages. The study increased our understanding on how ProScale can assist in identifying chemical safety issues in the life cycle of products. It also highlighted areas for further development including human toxicity and ecotoxicity assessment.

● A case study using ProScale on the comparative assessment of human toxicity potential via direct exposure during the production of polyamide with two different flame retardants has been published.

● By use of advanced digital methods, such as AI and machine learning (part of the Mistra SafeChem *in silico* toolbox and additional tools), procedures are being developed to populate USEtox and ProScale with substance property data to increase their coverage and make possible high throughput assessment.

● A prioritization framework has been developed to assess the potential of developing machine learning-based approaches to fill input data gaps in human and ecosystem toxicity characterization.

Participants in WP5

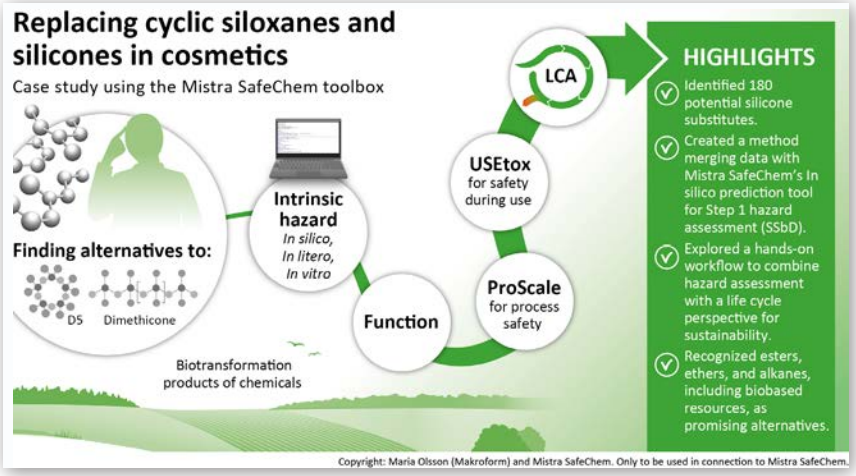
AstraZeneca, BASF, Cytiva, DTU, IVL Swedish Environmental Research Institute, Perstorp, RISE, Volvo Cars. One PhD student.

WP leaders

Hanna Holmquist, IVL

Anna-Karin Hellström, RISE

Case studies



● **Siloxanes and silicones in cosmetics:** This case study aimed to investigate the environmental effects of siloxanes and silicones used as cosmetic ingredients from a life cycle perspective and to identify and evaluate safe and suitable substitutes. More than 175 alternative cosmetic ingredients with similar function to siloxanes/silicones in foundations and lotions were identified using a systematic search strategy. A screening assessment, utilizing existing data to follow Step 1 of the SSbD framework as proposed by the JRC (EU's Joint Research Centre), was established and used for initial prioritization. In total 67 ingredients were further assessed and prioritised with the Mistra SafeChem toolbox by evaluating exposure risk during chemical production (Step 2) and product use (Step 3). Additionally, a screening LCA was conducted to compare different environmental impacts (Step 4) based on the environmental footprint categories suggested by the EU. Input from the study has been provided as feedback to JRC with a focus on user friendliness and needs from an SME perspective. This methodology provides a means to simplify selection and prioritization of more sustainable chemicals used in formulations and chemical products.

● **Indoor environment of cars:** In a car cabin, humans might be affected by incoming air and emissions from interior materials. This case study has evaluated exposure to a selection of potentially hazardous chemicals and identified strategies to decrease or substitute these substances with healthier and more sustainable alternatives. We have used models and tools developed in the other work packages to evaluate their performance for real-world scenarios. We performed passive sampling using polydimethylsiloxane samplers in contact with the materials inside a car cabin, and air and deposition samples to map potential emission sources. We have also demonstrated how the Mistra SafeChem toolbox can be used to do an alternative assessment of plasticizers.

● **Three multidisciplinary case studies, assessing chemical hazards and environmental performance for processes developed in WP4:**

- Non-target screening of chemical content and life cycle assessment to inform process development in textile recycling to produce cellulose nano-crystals from either a traditional process using sulphuric acid, or from a new citric acid based process.
- Hazard assessment and life cycle assessment to support evaluation of a method for electrochemical hydrogenation of enones and alkenes using commercial nickel foam, against the conventional use of palladium on carbon and hydrogen gas.
- Assessment of potential hazards and risks to prioritize substrates and products in a process for the enzymatic formation of amide bonds, increasing overall process safety.

● **Environmental assessment in early process scale-up:** In this case study, the potential for identifying the most feasible settings for scale-up, from an environmental perspective, was explored. This was done by use of environmental assessment and the application of green chemistry principles. A study of the degradability of substances relevant to the processes and their breakdown products was included, where the Mistra SafeChem *in silico* degradability method was applied to verify the experimental prediction.

Participants in WP6

AstraZeneca, H&M, IVL Swedish Environmental Research Institute, KTH, Perstorp, RISE, Stockholm University, Volvo Cars.

WP leaders

Anneli Julander, IVL

Lisa Skedung, RISE

SHORT FACTS

Mistra SafeChem phase 1

Organisation

The research programme in phase 1 was constituted by a consortium of six research partners and thirteen industry partners. The consortium, funded by Mistra and the partners, was led by IVL Swedish Environmental Research Institute and reported to the Programme board.

Running time

2020– June 2024

Financier and budget

In total 103 MSEK

- 70 MSEK from Mistra
- 4.25 MSEK as cash contribution from industry partners
- 29 MSEK as in-kind contribution from research and industry partners

Programme lead

Programme director:
John Munthe, IVL

Deputy programme director:
Lennart Bergström, Stockholm University

Deputy programme director:
Ian Cotgreave, RISE

Programme manager:
Hanna Holmquist/Monika Witala, IVL

Programme communicator:
Ragnhild Berglund, IVL

Research partners

- International Chemical Secretariat (ChemSec)
- IVL Swedish Environmental Research Institute
- KTH Royal Institute of Technology
- RISE Research Institutes of Sweden
- Stockholm University
- Technical University of Denmark (DTU)

Industry partners

- AC2T
- AstraZeneca
- BASF
- Cytiva
- EnginZyme
- Holmen
- H&M
- IKEM
- Krahnen GmbH
- Perstorp
- RenFuel
- Stockholm Vatten och Avfall
- Volvo Cars
- Wargön Innovation

Work packages and leaders

- **WP1: Programme management, WP coordination and communication**
  John Munthe, IVL
  Hanna Holmquist, IVL
  Monika Witala, IVL
- **WP2: A vision and agenda for green and sustainable chemistry**
  John Munthe, IVL
  Lennart Bergström, Stockholm University
- **WP3: Hazard and risk screening – early warning and proactivity**
  Ian Cotgreave, RISE
  Jonathan Martin, Stockholm University
- **WP4: Design and management of chemicals, materials and processes**
  Belén Martín-Matute, Stockholm University
  Per-Olof Syrén, KTH
- **WP5: Life cycle assessment and management**
  Hanna Holmquist, IVL
  Anna-Karin Hellström, RISE
- **WP6: Case studies**
  Anneli Julander IVL
  Lisa Skedung, RISE

Programme board phase 1

Presented as standing in the picture:

Sara Brosché
Senior Advisor, IPEN
(International Pollutants Eliminations Network)

Krister Holmberg, Chair
Professor Emeritus, Chalmers

Anna Wiberg
CEO, Celluxtreme

Per Ängquist
Director General, Swedish Chemicals Agency

Malin Lindgren
Mistra (co-opted)

Patrik Andersson
Professor, Umeå University

SHORT FACTS

Mistra SafeChem phase 2

Organisation

The consortium in phase 2 consists of six research and nine industry partners.

Running time

July 2024 – June 2028

Financier and budget

In total 103 MSEK

- 70 MSEK from Mistra
- 30 MSEK in-kind including cash contribution from research and industry partners

Programme lead

Programme director:
John Munthe, IVL (until December 2024)
Patrik Andersson, IVL (from January 2025)

Deputy programme director:
Lennart Bergström, Stockholm University

Deputy programme director:
Ian Cotgreave, RISE

Programme manager:
Helene Juliusson, IVL

Deputy programme manager:
Monika Witala, IVL

Programme communicator:
Ragnhild Berglund, IVL (until March 2025)
Amelie Karlsson, IVL (from April 2025)

Programme financial officer:
Marianne Blückert, IVL

Research partners

- IVL Swedish Environmental Research Institute
- KTH Royal Institute of Technology
- RISE Research Institutes of Sweden
- Stockholm University
- Technical University of Denmark (DTU)
- Uppsala University

Industry partners

- AstraZeneca
- BASF
- Cambrex
- EnginZyme
- LigniCore
- Merck
- Nouryon
- Perstorp
- Stockholm Vatten och Avfall

Work packages and leaders

- **WP1: Programme management, WP coordination and communication**
  John Munthe, IVL (until December 2024)
  Patrik Andersson, IVL (from January 2025)
  Helene Juliusson, IVL
- **WP2: A vision and agenda for green and sustainable chemistry**
  John Munthe, IVL
  Lennart Bergström, Stockholm University
- **WP3: Hazard and risk screening – early warning and proactivity**
  Ian Cotgreave, RISE,
  Ulrika Nilsson, Stockholm University
- **WP4: Design and management of chemicals, materials and processes**
  Belén Martín-Matute, Stockholm University
  Per-Olof Syrén, KTH
- **WP5: Life cycle assessment and management**
  Tomas Rydberg, IVL,
  Anna-Karin Hellström, RISE

Case studies and leaders

- **CS1: Novel recyclable heterogeneous catalysts for sustainable organic synthesis**
  Jan-Erling Bäckvall and Belén Martín-Matute, Stockholm University
- **CS2: Sustainable catalytic processes for constructing functionalized organic molecules**
  Belén Martín-Matute and Jan-Erling Bäckvall, Stockholm University
- **CS3: Safe and sustainable production of thermosetting material from lignin for a specific application**
  Joseph Samec and Aji Mathew, Stockholm University
- **CS4: Safe and environmentally sustainable textile valorisation and recycling processes**
  Aji Mathew, Stockholm University
  Anna-Karin Hellström, RISE
- **CS5: Safer and more sustainable by design in biocatalysis**
  Per-Olof Syrén, KTH
  Tomas Rydberg, IVL

Programme board phase 2

Presented as standing in the picture:

Krister Holmberg, Chair
Professor Emeritus, Chalmers

Helen Håkansson
Professor Emerita, Karolinska Institutet

Nils Hannerz
Director of Industrial Policy, IKEM

Anna Wiberg
CEO, Celluxtreme

Jan Svärd
CEO, EasyMining

Fredrik Gunnarsson
Mistra (co-opted, missing in the picture)

DELIVERABLES 2024

You find links to all publications on the page Deliverables on our website mistrasafechem.se.

SCIENTIFIC PUBLICATIONS

WP3: Hazard and risk screening – early warning and proactivity

Abele, C., Perez, A., Höglund, A., Pierozan, P., Breitholtz, M., & Karlsson, O. (2024). Automated Image-Based Fluorescence Screening of Mitochondrial Membrane Potential in Daphnia magna: An Advanced Ecotoxicological Testing Tool. *Environmental Science & Technology*, 58(36), 15926–15937.

Carlsson, J., Dostberg, A., Åström, T., Matyjasiak, J., Kallin, A., Juric, S., & Nilsson, U. (2024). Health risks from exposure to chemicals in clothing—Non-regulated halogenated aromatic compounds. *Chemosphere*, 363, 142930.

Liagkouridis, I., Giovanoulis, G., & Thorsén, G. (2024). Assessing the environmental transformation of alternative chemicals using *in silico* tools, (bio)degradation testing and suspect screening – a case study of emerging alternative plasticizers. *Emerging Contaminants*, 100430.

Peets, P., Rian, M. B., Martin, J. W., & Kruve, A. (2024). Evaluation of Nontargeted Mass Spectral Data Acquisition Strategies for Water Analysis and Toxicity-Based Feature Prioritization by MS2Tox. *Environmental Science & Technology*, 58(39), 17406–17418.

Pierozan, P., Höglund, A., Theodoropoulou, E., & Karlsson, O. (2024). Perfluorooctanesulfonic acid (PFOS) induced cancer related DNA methylation alterations in human breast cells: A whole genome methylome study. *Science of The Total Environment*, *949*, 174864.

Strand, D., Lundgren, B., Bergdahl, I. A., Martin, J. W., & Karlsson, O. (2024). Personalized mixture toxicity testing: A proof-of-principle *in vitro* study to evaluate the steroidogenic effects of reconstructed contaminant mixtures measured in blood of individual adults. *Environment International, 192,* 108991.

Strand, D., Nylander, E., Höglund, A., Lundgren, B., Martin, J. W., & Karlsson, O. (2024). Screening persistent organic pollutants for effects on testosterone and estrogen synthesis at human-relevant concentrations using H295R cells in 96-well plates. *Cell Biology and Toxicology, 40*(1), 69.

Åström, T., Ruiz-Caldas, M.-X., Skedung, L., Chelcea, I., Nilsson, C., Mathew, A. P., … Nilsson, U. (2024). The fate of hazardous textile pollutants in an upcycling process for post-consumer garments. *Cleaner Engineering and Technology, 22,* 100794.

WP4: Design and management of chemicals, materials and processes

Apostolopoulou-Kalkavoura, V., Fijoł, N., Lombardo, S., Ruiz-Caldas, M.-X., & Mathew, A. P. (2024). In Situ Functionalisation and Upcycling of Post-Consumer Textile Blends into 3D Printable Nanocomposite Filaments. *Advanced Sustainable Systems,* in press, 2400132.

Kaewmuangphet, S., Samec, J. S. M., & Tungasmita, D. N. (2024). Ethyl levulinate production from agricultural residue through tin oxide with grafted propylsulfonic Faujasite catalysis. *Journal of Cleaner Production, 466,* 142896.

Muangmeesri, S., Baddigam, K. R., Navare, K., Apostolopoulou-Kalkavoura, V., Witthayolankowit, K., Håkansson, H., … Samec, J. S. M. (2024). Recycling of Polyesters by Organocatalyzed Methanolysis Depolymerization: Environmental Sustainability Evaluated by Life Cycle Assessment. *ACS Sustainable Chemistry & Engineering, 12*(10), 4114–4120.

Neiva, D. M., Ek, M., Sels, B. F., & Samec, J. S. M. (2024). Toward sustainable upgrading of bark. *Chem Catalysis, 4*(9), 101022.

Phan, H., Gueret, R., Martínez-Pardo, P., Valiente, A., Jaworski, A., Slabon, A., & Martín-Matute, B. (2024). Synthesis of Benzoic Acids from Electrochemically Reduced CO_2 Using Heterogeneous Catalysts. *ChemSusChem,* in press, e202401084.

Ruiz-Caldas, M.-X., Apostolopoulou-Kalkavoura, V., & Mathew, A. P. (2024). Unlocking the potential of post-consumer garments as a source of nanocellulose. *Cell Reports Physical Science, 5*(2), 101795.

Ruiz-Caldas, M.-X., Apostolopoulou-Kalkavoura, V., Pacoste, L., Jaworski, A., & Mathew, A. P. (2024). Upcycling Textile Waste into Anionic and Cationic Cellulose Nanofibrils and Their Assembly into 2D and 3D Materials. *ChemSusChem,* in press, e202402103.

Ruiz-Caldas, M.-X., Schiele, C., Hadi, S. E., Andersson, M., Mohammadpour, P., Bergström, L., … Apostolopoulou-Kalkavoura, V. (2024). Anisotropic foams derived from textile-based cellulose nanocrystals and xanthan gum. *Carbohydrate Polymers, 338*, 122212.

Söderberg, E., von Borries, K., Norinder, U., Petchey, M., Ranjani, G., Chavan, S., … Syrén, P.-O. (2024). Toward safer and more sustainable by design biocatalytic amide-bond coupling. *Green Chemistry, .*

Tortajada, P. J., Kärnman, T., Martínez-Pardo, P., Nilsson, C., Holmquist, H., Johansson, M. J., & Martín-Matute, B. (2024). Electrochemical Hydrogenation of Alkenes over a Nickel Foam Guided by Life Cycle, Safety and Toxicological Assessments. *Green Chemistry,* in press.

Witthayolankowit, K., Ramazanova, L., Baddigam, K. R., Marson, A., Apostolopoulou-Kalkavoura, V., Lebedeva, D., … Samec, J. S. M. (2024). Valorization of Tops and Branches to Textile Fibers and Biofuel: Value Chain Explored Experimentally; Environmental Sustainability Evaluated by Life Cycle Assessment. *ACS Sustainable Chemistry & Engineering, 12*(1), 526–533.

WP5: Life cycle assessment and management

Cappucci, G. M., Neri, P., Ferrari, A. M., & Fantke, P. (2024). Evaluating toxicity impacts of local chemical emissions in Life Cycle Assessment. *The International Journal of Life Cycle Assessment, 29*(4), 669–682.

Huang, L., Aurisano, N., Fantke, P., Dissanayake, A., Edirisinghe, L. G. L. M., & Jolliet, O. (2024). Near-field exposures and human health impacts for organic chemicals in interior paints: A high-throughput screening. *Journal of Hazardous Materials, 465,* 133145.

REPORTS AND BRIEFS

Aleksandra Sebastian, Dämien Bolinius, Georgios Giovanoulis, Jeffrey Phan and Maria Bernander (2024). Indoor air quality – materials inside the car cabin– WP6 Case Study Summary

Anneli Julander, Monika Witala, Emelie Apell, Lisa Skedung and Dämien Bolinius (2024). Case Study Summary Report – Summary of WP6 of Mistra SafeChem

Josefin Neuwirth, Håkan Fridén, Nilay Elginoz Kanat, Hanna Holmquist, Monika Witala, John Berggren, Oleg Pajalic (2024). Environmental assessment in early process scale up

Joy Ngozi Onwumere and Zhehao Huang (2024). Crystal Engineering for Water Treatment

Jutta Hildenbrand, Steffen Schellenberger, Anna-Karin Hellström, Mikael Larsson, Hanna Holmquist, Tomas Rydberg and Kerstin von Borries (2024). Towards safe and sustainable chemistry – Guidance to the use of the Mistra SafeChem toolbox for life cycle based assessments

Therese Kärnman (2024). ProScale applied in a Mistra SafeChem case study with BASF – A comparative assessment of the human toxicity potential via direct exposure of a polyamide produced with two different flame retardants

PhD THESES

Carlsson, J. (2024). Is your wardrobe making you sick? Textile Chemicals with Focus on Skin Sensitizers – Analytical Methods, Occurrence and Dermal Exposure. (Doctoral Thesis in Analytical Chemistry.) Stockholm University, Stockholm.

Phan, V. D. H. (2024). Catalytic Transformations of CO_2 into Organic Compounds. (Doctoral Thesis in Organic Chemistry.) Stockholm University, Stockholm.

Ruiz-Caldas, M.-X. (2024). Discarded Textiles as an Under-explored Source of Cellulose Nanomaterials: Processing, Properties, and Applications in Lightweight Materials. (Doctoral Thesis in Materials Chemistry.) Stockholm University, Stockholm.

von Borries, K. (2024). Advancing life cycle based chemical toxicity characterization through digitalization. (Doctoral Thesis in Quantitative Sustainability Assessment.) Technical University of Denmark, Lyngby.

OUTREACH ACTIVITIES IN 2024

Presentations and lectures at several webinars and conferences, among those:

- Meeting at the EU's Joint Research Centre (January)
- Lectures in Germany, Italy and Belgium (January, February and June)
- Final tour with stops at Perstorp, AstraZeneca, Swedish Chemicals Group at RISE, West Swedish Chemistry and Materials Cluster (spring of 2024)
- Mistra Jubilee (seminar in March, conference in September)
- Materials Research Society 2024, virtual conference (May)
- SETAC Annual meeting, Society of Environmental Toxicology and Chemistry, Seville, Spain (May)
- Green Chemistry Conference, Dresden, Germany (May)
- Mistra SafeChem Final Webinar (June)
- SETAC Europe 26th LCA Symposium, Gothenburg, Sweden (October)
- SSbD24 Conference, Monte Veritá, Switzerland (November)

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