2023 ANNUAL REPORT MISTRA SAFECHEM

MISTRA

MISTRA SAFECHEM

CONTENT

This is the annual report for 2023 from Mistra SafeChem,
a reseach programme funded by Mistra,
The Swedish Foundation for Strategic Environmental Research.

MISTRA

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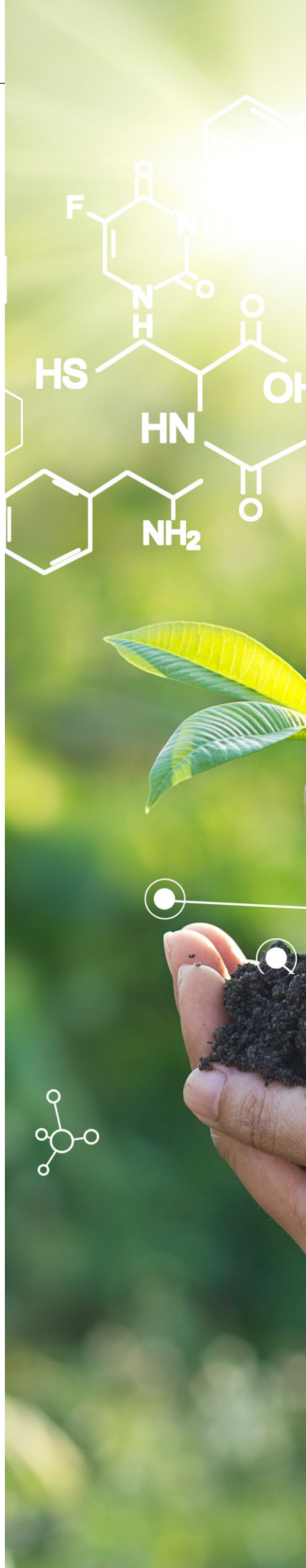


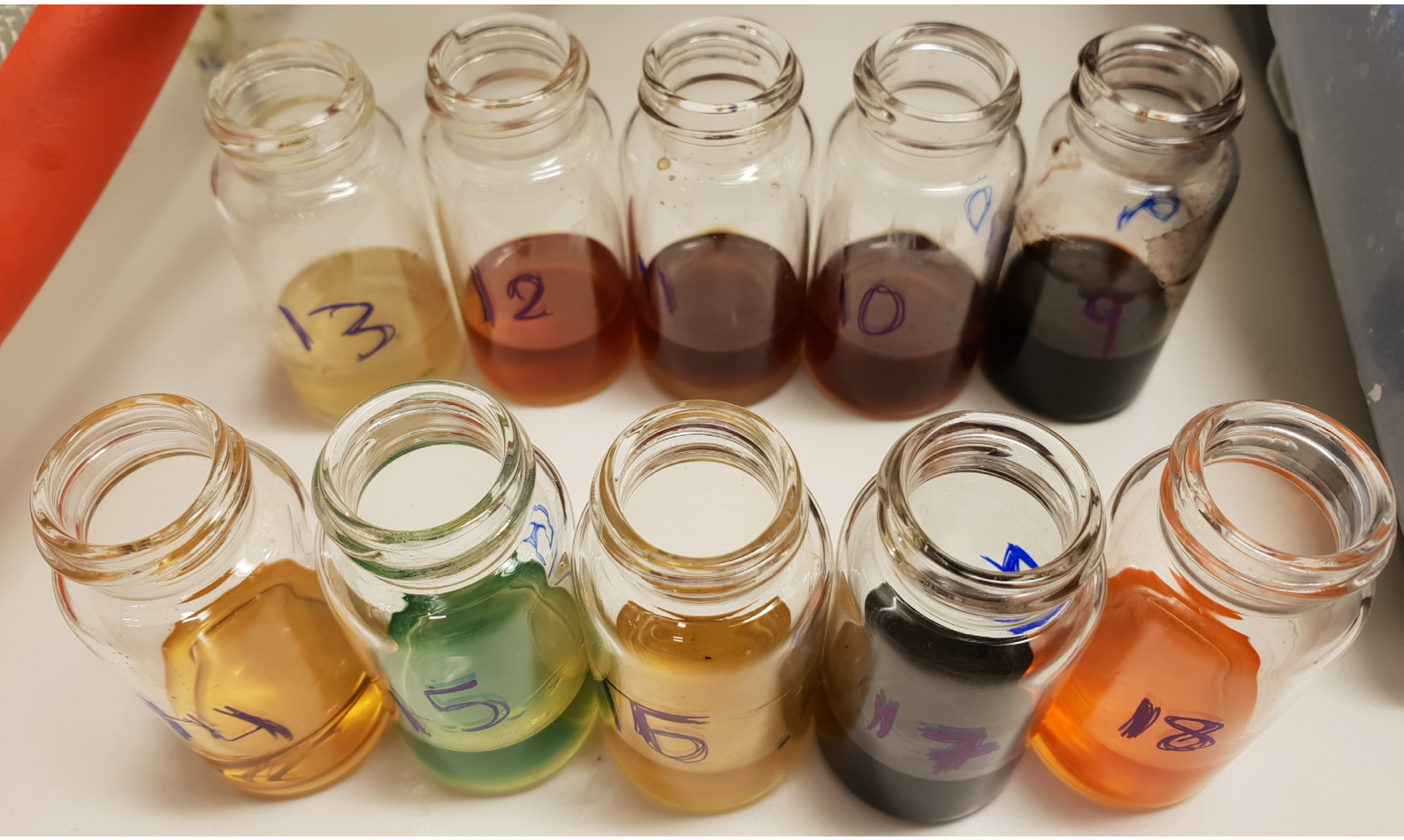
MISTRA SAFECHEM

ANNUAL REPORT FOR 2023

The vision of Mistra SafeChem is to enable and promote the expansion of a safe, sustainable and green chemical industry

PARTNERS

AstraZeneca, BASF We create chemistry, chemsec International Chemical Secretariat, cytiva, DTU, EnginZyme, H&M, HOLMEN, ivl Swedish Environmental Research Institute, IKEM Innovations- och kemiindustrierna i Sverige, KRAHNEN WIR SAUGEN MIT SICHERHEIT, KTH Vetenskap och Konst, Perstorp, RENFUEL Lignin Bio Oils & Materials, RI.SE, Stockholm University, Stockholm Vatten och Avfall, Wargön Innovation, Volvo



ABOUT MISTRA SAFECHEM 2023:

An intense last year with a focus on both results and future work

2023, the last full year of Mistra SafeChem phase 1, was intense. We continued the research activities at full steam and started the planning for final deliverables and dissemination of the results in the last six months of the programme period. In addition, a proposal for continuation in a second phase was prepared and submitted to Mistra.

To summarise and integrate the results of four years of research, more than 80 scientific publications and reports and the experiences of a large group of scientists from different disciplines is a challenging but also rewarding task.

During this process, a key achievement of the first years of the programme was identified to be the creation of a multidisciplinary research community enabling cooperation between experts on toxicology/ecotoxicology, catalytic and biocatalytic synthesis, advanced analytical chemistry, life cycle assessment, exposure assessment, machine learning and programming.

A toolbox for end-users

A key initiative for the integration and presentation of results was the Mistra SafeChem toolbox created to enhance the dissemination of our results. Currently, many of the tools are only available for internal use in the programme, but a selection will be open for end-users once they are fully developed.

By the end of 2023, the toolbox contains 37 individual tools – but more are expected to come. These tools are for new chemical processes, analytical methods, methods for prediction and testing human toxicity and ecotoxicity, and methods for life cycle assessment including process safety and chemical footprint. The tools are presented in short descriptions and what they can be used for, with links to

publications and contact persons. The toolbox will continue to develop in the final stage of the programme.

Long planning for future phase

The work to plan and prepare a proposal for phase 2 was initiated already in 2022 and involved discussions with current and new partners on both scientific contents and the organisational structure of a new programme phase. The proposal was submitted in late November and a decision by the Mistra Board is expected in late March. Hopefully, a second phase can start on July 1, 2024.

Together with the proposal, a progress report was submitted where the research performed so far was summarised along with other facts and information about the programme. In line with the focus in 2023 to summarise and disseminate the results to date, this annual report is to a large part based on the progress report.

Strong focus on the SSbD concept

Mistra SafeChem partners have also been active in the ongoing work with the implementation of the EU Chemicals Strategy for Sustainability (CSS) especially about the definition and development of the concept of Safe and Sustainable by Design (SSbD).

The life cycle perspective highlighted in Mistra SafeChem along with the strong knowledge base on LCA methodologies, hazard screening and chemical footprints provides an excellent basis for support in the development of criteria and methods for SSbD assessment of products and value chains. In addition, Mistra SafeChem partners participate in several EU-funded projects where SSbD methods are tested and applied to specific materials and products.

The spring of 2024 will be very intense for Mistra SafeChem with several final deliverables from all work packages, focused dissemination activities to round up phase 1 and, hopefully, planning the start-up of phase 2.

John Munthe,
IVL Swedish Environmental Research Institute, Programme Director

Hanna Holmquist,
IVL Swedish Environmental Research Institute, Programme Manager

2023 in numbers

For those of you who like numbers the following list can in part summarize Mistra SafeChem in 2023:

102
researchers and industry representatives active in the programme

37
tools launched in the Mistra SafeChem toolbox

27
scientific articles published

21
news articles published on the website

6
major case studies active

15+
presentations at external seminars and conferences

3
meetings for all persons involved in the programme

1
external report published

CHAIRMAN OF THE BOARD:

Collaboration is a keyword

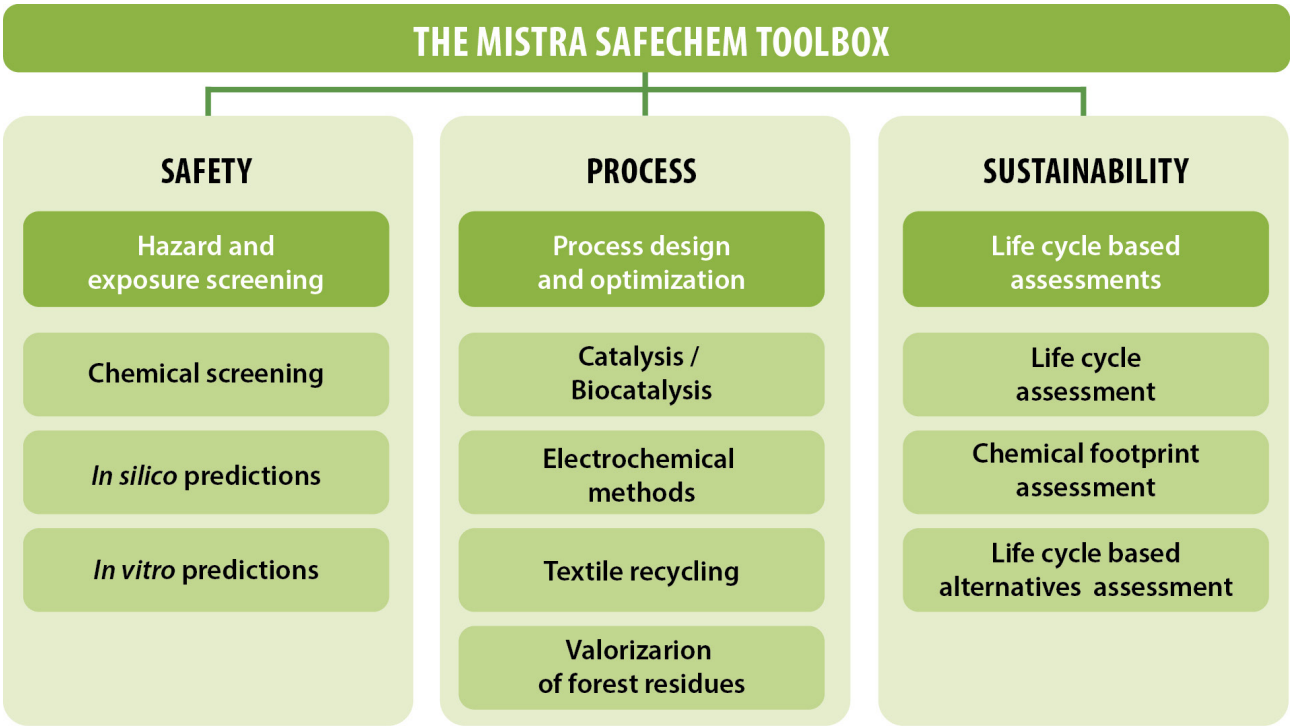
Mistra SafeChem's first phase is approaching the end and an application for a second phase has been reviewed by an international panel. We now know the evaluation was positive and expect continued funding.

This means that we can look ahead but there are also reasons to pause and look back.

Mistra SafeChem is a large research programme with a broad scope. Taken together, the programme is a collaboration for a safe and sustainable green chemistry and a key word is "collaboration". The programme management has strived to foster collaborations between the many rather disparate research areas and the board has encouraged that ambition.

It is obvious that Mistra wants to see that its money is invested so that the outcome is larger than the sum of many individual projects. One tool for stimulating joint work between different disciplines is the programme reserve. Therefore, the board has made it clear that the reserve should primarily be used to support activities across work packages.

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



HIGHLIGHT FROM 2023:

The Mistra SafeChem toolbox is launched

A central part of Mistra SafeChem's work is to develop and disseminate tools that facilitate the transition to a safe, sustainable and green chemical industry. Now, after four years of work, we can proudly present our toolbox. It is well filled, but not full.

– It's a fantastic job by all Mistra SafeChem's researchers and PhD students who have contributed to these tools for a greener chemical industry, says Anneli Julander, IVL Swedish Environmental Research Institute, who has been responsible for compiling all the methods and processes into a toolbox.

37 tools and processes developed – so far

The Mistra SafeChem toolbox includes new chemical processes, developed to contribute to sustainable development, analytical methods, methods for prediction and testing of human toxicity and ecotoxicity, and methods for life cycle assessment including process safety and chemical footprint.

By the end of 2023, 37 different tools and processes were included in the programme's toolbox.

– We plan to update the toolbox gradually as tools are developed and tested, says Hanna Holmquist, IVL, in the Mistra SafeChem programme lead.

Many of the tools are for the time being fully available only for internal use in the programme.

– 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 eventually. As research results become available we will include additional methodological aspects and more examples of use. The toolbox will then become more accessible to practitioners in the chemical industry. For example, life cycle analysts should be able to pick a certain method for use in their work, says Hanna Holmquist.

The toolbox has attracted media interest, with articles in several industry magazines.

Tools for three areas

The Mistra SafeChem toolbox is divided into three "compartments":

- Safety – which includes hazard and exposure screening.
- Process – with methods and models for process design and optimization.
- Sustainability – where you find tools for life cycle based assessments.

See the Mistra SafeChem toolbox on the webpage mistrasafechem.se/projekt/mistra-safechem/toolbox.

HIGHLIGHT FROM WP2: A VISION AND AGENDA FOR GREEN AND SUSTAINABLE CHEMISTRY

Study about the EU taxonomy regulation

Policymakers are moving towards a more open view on data sharing which will enable new legislation. This is an important conclusion from a Mistra SafeChem study on the EU taxonomy regulation.

The report is written by Kristina Andersson, Anna-Karin Hellström and Jenny Lundahl, all from RISE. They have used policy lab processes, which bridge the gap between the legislative domain responsible for developing regulatory frameworks and the innovative companies that create solutions for emerging markets using new technologies and opportunities. These processes have been applied to the EU taxonomy regulation to identify challenges and opportunities related to chemical safety and usage for manufacturers of complex products.

– The EU taxonomy regulation represents a serious effort to establish standardized sustainability reporting. But it is still in its early stages and lacks maturity, comments Kristina Andersson.

Certain ambiguities within the regulation currently prevent a comprehensive comparison of companies due to the development of other legislations. Addressing these gaps depends on the future development of, for example, REACH.

– We conclude that the EU taxonomy regulation is part of a larger movement that reflects the policymakers' intentions. This includes increased data sharing at a significantly different level compared to current practices. This shift will enable authorities to access the data and develop new legislation, says Jenny Lundahl.

The specific focus of the study is on the objective of pollution prevention and control regarding the use and presence of hazardous substances listed in appendix C of the EU taxonomy regulation.

Read the report: Challenges and opportunities with the EU Taxonomy Regulation – with focus on chemical safety and usage in complex products

HIGHLIGHT FROM WP4: DESIGN AND MANAGEMENT OF CHEMICALS, MATERIALS AND PROCESSES

Bark beetle damaged wood can replace cotton

Wood damaged by bark beetles can be converted into fiber that can replace cotton. It can also be used in the chemical industry or as biofuel.

Stockholm University professors Joseph Samec and Aji Mathew, researchers within Mistra SafeChem, lead a project which has shown that bark beetle damaged wood can generate high-quality textile fiber. It can replace cotton for several functions within, for example, healthcare. It is also possible to produce environmentally friendly (or green) chemicals that can be used in the chemical industry or as biofuel, such as aviation fuel.

This chemical innovation can enable new areas of application for damaged wood.

– We have succeeded in making dissolving pulp for fibre from bark beetle infected spruce that has the quality for regeneration. Now we will scale up and make fibre from it, which later may be used to make clothes. We are very happy with it, Joseph Samec says.

The conclusion is that this residual stream from the forest can generate a high-quality fiber which has significantly lower impact than cotton regarding water consumption, climate change, land use and resource use.

Read the article: Valorization of beetle infected spruce to produce textile fibers and biofuels: Environmental sustainability evaluated by life cycle assessment, *Chemical Engineering Journal*

HIGHLIGHT FROM WP3: HAZARD AND RISK SCREENING – EARLY WARNING AND PROACTIVITY

A method developed to avoid rabbit eye test

Mistra SafeChem researchers describe a new *in silico* method that permits differentiation between liquids causing eye damage or irritation, and those with no need for such classification. It can be applied to liquids still at the desktop design stage. But it all started with a cruel test on a rabbit...

Martin Andersson, Ian Cotgreave, Swapnil Chavan, RISE, and Ulf Norinder, Stockholm University, are the men behind this progress. Martin Andersson describes it from a personal point of view:

"Back in 1985 Swedish television sent a program about animal experiments and I remember choosing to present about this topic in school. From that day, the cruel Draize test where eye irritation is evaluated in the rabbit eye got stuck in my mind.

Fast forward to 2016. I worked at RISE with the replacement of solvents in products using the Hansen Solubility Parameter (HSP) concept, and one day a poster on eye irritation caught my eye. On the poster, organic solvents were discussed in the context of their eye-irritation potential.

I thought: 'Could the cornea possibly be treated as a biopolymer with a specific set of HSP parameters? If this is true, then eye irritant solvents should be identifiable via their Hansen parameters!'

I just had to make a small test on the computer to find out, and it looked promising – eye irritants seemed to be clustered in a specific region in HSP space and non-irritants were scattered outside this sphere!

I announced the news at an internal meeting at RISE and got support for a small feasibility study together with colleagues which resulted in a presentation at the HSP50 conference in York in April 2017. Now the project accelerated, with further substantial support from RISE, Mistra SafeChem and the Swedish Fund for Research Without Animal Experiments.

And now, 28 years after my presentation as a 14-year-old, we have published a paper describing a pure *in silico*-method where the outcome of a Draize rabbit eye test can be predicted directly from the chemical structure of a pure liquid only, with a sensitivity of 84.6 percent and a specificity of 81.8 percent, without the need for any animal experiments – or any experimental data at all.

The next step is to get the method accepted for inclusion in the OECD guidelines as a prescribed method that must be used instead of animal tests."

Read the article: *In Silico* Prediction of Eye Irritation Using Hansen Solubility Parameters and Predicted pKa Values, *Sage Journals*

HIGHLIGHT FROM WP5: LIFE CYCLE ASSESSMENT AND MANAGEMENT

Machine learning can address critical data gaps

How can machine learning help bridge the gaps in chemical data assessments? That is the subject of an article, written by Mistra SafeChem researchers Kerstin von Borries and Peter Fantke, DTU, Hanna Holmquist, IVL, and others.

The article is the result of Kerstin von Borries' PhD project investigating the potential of machine learning to address critical data gaps associated with the characterization of chemical toxicity effects.

Machine learning is increasingly used to fill data gaps in assessments to quantify impacts associated with chemical releases and chemicals in products. However, the systematic application of machine learning based approaches to fill chemical data gaps is still limited, and their potential to address a wide range of chemicals was largely unknown before this study.

The study resulted in 13 out of 38 parameters prioritized for developing machine learning based approaches, with the potential to derive data for up to 46 percent of marketed chemicals, depending on the property predicted. Nine parameters were flagged for critical data gaps.

Kerstin von Borries' PhD project is the base for the article.

The results can systematically inform future machine learning model development efforts to address data gaps in chemical toxicity characterization.

Read the article: Potential for Machine Learning to Address Data Gaps in Human Toxicity and Ecotoxicity Characterization, *Environmental Science & Technology*.

HIGHLIGHT FROM WP6: CASE STUDIES

Cosmetics study invited to EU workshop on SSbD

The Mistra SafeChem case study on finding alternatives to siloxanes in cosmetics was one of the special invited studies to be presented at an EU workshop on the Safe and Sustainable by Design framework.

The 4th Stakeholder Workshop on Safe and Sustainable by Design was held in Brussels by the EU Joint Research Centre. The focus was on the outcomes of the first reporting period of the SSbD framework. From Mistra SafeChem, Nina Melander from the Swedish Centre for Chemical Substitution took part.

The workshop's primary goal was to figure out if the framework is user-friendly for industries and other intended users and, if not, pinpoint the tweaks needed to integrate safety and sustainability into operations in real life.

– In 2023, the EU gathered feedback from practical case studies to understand the good, the bad, and the ugly. This was presented during the workshop, as well as approaches and insights from practical case studies or more strategic national initiatives, Nina Melander says.

Almost 50 case studies were reported to the EU during the feedback period of 2023.

Nina Melander took part in the SSbD workshop in Brussels.

– We were one of the selected cases to present partial results from our Mistra SafeChem case study on finding alternatives to siloxanes in cosmetics. I shared our insight on how to tackle step 1 for assessing hazards from an SME perspective, using previous experiences and tools from chemical substitution. I also shared our experiences from educational initiatives by the Swedish Centre for Chemical Substitution to promote the framework.

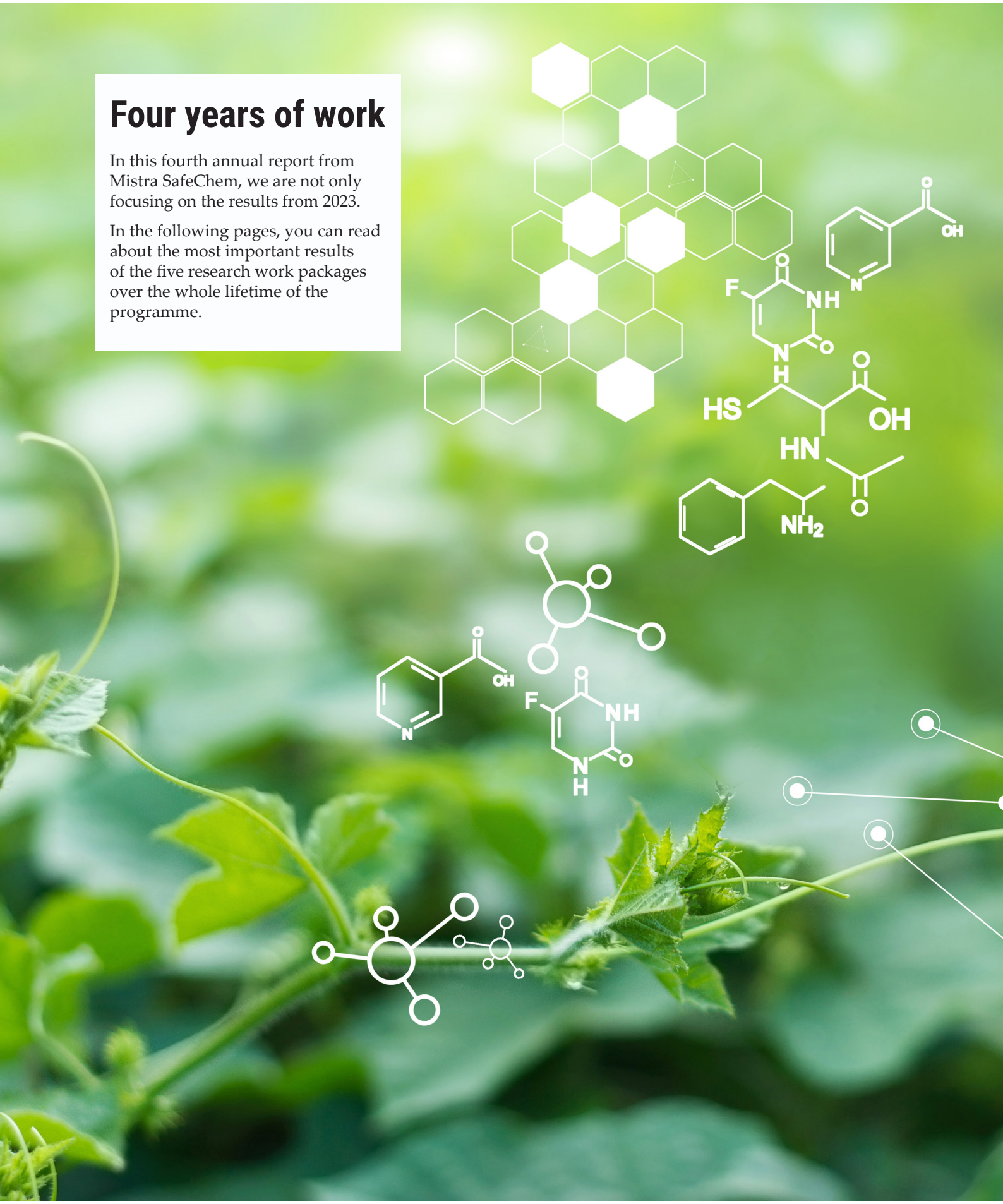
Nina Melander's work in the substitution center is focused on making chemical substitution and alternative assessment more practical and hands-on, especially for SMEs, small and medium-sized enterprises.

– The feedback for our work has been overwhelmingly positive as well as for the speech during the workshop. I think this is a testament to our thoughts on how to make SSbD more accessible.

Four years of work

In this fourth annual report from Mistra SafeChem, we are not only focusing on the results from 2023.

In the following pages, you can read about the most important results of the five research work packages over the whole lifetime of the programme.



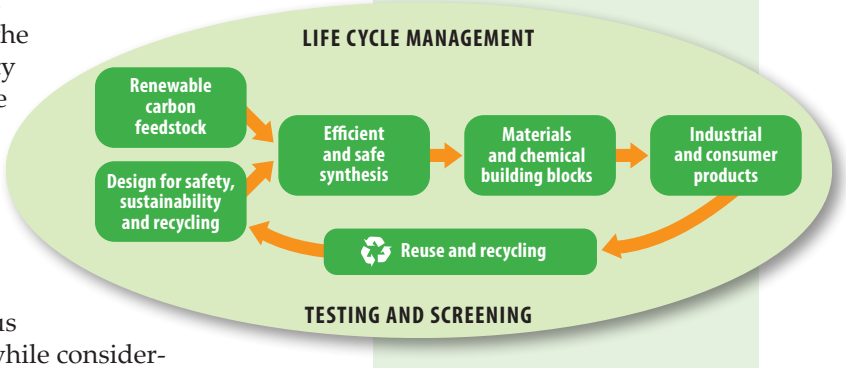
KEY ACHIEVEMENTS: WORK PACKAGE 2

A vision and agenda for green and sustainable chemistry

● An early task was to devise a simplified concept for visualising and communicating the Mistra SafeChem version of safe, green and sustainable chemistry (see figure to the right). This concept is also intended to be used as a framework for illustrating how individual research results are linked to a common concept and aim.

● A compilation of information on the Swedish chemical industry, data on the import, export and use of selected chemicals as well as interviews with representatives of the chemical industry has been made. This information is used to formulate opportunities and obstacles to enable a green and sustainable chemistry. Main conclusions include that the EU CCS and associated industry initiatives as well as current and planned research initiatives provide a strong framework for coordinated action towards a vision of safe, sustainable and green chemistry. Identified obstacles include the complexity of chemical value chains, the international/global aspect of these value chains and the inclusion of all societal sectors.

● A policy lab approach, with a focus on the EU Taxonomy Regulation, has been used to identify challenges and opportunities related to chemical safety and usage for manufacturers of complex products. The main challenge is the need to enhance transparency and traceability throughout supply chains. Overcoming these challenges requires addressing barriers, such as the lack of a harmonized regulatory framework across the value chain, the need for faster identification and restriction of hazardous substances, and the reinforcement of stronger enforcement measures. The enabling of a full declaration of the hazardous properties and functions of the substances, while considering the balance between information disclosure and protecting trade secrets, would reduce the need for extensive tracking of substances of very high concern along the value chain.



● The Mistra SafeChem symposium on green and sustainable chemistry was arranged at AstraZeneca, Mölndal, on September 26, 2022. About 100 persons attended on-site and 150 digitally. The keynote speaker was Professor Paul Anastas, Yale University, other speakers were Professor Lutz Ackermann, Georg-August-University Göttingen, Stewart Owen, Principal Environmental Scientist at AstraZeneca, and researchers from Mistra SafeChem.

● Inspired by Mistra SafeChem and with contributions from programme partners, the master's Program in Sustainable Chemistry at Stockholm University completed its first full curriculum for first- and second-year students in 2022.

● Chemical industry representatives were interviewed to identify opportunities and obstacles and participated in the policy lab where also the Swedish Chemicals Agency took part.

FACTS ABOUT WP2

Objectives

- To define a conceptual structure for green chemistry in Sweden.
- To assess opportunities and obstacles in markets and policies for expanding green chemistry in Sweden.
- To identify and assess novel evaluation criteria in the legal framework.
- To create a vision and agenda for green chemistry in Sweden.
- To prepare for establishment of a permanent platform for research and implementation of green chemistry.
- Competence development, education and communication.

Participants

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

WP leaders

John Munthe, IVL Swedish Environmental Research Institute

Lennart Bergström, Stockholm University

KEY ACHIEVEMENTS: WORK PACKAGE 3

Hazard and risk screening – early warning and proactivity

● We have developed an *in silico* toolbox for early hazard screening, using traditional machine learning and AI-based approaches, so far mainly available within the programme. This has resulted in state-of-the-art tools, particularly in skin irritation and sensitization, and hazards such as carcinogenicity, mutagenicity, and reproductive toxicity screening.

● Another cutting-edge attempt is introducing non-descriptor based structural designation by "molecular embeddings" when developing deep learning tools. We have introduced computational tools to predict metabolic stability or breakdown of compounds in the human body and the ecosphere. We have also introduced uncertainty analysis into computational models.

● 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 a cluster of cell-based assays to fill in 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 potentially complex mixtures of both desired and undesired products. We have developed a series of non-target analytical tools to identify unknowns, both in chemical processes and resulting human and ecological exposomes. Further development has provided a unique, solvent-free method that screens for semi-volatile chemicals likely to migrate from skin-close garments to human skin.

● We have created an analytical method to detect polar substances. These can be predicted *in silico* to aid the identification of potentially hazardous molecules in water or leachates from commercial products. The work has facilitated the development of an *in silico* tool called MS2Tox that can accurately predict the acute toxicity of unknown substances in untargeted water analysis.

● Co-development of clusters of *in silico* and *in vitro* tests covering regulatorily relevant hazards has laid the foundations for several important approaches which can be used to screen for potential hazards.

● The non-target analysis tools have provided input to the identification of potential "bad actor" chemicals produced in chemical processes, particularly in the textile processing case. The methods developed for complex mixture analysis provided great opportunities for industrial partners to speed up the identification of chemical structures.

● The *in silico* toolbox has been applied to a PARC case study on defining alternatives to bisphenol A. Preliminary results show it can support rapid read-across hazard assessments for structural alternatives where little experimental information is available.

● The mutagenesis and skin sensitization bioassays have been applied in concert with *in silico* tools in the textile processing case study, paving the way for the development and deployment of Defined Approaches combining *in silico* and *in vitro* assays in a tiered approach to hazard assessment within the programme.

FACTS ABOUT WP3

Objectives

WP3 will construct and maintain a framework of capabilities and competencies providing a workflow moving through the following steps:

- Initial mitigation planning for hazard identification, exposure estimations and risk assessment, from both the human and environmental perspectives.
- *In silico* screening of available human and ecotoxicological/environmental fate data, read-across data by structural QSAR (quantitative structure-activity relationship) and application of other predictive computational toxicological tools.
- *In vitro* screening for critical human and ecotoxicological adversities relevant for risk assessment, including for combinatorial exposures.
- Development and application of analytical methodologies and techniques, including non-target analyses of exposures and bio-stability, particularly from the ecosystem perspective.
- Integrated hazard and risk assessments which are fit for purpose in appropriate material/process developments and case studies.

Participants

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: WORK PACKAGE 4

Design and management of chemicals, materials and processes

● Initial work focused on upcycling postconsumer textiles into nanocellulose using sulphuric acid hydrolysis (conventional route) and developed a new milder processing route with citric acid. The cotton fraction was upcycled into cellulose nanocrystals (CNC) while the polyester or acrylics were recovered without any decrease in molecular weight.

● A screening life cycle assessment (LCA) showed that producing the 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 have found a simple method to recover around 60 percent of the citric acid with a purity above 90 percent. This has contributed to a patent (pending) and a spin-off, Cellucircle AB.

● We have developed methods to regenerate and spin viscose fibres from forestry tops and branches. An LCA shows beneficial results on the footprint categories.

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

● We have developed a sequence-based protein engineering pipeline to generate biocatalysts with enhanced robustness. We explored the safety and sustainability of this pipeline in biocatalytic amide bond synthesis by applying tools developed in the programme. Benefitting from the high stability of our enzymes, we generated a chemoenzymatic approach to upcycle inert wood-based building blocks into monomers and biopolymers – a novel family of bio-based polyesters. We also showed how CO_2 could be used as feedstock to make chemical building blocks for material applications by synthetic biology applications.

● We have developed new recyclable metal catalysts to construct enantiomerically pure chiral organic compounds, including important natural products and biologically active compounds.

● One of them is a heterogeneous palladium catalyst immobilized on crystalline nanocellulose for selective oxidative carbonylation which could be recycled up to nine times without any significant change in yield.

● We have pioneered catalytic techniques for the late-stage functionalization of complex pharmaceuticals. This facilitates the selective alteration of drug molecules creating new drug candidates in a single synthetic step, eliminating the necessity for de novo synthesis.

● Hydrogenation reactions are broadly used in the industry. In those, fossil-derived hydrogen gas and the scarce metal palladium are traditionally used. We have published a method using water instead of hydrogen as the reductant of alkynes and alkenes and a recyclable nickel foam as the catalyst instead of scarce palladium.

● We have developed a protocol that enables the use of CO_2 as a carbon source to produce chemicals.

FACTS ABOUT WP4

Objectives

- Optimize material use, re-use and recycling for maximum benefits for resource efficiency and sustainability.
- Develop green chemistry industrial processes aiming at replacing/minimizing the use of toxic chemicals and minimizing waste.
- Rational design of first-row transition metal and enzyme catalysts, upscaling of green catalytic processes towards industrial scale.
- Development of methods to define and quantify resource efficiency and circularity of value chains.
- Providing data for evaluation and understanding toxicology determinants of the developed processes.

Participants

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

WP leaders

Belén Martin-Matute, Stockholm University

Per-Olof Syrén, KTH

KEY ACHIEVEMENTS: 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.

● 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 and ProScale are already in use by both industry and academia, and the possibility of integrating them into the European framework for assessment of Safe and Sustainable by Design is under investigation.

● 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 on indoor wall paint, about the applicability of ProScale in product environmental footprint (PEF), has been described in a brief report. 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 is expected to increase the understanding of how ProScale can help identify chemical safety issues in the life cycle of products and on priorities for further advancements of ProScale for human toxicity and ecotoxicity.

● 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-related gaps in human and ecosystem toxicity characterization.

● The life cycle based chemicals assessment toolbox has been explored as decision support in process optimization in early design stages and CAA. Early screening LCA studies including "chemical footprint" was shown to be useful for understanding and improving the environmental performance and life cycle toxicological potentials of lab-scale routes. In one of the substitution case studies initial life cycle considerations were included by qualitative risk mapping, effectively guiding the further assessment.

FACTS ABOUT WP5

Objectives

- To develop and provide a life cycle based chemicals assessment toolbox.
- To develop a tool for high throughput alternatives assessment for chemical substitution.
- To develop a model fit-for-purpose for estimating near-field human exposure for different product application contexts for integration into life cycle assessment and alternatives assessment.
- To provide ProScale and USEtox LCIA characterization factors for human toxicity and eco-toxicity for all case study relevant chemicals that are within the scope of the included methods.
- To compile all relevant information from LCA carried out from case studies.
- To deliver guidelines and training on how to apply life cycle approaches/assessment in case studies and along the design process.

Participants

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

WP leaders

Hanna Holmquist, IVL Swedish Environmental Research Institute

Anna-Karin Hellström, RISE

KEY ACHIEVEMENTS: WORK PACKAGE 6

Case studies

● **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 on plasticizers.

● **Siloxanes and silicones in cosmetics:** Silicone chemistry is not in line with green chemistry principles. This case study aimed to investigate the environmental effects of siloxanes and silicones from a life cycle perspective and to identify and evaluate possible substitutes. More than 175 alternative ingredients to silicones in foundation and lotions were identified using a systematic search strategy. A screening assessment using existing data to follow step 1 in the SSbD framework as proposed by JRC (EU's Joint Research Centre) was established and used for a first prioritisation. In total 67 ingredients were further assessed and prioritised with the Mistra SafeChem toolbox. This methodology could simplify when screening and prioritizing among substances for use in a formulation or when choosing chemical products. Input from the study has been provided as feedback to JRC with a focus on user-friendliness and needs from an SME perspective.

● **Three multidisciplinary case studies have been performed, 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 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.

● **Process optimization and intensification:** In this case study, the potential for identifying the most feasible settings for scale-up, from an environmental perspective, is 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.

FACTS ABOUT WP6

Objectives

- To coordinate the interaction between the case studies and the various tools and methods generated in WP3, WP4 and WP5.
- To transform industrial challenges into cases fit for the programme and for evaluation of the tools.
- To formulate the results from the case studies into general conclusions with respect to efficiency and reliability of the toolbox.

Participants

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

WP leaders

Anneli Julander, IVL Swedish Environmental Research Institute

Lisa Skedung, RISE

SHORT FACTS

This is Mistra SafeChem

Organisation

The research programme is constituted by a consortium of six research partners and thirteen industry partners.
The consortium, funded by Mistra and the partners, is led by IVL Swedish Environmental Research Institute and reports to the Programme board.

Running time

December 2019 – 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, IVL

Deputy programme manager:
Monika Witala, IVL

Programme communicator:
Ragnhild Berglund, IVL

Research partners

- International Chemical Secretariat (ChemSec)
- Technical University of Denmark (DTU)
- IVL Swedish Environmental Research Institute
- Royal Institute of Technology (KTH)
  Fibre and Polymer Technology
  SciLifeLab
- RISE Research Institutes of Sweden
- Stockholm University
  Department of Computer and System Sciences (DSV)
  Department of Environmental Science (ACES)
  Department of Materials and Environmental Chemistry (MMK)
  Department of Organic Chemistry (OrgChem)

Industry partners

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

Work packages

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

Programme board

Presented as standing in the picture to the right:

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

Krister Holmberg, Chair
Professor Emeritus, Chalmers

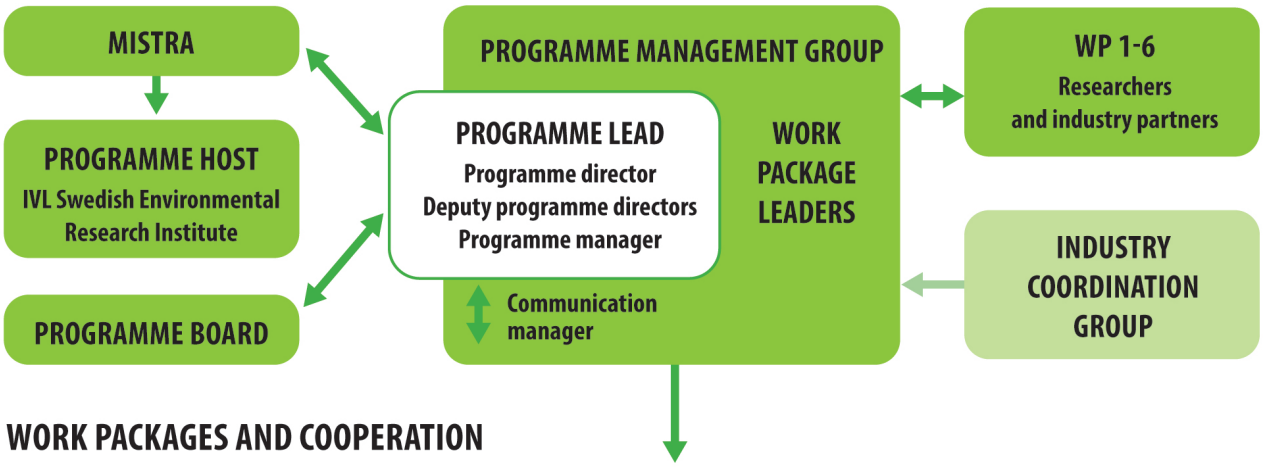
Anna Wiberg, CEO, Celluxtreme

Per Ängquist, Director General, Swedish Chemicals Agency

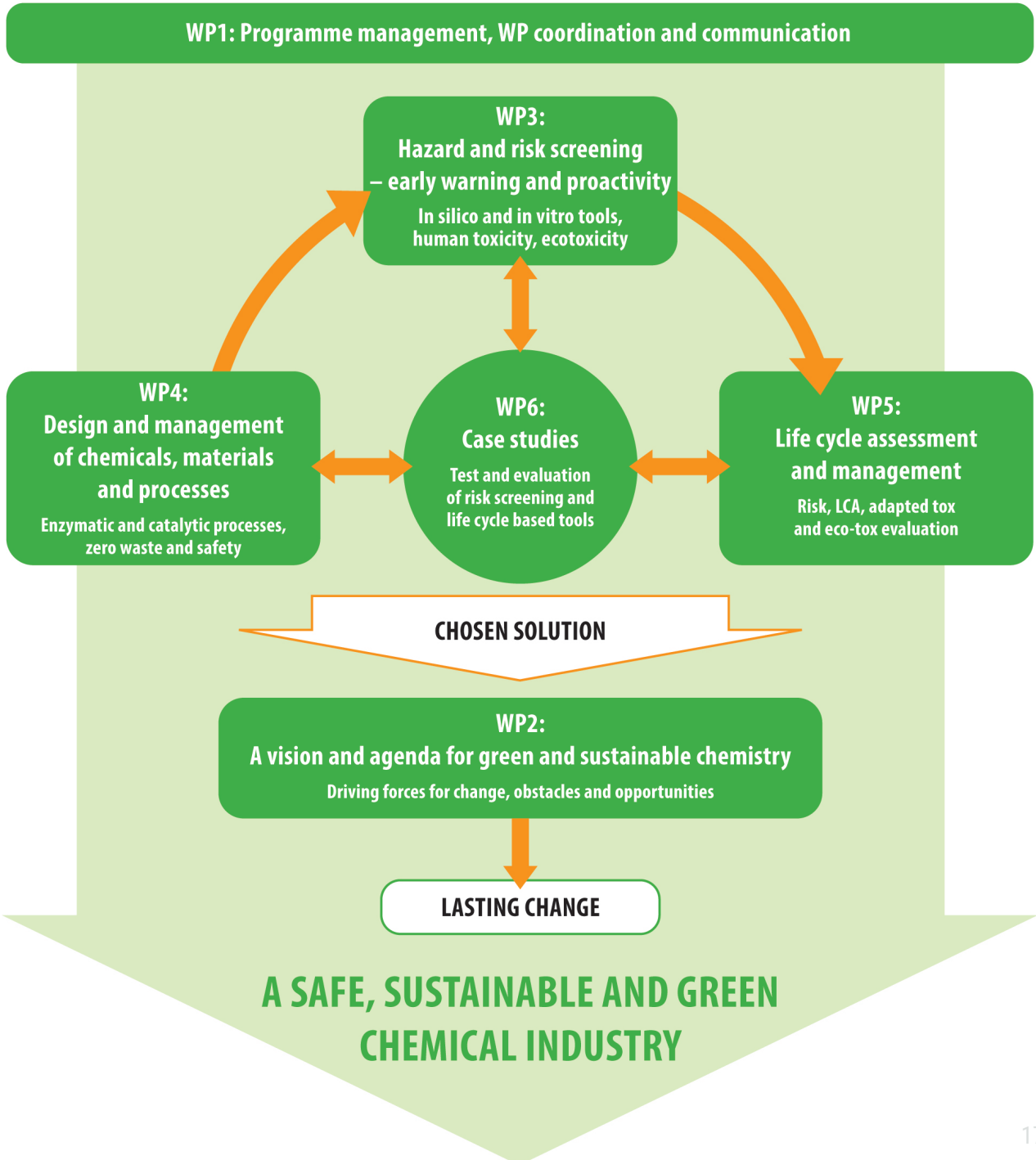
Malin Lindgren, Programmes Director, Mistra (co-opted)

Patrik Andersson, Professor, Umeå University

ORGANISATION OF MISTRA SAFECHEM



WORK PACKAGES AND COOPERATION



DELIVERABLES 2023

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

Andersson, M., Norinder, U., Chavan, S., & Cotgreave, I. (2023). In Silico Prediction of Eye Irritation Using Hansen Solubility Parameters and Predicted pKa Values. *Altern Lab Anim,* 51(3), 204-209.

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REPORTS AND BRIEFS

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MASTER THESES

Castiella Ona, G. (2023). Enantioselective palladium-catalyzed carbocyclization reaction of allene derivatives. The use of enantiotopic olefin chains in carbocyclization. (Department of Organic Chemistry, Stockholm)

Pires Vilela, I. (2023). Regio- and Chemoselectivity of Palladium-Catalysed Carbocyclisation of Enallenes. Substrate scope and mechanistic studies. (Stockholm University and Instituto Superior Técnico, Stockholm/Lisabon)

OUTREACH ACTIVITIES IN 2023

- **Presentations at several webinars, among those:**
  - The industrial adoption of the SSbD (Safe and Sustainable by Design) tools, arranged by Change Chemistry
- **Presentations at conferences and meetings, among those:**
  - 2023 GC3 European Forum, Leverkusen
  - Northtox 2023, Stockholm: Toxicology in the Anthropocene
  - 4th Stakeholder Workshop on Safe and Sustainable by Design, Brussels, arranged by the EU Joint Research Centre
  - The TOKS XVIII symposium at South Danish University, Odense (meeting for organic chemistry students)
  - The WISE Welcome meeting, Kolmården
  - Adam Mickiewicz University (AMU), Poznan
  - EuCOMC XXV, Madrid
  - Gesellschaft Deutscher Chemiker lecture at Bayer, Wuppertal
  - The Stockholm Trio-UT workshop, Tokyo,
  - The 16th International Conference on Materials Chemistry, Dublin
  - The 5th International Cellulose Conference, Kyoto
  - ISWFPC-23, Venice
  - PARC
  - The Swedish network for substitution
- **Articles in the media, a selection:**
  - Kemisk tidskrift (the Swedish Chemical Journal)
  - Process Nordic (magazine)

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