2021 ANNUAL REPORT MISTRA SAFECHEM

MISTRA
The Swedish Foundation for Strategic Environmental Research

MISTRA SAFECHEM

CONTENT

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

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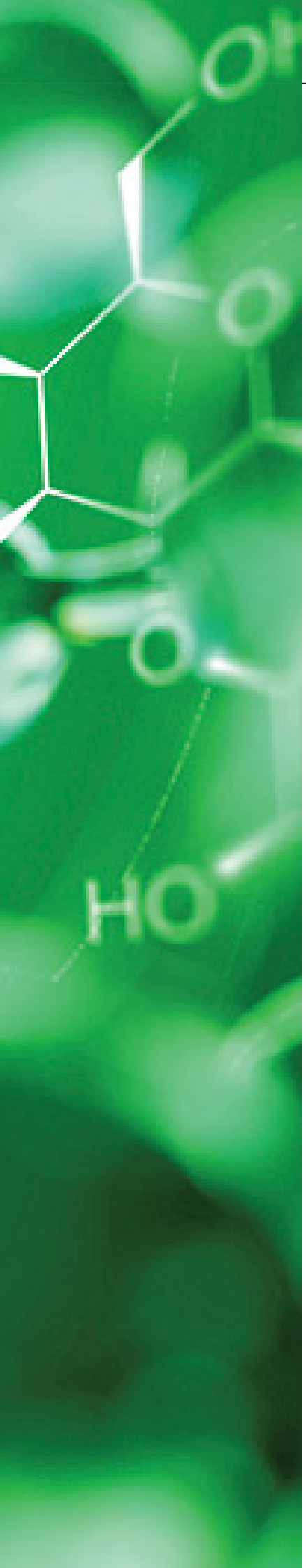


MISTRA SAFECHEM

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

PARTNERS

ACT Research · AstraZeneca · BASF We create chemistry · chemsec International Chemical Secretariat · cytiva · DTU · H&M · HOLMEN · ivl Swedish Environmental Research Institute · IKEM · KRAHNEN · KTH Vetenskap och Konst · Perstorp · RenFuel Lignin Bio Oils · RI.SE · Stockholm University · Stockholm Vatten och Avfall · Wargön Innovation · Volvo

ABOUT MISTRA SAFECHEM 2021:

A first full year of increased interaction and excellent research

Mistra SafeChem is based on the concept of green chemistry and has the overarching vision to enable and promote the expansion of a safe, sustainable, and green chemical industry in Sweden.

Through research and development, the programme aims to contribute to a reduction of hazardous chemical exposure of the human population and the environment. Key features are the advancement of safe and green industrial synthesis processes and implementing the use of a toolbox system for hazard screening, risk quantification, life cycle assessments and materials management developed within the programme.

Mutual understanding of requirements

The research programme started officially at the beginning of 2020, but due to delays caused by the covid-19 pandemic, practical work didn't start until the autumn of 2020. Hence, by the end of 2021, the first full calendar year of the programme came to an end.

We in the programme lead are very happy to see all the excellent research carried out in the programme. Not only in the initially planned research fields within each work package, but also in the transdisciplinary case studies where researchers and industrial partners collaborate to advance the research by testing and refining tools and methods developed in the programme. These interactions increase our understanding of each other's requirements and challenges, as well as knowledge about what can be learnt regarding safety and sustainability already in the design phase of a chemical or material. During the year several new collaboration activities were identified which resulted in an expansion of the programme's transdisciplinary case studies by 3 MSEK (read more on pages 8 and 16-17).

A real milestone during the year was the possibility

for all partners to meet and greet in person at a programme conference (read more on page 9).

A new strong partner

By the end of 2021 one additional industrial partner was affiliated to Mistra SafeChem. Cytiva, based in Uppsala and a global provider of life science technologies and services, joined the programme with the research aim of expanding the hazard prediction toolbox to also include reactive intermediate in chemical synthesis. This research activity is a valuable addition as the potential hazards of reactive chemicals are a common challenge for many chemical producers and material manufacturers.

In line with the EU chemicals strategy

Looking outside the Mistra SafeChem programme, the advancement of implementing the EU chemical strategy for sustainability proceeded during 2021. Many of the key elements in the strategy are well aligned with the aims and plans for the research in Mistra SafeChem. An interesting point is that the strategy also includes initiatives to ensure how safe and sustainable chemicals and materials can contribute to the Green Deal and the necessary transformations to a climate neutral and sustainable society. The implementation of the strategy has begun in 2021 and expert groups and consultation processes have been initiated as well as plans for EU-funded research on topics relevant to the strategy.

The programme made an initial analysis of where and how the programme can contribute to the implementation of the strategy. This analysis along with general information about the strategy was in February presented and discussed at a breakfast seminar arranged in cooperation with SusChem Sweden.

John Munthe, IVL Swedish Environmental Research Institute, Programme Director

Richard Lihammar, IVL Swedish Environmental Research Institute, Programme Manager

Hanna Holmquist, IVL Swedish Environmental Research Institute, Deputy Programme Manager

2021 in numbers

For those of you who like numbers the following list can in part summarize Mistra SafeChem in 2021:

92 researchers and industry representatives active in the programme

21 scientific articles published

16 news articles published on the website

4 new case studies launched

4 programme forums

3 external seminars on programme tools and green chemistry

2 research student group meetings

1 programme conference with external attendees

CHAIRMAN OF THE BOARD:

Activities are at full speed

The board is very pleased by how Mistra SafeChem develops.

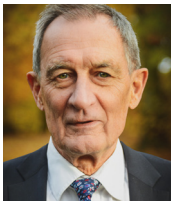
The activity is high in all the work packages and what is particularly satisfactory is to see how different work packages have started to interact with each other. Collaboration between groups with different research focuses may result in outcomes that are novel and sometimes groundbreaking.

At its last meeting during 2021, the board was given the difficult task to prioritize among research proposals that would receive funding from the programme reserve. There were many good proposals – more than what could be funded – and the majority involved joint work between two or more work packages. The programme management has evidently succeeded in fostering collaborations between research groups.

The conference in November 2021 was the first large gathering of all people involved in the programme. We, the board, were pleased by what we saw and heard.

The activities are now running at full speed. The future looks bright.

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



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 report to the Programme board.

Research partners

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

Industry partners

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

Running time

December 2019 – June 2024

Financier and budget

In total 101 MSEK

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

Work packages

- **WP1:** Programme management, WP coordination and communication
- **WP2:** A vision and agenda for green and sustainable chemistry
- **WP3:** Hazard and risk screening – early warning and proactivity
- **WP4:** Design and management of chemicals, materials and processes
- **WP5:** Life cycle assessment and management
- **WP6:** Case studies

Programme board

Presented as standing in the picture above:

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

Krister Holmberg
Professor Emeritus, Chalmers (Chair)

Anna Wiberg
Celluxtreme (former Programme manager, BioInnovation)

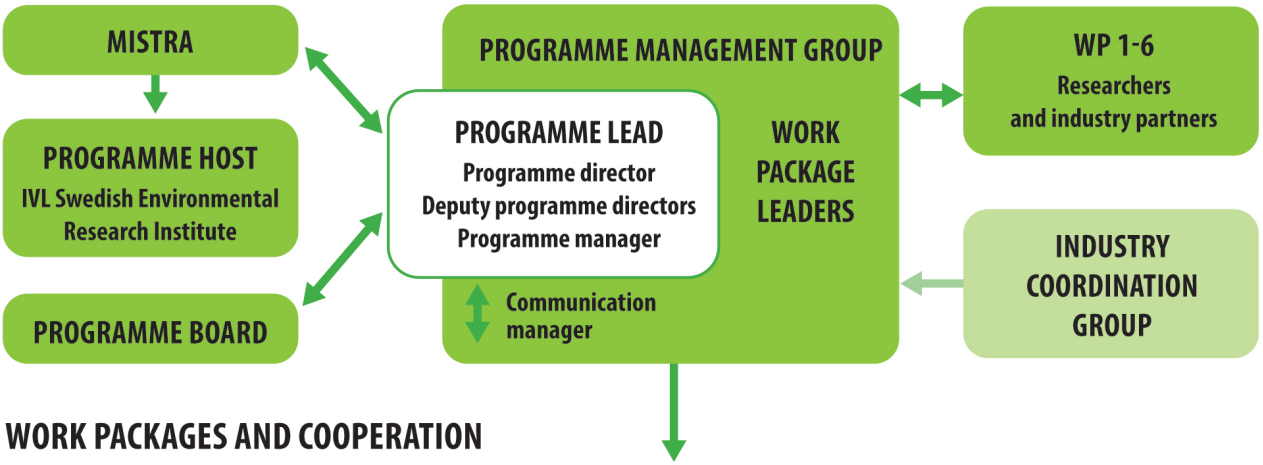
Per Ängquist
Director General, Swedish Chemicals Agency

Malin Lindgren
Programmes Director, Mistra (co-opted)

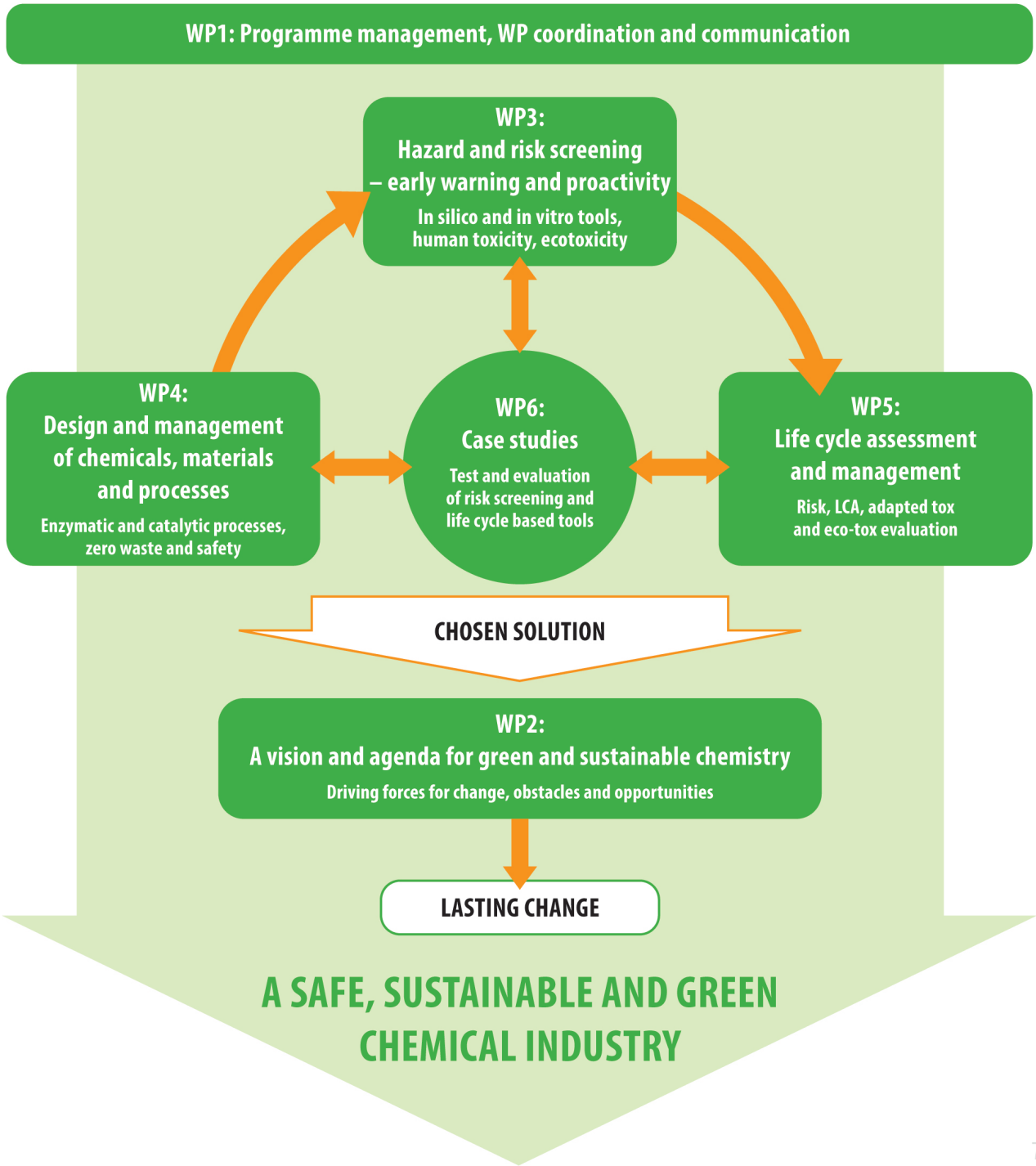
Patrik Andersson
Professor, Umeå University

Therese Jacobson, Swedish Society of Nature Conservation, left the board during the year.

ORGANISATION OF MISTRA SAFECHEM



WORK PACKAGES AND COOPERATION



SEVERAL NEW CASE STUDIES STARTED

Interaction is the best way forward

In Mistra SafeChem case studies have emerged as a most efficient way forward to ensure interactions within the complex programme. In case studies transdisciplinary research is created which is needed to reach the programme vision to enable and promote the expansion of a safe, sustainable and green chemical industry in Sweden.

In the case studies, the toolbox of new methods for hazard screening, risk quantification, life cycle assessments and materials management is applied to test and evaluate specific processes' adherence to the green chemistry principles and sustainability. Methods for analytical screening of chemicals of emerging concern are being refined and applied for different materials and media.

As of 2021 a wide variety of case studies are executed. The two initially planned cover chemical substitution in materials in consumer use. During the year studies were added focusing on development in catalysis, recycling and resourcing to biobased materials.

Pedro Tortajada Palmero, Stockholm University, introducing a new chemical reaction to Therese Kärnman, IVL Swedish Environmental Research Institute.

Herein we look into two of the new case studies in detail: **The sustainability assessment of a novel hydrogenation reaction process** and **Biocatalytic routes to amides for safer and more sustainable by design in discovery chemistry**.

A new hydrogenation reaction process

The sustainability assessment of a novel hydrogenation reaction process has its focus on electrochemical proton reduction over nickel foam as an alternative to the use of noble metals, i.e. palladium, for the hydrogenation reaction. The use of earth-abundant metals hold promise with regards to issues with resource scarcity, but the novel reaction has the potential to also reduce the need for fossil-based hydrogen production and transportation due to *in situ* hydrogen generation.

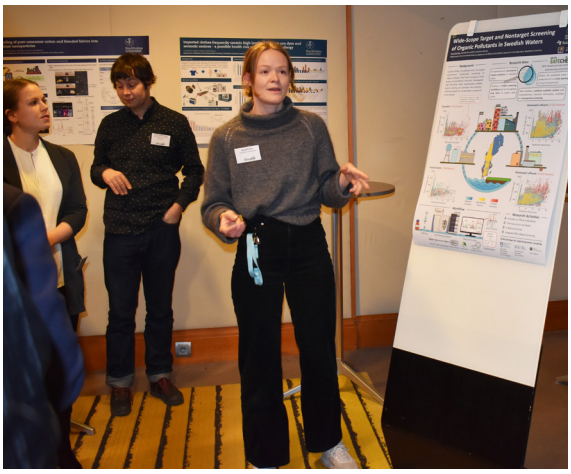
In this case study, the Mistra SafeChem toolbox is applied to explore if a nickel foam catalysed hydrogenation of alkenes to alkanes has an improved environmental and human health performance compared to a scenario where the conventional technique is applied. The toolbox is applied in an iterative process starting from hazard and exposure assessment for the chemicals in the reaction process, a screening life cycle assessment (LCA) with a broad scope in impact categories and a global material flow analysis (MFA) for nickel and palladium. The LCA is currently being extended with additional focus on chemical footprint and upscaling of the process.

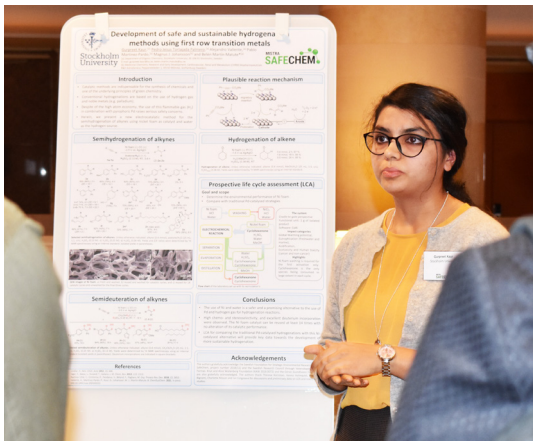
Biocatalytic routes

The formation of amide bonds is an important transformation in the production of organic molecules. Amides are used in a wide range of fields, and as a synthetic intermediate product. The classical synthetic method to produce amides using harsh chemical routes has many drawbacks, one is the generation of large quantities of waste. Also, some of the activating agents are not environmentally friendly.

One alternative route to acquire the amide functionality would be to use biocatalysts, enzymes. Research has reported that biocatalytic reactions using engineered enzymes would be highly competitive for large scale production of pharmaceuticals in terms of efficiency and sustainability. To assess if these benefits exist also for amide bond synthesis a case study is conducted.

The Mistra SafeChem toolbox is applied to explore if products are safe and more sustainable. Extensive amounts of amide containing molecules, important for the pharmaceutical industry, have been identified and the molecules are assessed using the *in silico* model for hazard prediction, developed within the programme, to identify safe building blocks. Life cycle thinking is applied to avoid potential burden shifting from one impact to another and an LCA is planned for an upscaled process for biocatalyst production.





At the programme conference the participants in Mistra SafeChem finally got to meet, both each other and external guests.
The research students gave poster presentations of their work, among them May Britt Rian (upper right) and Gurpreet Kaur (lower left).

COMMUNICATION AND DISSEMINATION

Personal chemistry – at last!

Like all other work in Mistra SafeChem, communication and dissemination have accelerated in 2021.

A real milestone was the possibility to meet and greet in person at the programme conference in Stockholm in November. For readers of this annual report in the far future, this might not sound like a milestone, but for 2021, a year that was characterized by several covid-19 related restrictions and digital meetings, this was a well-needed event.

Half of the conference was open to external participants, but due to the contagion situation, only around 20 people came. More than 60 people from the programme took part.

All work packages as well as the PhD students enrolled in the programme gave an update on the progress of the research. A panel discussion on how to reach the programme vision was held where many valuable insights were shared and discussed.

The programme has started a series of breakfast webinars, mainly aimed at the Swedish chemical industry, where scientists and industry partners from the work packages talk about their mutual work. The first two were held in the autumn of 2021. The title **Green and sustainable chemistry** attracted around 80 listeners, and **Screening tools for safe-by-design chemistry** drew 65 people. Three more webinars are planned for the spring of 2022.

The website mistrasafechem.se, which had more than 500 visitors each month in 2021, is regularly updated with news from the programme. The news published on the web is summarized in newsletters. During the year five newsletters were sent out, and several posts on social media were made that drew further attention to the work.

Ragnhild Berglund,
IVL Swedish Environmental Research Institute,
Programme Communicator

WORK PACKAGE 2: A VISION AND AGENDA FOR GREEN AND SUSTAINABLE CHEMISTRY

A framework to illustrate challenges for the chemical industry in Sweden

The research in WP2 is aimed at developing a conceptual framework for green and sustainable chemistry in Sweden and to identify future challenges for research and innovation in chemical industry and value chains. WP2 will also evaluate potential needs for adaptation of the chemical regulatory system to support a shift to green and sustainable chemistry and promote education and research exchange between academia and industry.

Achievements in 2021

The work has focused on the development of a simple concept for green and sustainable chemistry relating to both the research performed in the programme and to challenges facing the chemical industry. In the current version, the concept is a simple illustration providing a common framework where all components of the research performed in the programme can be represented.

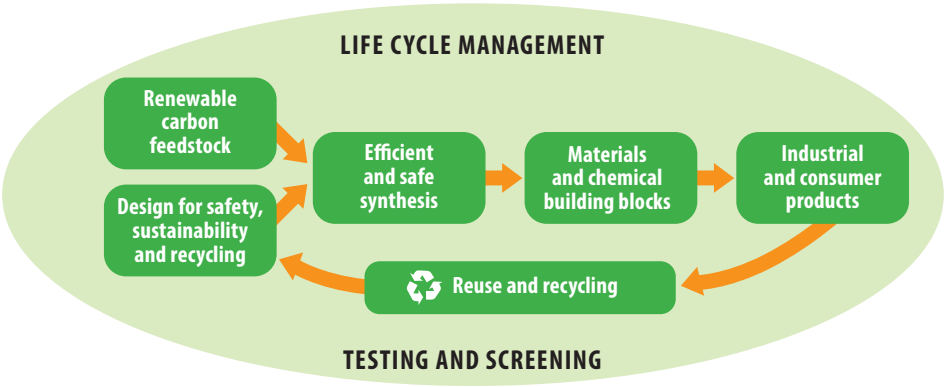
A second activity in WP2 has been to analyse how the programme can contribute to the EU's chemicals strategy for sustainability which will be implemented in the coming years. The chemicals strategy has many things in common with the 12 principles of Green Chemistry but with more focus on sustainability and a circular economy. The strategy also emphasises the role of chemicals in the Green Deal and transformation to a sustainable and climate neutral EU. The implementation plan of the strategy contains a number of critical topics which will require large efforts in research and innovation. Mistra SafeChem research can contribute significantly to this with e.g. tools for hazard screening (WP3) and life cycle assessment (WP5) as well as catalysis-based synthesis processes (WP4) and practical examples of green chemistry from industry (WP6).

In 2021, an activity to map the chemical industry and the production and use of chemicals in Sweden was initiated. The task to provide a definition of "chemicals" and "chemical industry" that is relevant to Sweden and Swedish industry, and for continued use in the Mistra SafeChem programme, proved to be very complex. Both in relation to providing clear definitions of the very diverse chemical

industry and to the task of finding relevant data and information to expand the conceptual framework to quantitative descriptions of the production, value chains and chemical flows involved. Adding to this is the inherent complexity of global chemical value chains and the lack of publicly available information.

Interaction with other WPs

WP2 has interactions with all activities in the programme by providing a concept for green and sustainable chemistry to which research in all WPs can be related. This concept will also provide a basic structure for the programme synthesis to be prepared towards the end of phase 1.



A simple concept for Green Chemistry in Sweden – and a framework to illustrate how the research performed in Mistra SafeChem contributes.

FACTS ABOUT WP2

A vision and agenda for green and sustainable chemistry

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 IVF, Stockholm University and Volvo Cars.

Activities 2021

- Surveys, data gathering and assessment
- Workshops and dialogue

WP leaders

John Munthe, IVL Swedish Environmental Research Institute

Lennart Bergström, Stockholm University

Screenings of recycled textiles, usig the analytical toolbox of WP3, revealed that they contain hundreds of compounds, including some with health and environmental concerns.

WORK PACKAGE 3: HAZARD AND RISK SCREENING – EARLY WARNING AND PROACTIVITY

Development of tools for analysis of textiles, water and much more

The main focus for WP3 is to develop tools for early assessment of hazards and risks of chemicals. The development of *in silico*, *in vitro* and analytical tools are presented for each research area.

Achievements in 2021

***In silico* toolbox:** Many computational tools were delivered and placed on a web-based server for use, including a battery of *in silico* models for endocrine disrupters, ready biodegradation, reproductive toxicity, carcinogenicity, mutagenicity, eye irritation and bioconcentration factor in fish and persistence in soil. Some models have been extended to Chemsec's SINimilarity tool for public use.

A post-doctoral position sponsored by Cytiva has been established to produce models based on quantum mechanical aspects for reactivity with respect to skin sensitization.

AstraZeneca has contributed with substance-based data from their screen libraries, which are being used to tune the various *in silico* models in the toolbox.

The models have been successfully applied to three cases in WP4 (amide bond synthesis, hydrogenation and textile processing), where they have been used to bring comparative hazard identification into decision making in their respective process designs.

The toolbox has also been applied in WP6 to the silicon-based chemistries involved in the H&M and Volvo Cars cases.

***In vitro* toolbox:** Several human toxicity end-

point models were either established or scoped for establishment. These include hepatotoxicity and mitochondrial toxicity, skin sensitization, phototoxicity and genotoxicity. Additionally, for hepatoxicity AstraZeneca has contributed with a set-up using a high content imaging assay.

On the side of ecotoxicological testing, a high throughput, high content, image-based screening platform has been installed at SciLifeLab, which has been initially applied to establishing one of the *in vitro* methods in the programme, but also expanded to human breast epithelial cells for hormone disruption assay.

Analytical toolbox: A workflow for suspect and non-target screening to identify chemicals leaching from textiles has been established and used. Analysis of clothing garments imported to the Swedish market revealed hundred chemicals from a wide range of compound classes. Nitroanilines with suspected mutagenic and possible skin sensitization properties, and quinoline, a carcinogenic compound, were among the compounds occurring at the highest concentrations, which at times came close to REACH legislation guidelines.

A similar workflow has been applied on cellulose nanocrystals made from recycled textiles and used by researchers in WP4. The screenings revealed that both the recycled textiles and the cellulose contain hundreds of compounds, including some with health and environmental concerns. However, the concentrations of identified health hazards were found to be below EU limits.

The techniques are also being applied to directed analysis of classes of contact allergens in garments such as azo dyes, arylamines and halogenated nitrobenzenes. Initial hazard assessments of identified chemicals have begun, including the use of computational tools for data gap filling.

Analytical approaches have been established for application non-target analysis of samples taken from the Volvo Cars case study in WP6. These techniques are also being applied to a project focusing on non-target and wide-scope target screening of organic pollution in Swedish waters. Wastewater and groundwater samples have been collected by The Geological Survey of Sweden and from households and wastewater treatment plants by Stockholm Vatten och Avfall.

Interaction with other WPs

Work has begun to integrate the efforts of WP3 and WP5 more closely, particularly in the area of the flow of digital information from hazard assessment into appropriate LCAs in the case and process studies in WP4 and WP6.

FACTS ABOUT WP3

Hazard and risk screening – early warning and proactivity

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 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, RISE IVF, Stockholm University. Four PhD students and one postdoc.

Activities

- Computational toolbox expanded with new toxicity, physicochemical and dispositional predictive tools, access provided via web-based interface. Cytiva postdoc recruited.
- Analytical tools for non-target and suspect screening established and matched to case and process study demands.
- Computational tools and analytical approaches established for WP6 cases and WP4 workstreams.
- Data generated and comparative hazard assessments begin to steer decisions in alternatives selection and process development.
- Work begun concerning the flow of digital information in hazard assessments into LCA in WP5.

WP leaders

Ian A Cotgreave, RISE

Magnus Breitholtz, Stockholm University

In the search of more sustainable processes, electrochemistry offers a tool which can enable greener and safer reactions for organic chemistry.

WORK PACKAGE 4: DESIGN AND MANAGEMENT OF CHEMICALS, MATERIALS AND PROCESSES

Progress is made in replacing scarce metals and fossil resources

In WP4, researchers in organic and inorganic chemists aim to develop novel reactions, processes and materials to be used in green and sustainable chemical production.

Achievements in 2021

One focus is the replacement of catalysts based on scarce metals by abundant metals i.e. iron (Fe), copper (Cu) and nickel (Ni). The team has developed a method to access complex organic molecules using a nanocopper catalyst immobilized on cellulose, instead of a palladium (Pd) catalyzed method. A further contribution has been in the field of hydrogenation of organic molecules which is an extremely important reaction for the chemical industry. A new method has been found using a Ni catalyst instead of Pd. The reaction can use water as a reductant, instead of the typical hydrogen gas, derived from fossil resources. These ways of synthesizing organic molecules are currently being assessed in terms of LCA and toxicology.

Within the area of catalysis, work has been performed in close collaboration with AstraZeneca on the late-stage functionalization of different drugs. Drug analogues were prepared in a single synthetic step, instead of embarking on individual full synthesis routes, thus saving enormous amounts of chemicals. The studies were facilitated by automated testing via high throughput screening.

Progress has also been made towards the use of

enzymes as catalysts for the synthesis of chemicals. Chemoenzymatic routes for upcycling of wood-based side-streams into sustainable advanced functional materials were developed. Major progression in designer enzymes allowed the generation of circular polyesters from wood-derived side streams. Also, significant progress in safe and sustainable amide bond chemistries were achieved.

Towards developing green chemical processes for fine particle recovery and reuse, a recently developed nanoscale spectroscopic method has been used and applied for soot nanoparticles generated in motor oil. This is an important step for identifying chemical hazards in lubricants. This has also given a reference for developing green systems for biobased-coatings and nanoparticle substitutes. To achieve this, WP4 has studied the depolymerization of lignin using electrochemistry and applying green chemistry metrics.

WP4 has made a lot of progress in the recycling of textile and forest residues to produce chemicals and cellulose nanocrystals. One study has demonstrated the reductive catalytic fractionation of hemp hurd to produce a bio-oil and a cellulose fraction, which can be used as raw material for textile. Another method enables the conversion of beetle infected spruce to produce dissolving grade pulp.

Also, a methodology to depolymerize PET plastics that potentially could be applied to polycotton fabrics has been developed and the route has been assessed by LCA, life cycle assessment. In the area of textiles recycling, a route to isolate cellulose nanocrystals from cotton waste has been developed. Their morphology, thermal, and colloidal properties were statistically equivalent and were found to be indistinguishable from cellulose made from virgin cotton, despite the presence of residual impurities. The initial findings based on non-targeted screening also show that the residual impurities were at trace levels.

Interaction with other WPs

Close collaborations with WP3 and WP5 are going on. In the subarea of green and sustainable catalysis, LCA and toxicology studies are in progress, also together with AstraZeneca and DTU.

Collaborations between KTH, Astra Zeneca, IVL and RISE have resulted in a library of pharmaceutically relevant compounds with predicted minimal toxicity to humans and the environment. Experimental evaluation and validation of green synthesis routes by enzymes are ongoing.

Collaboration with WP3 for non-targeted screening of nanocellulose from textiles and LCA in collaboration with WP5 on crystalline nanocellulose processing from textile waste is ongoing.

FACTS ABOUT WP4

Design and management of chemicals, materials and processes

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

AC2T Research, AstraZeneca, Holmen, Krahnen, KTH, Perstorp, RenFuel, Stockholm University, Wargön Innovation. Six PhD students and four postdocs.

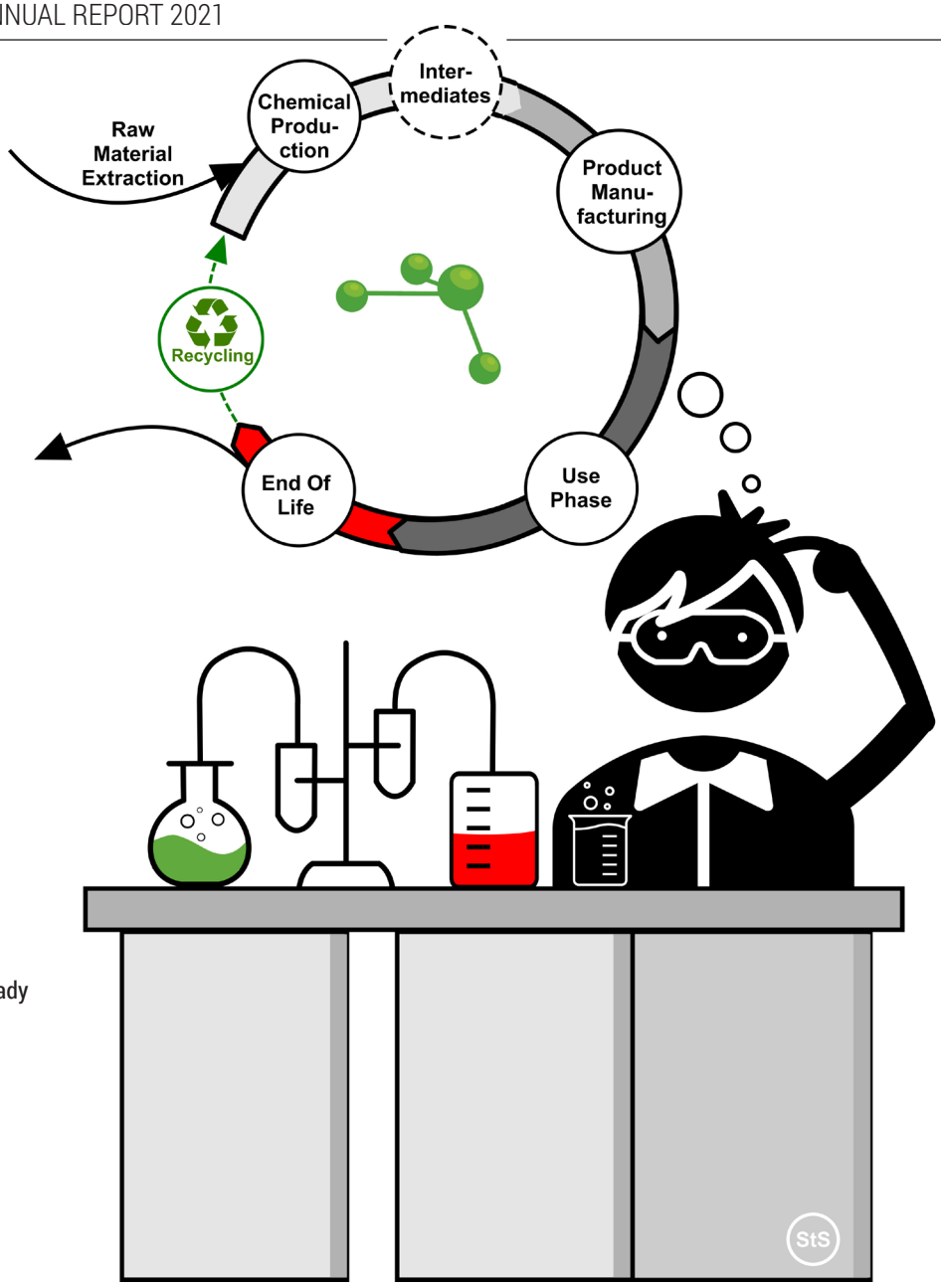
Activities

- Developed an oxidative toolbox to valorize biomass into new green building blocks and polymers.
- Significant progress in the development of designer enzymes for sustainable amide-bond formation.
- Developed a reduction method using a Ni catalyst and water as the hydrogen source.
- Developed methods for the late-stage functionalization of drugs.
- Carried out a nanoscale spectroscopic study on carbon soot particles from industrial engines.
- Biodegradable and toxicological aspects benchmarking of biobased coatings was stablished.
- Cellulose nanocrystals with over 97 percent purity successfully isolated from cotton textile blends, and the process was evaluated using non-targeted screening.
- PET and acrylics isolated from textile waste without significant decrease in molecular weight.
- Developed a carbocyclization with first row metal nanoparticles on cellulose and carried out LCA.
- Developed a metalloenzymatic deracemization of amines with cellulose as an artificial plant cell wall.

WP leaders

Belén Martin-Matute, Stockholm University

Per-Olof Syrén, KTH



An important part of WP5 is to make the inclusion of life cycle thinking possible already in the design phase.

WORK PACKAGE 5: LIFE CYCLE ASSESSMENT AND MANAGEMENT

LCA training for all partners has facilitated transdisciplinary research

In the WP5 work in 2021, focus lay on the development of a life cycle based chemicals assessment toolbox with associated guidelines. This toolbox can be applied to chemical alternatives assessment, chemical footprints and life cycle assessment (LCA).

Achievements in 2021

During 2021 WP5 activities intensified, and work is now ongoing in all tasks of the WP.

The life cycle based chemicals assessment toolbox was further advanced during the year, with focus on two life cycle impact assessment (LCIA) models for toxicity characterization, USEtox and ProScale Recommendations for the exposure and toxicity characterization of chemical emissions and chemicals in products in the USEtox model was published. Herein consumer exposure and emission-based exposure was combined in a matrix system, integrating far-field and near-field exposure. A probabilistic dose-response approach for toxic effects, combined with a decision tree for identifying reliable points of departure for non-cancer effects was also implemented. Peer-reviewed articles reporting on results from the use of this further advanced model rendered large media attention.

ProScale (E) models were further advanced via a case study on indoor paint adapted to fit the EU Product Environmental Footprint concept and by the development of normalization scores. Both impact assessment models, USEtox and ProScale, were applied in case studies (see further below).

The PhD project "Advancing life cycle based chemical toxicity characterization through digitalization", a collaborative effort between DTU and IVL, hosted by DTU, was started. In the PhD project there are strong interactions with WP3. A structured inventory of LCIA data gaps and potentially applicable digitalization techniques is ongoing. This includes the definition and evaluation of criteria to derive data gap importance and characterize machine learning algorithms for their appropriateness to address given data gaps. In addition to this PhD project, students have been engaged in the WP's research via internships at IVL and master level LCA course work at DTU.

Results of the research in WP5 have been disseminated via conference participation at Setac Europe and Eurotox and by the publication of a number of articles as well as news stories on the programme website.

Interaction with other WPs

To facilitate interactions and transdisciplinary research within the programme, LCA training was offered to all partners in a workshop series. These workshops were highly appreciated by the many programme participants not familiar with LCA and gave good stepping stones on the route to scoping the life cycle based assessments in the programme-wide case studies.

During the year, WP5 experts have been involved in both industrial and academic case studies in WP4 and WP6 to incorporate life cycle thinking in general, and for chemicals in particular, by applying the life cycle based chemicals assessment toolbox.

A joint working group between WP5 and WP3 was formed to facilitate data transfer between the WPs. The aim is to map and identify data needs in a life cycle based chemicals assessment toolbox that could be filled by *in silico* data generation.

As part of the PhD project on digitalization, there are close interactions between WP5 and WP3 in the mapping and joint development of digitalization tools for application in LCA. Collaboration is currently focused on the criteria evaluation for the machine learning algorithm characterization mentioned above. In parallel, suitable candidates for priority gaps with large available data sets have been identified, of which one will be selected to train and compare different machine learning algorithms.

FACTS ABOUT WP5

Life cycle assessment and management

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/ProScaleE 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 build a database compiling 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, Perstorp, RISE IVF, Volvo Cars. One PhD student.

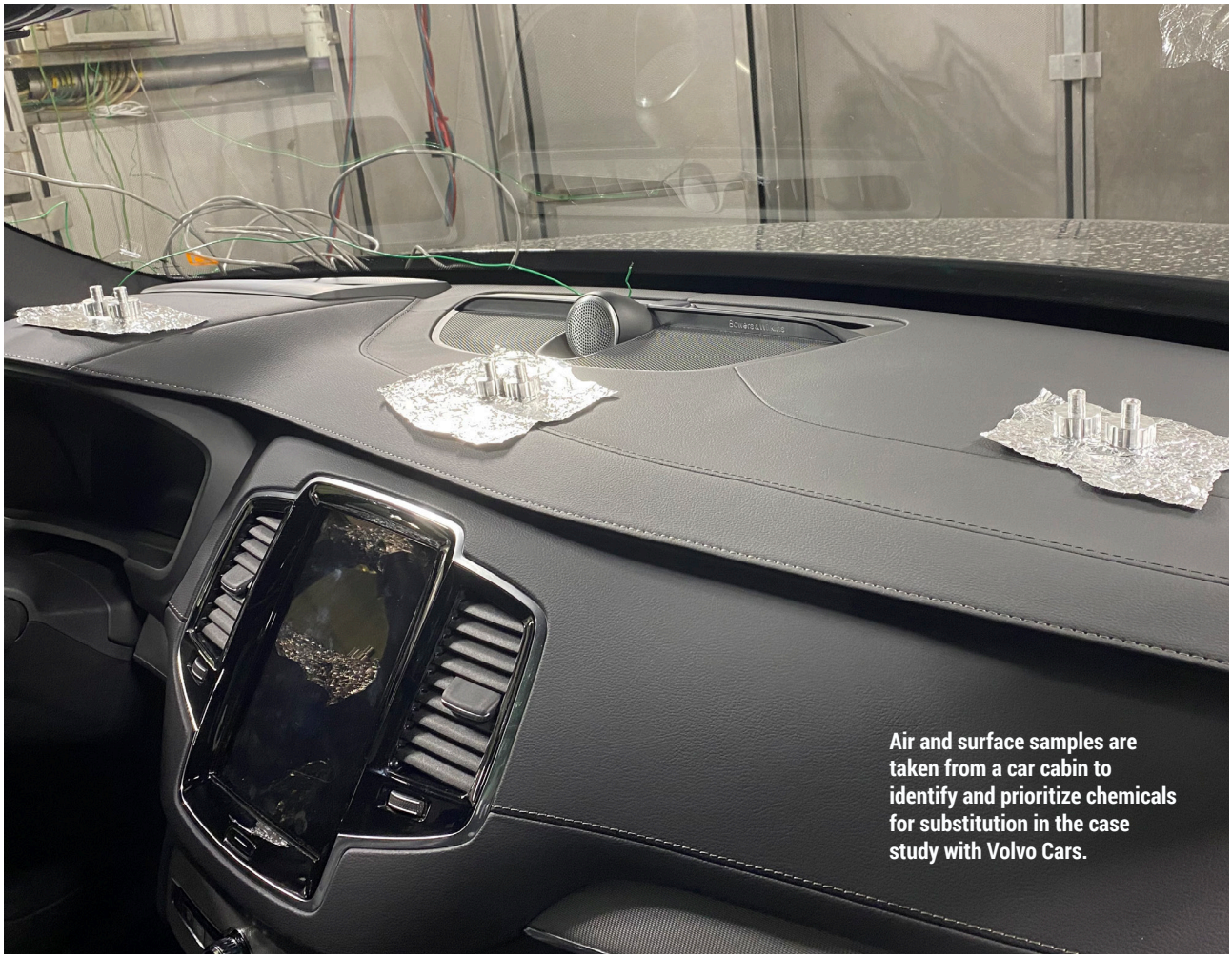
Activities

- Inter/intra WP coordination
- Workshops and training on the life cycle based toolbox and its individual elements
- Application of the life cycle based toolbox in case studies
- Advancement of data and models within the toolbox

WP leaders

Hanna Holmquist, IVL Swedish Environmental Research Institute

Anna-Karin Hellström, RISE IVF



Air and surface samples are taken from a car cabin to identify and prioritize chemicals for substitution in the case study with Volvo Cars.

WORK PACKAGE 6: CASE STUDIES

Tools and workflows are evaluated in challenging scenarios

In WP6 of Mistra SafeChem, the tools and workflows developed in the different work packages are brought together and evaluated with the use of real scenario challenges. Feedback is collected on how they perform, how they match the needs of the industry and how they can be developed further. Overall, the goal of WP6 is to offer a platform for collaboration for both existing and new partners.

At the end of 2021, WP6 includes both larger case studies planned since the start of the program, as well as a series of smaller case studies developed during the year.

Achievements in 2021

In 2021, work has successfully started in the two initial case studies with Volvo Cars and H&M.

In the case study with Volvo Cars, air and material samples were taken from a car cabin for targeted analysis. Also, a mapping was made to enable assessments of alternative plasticizers. Finally, work has started on the generation of toxicological and ecotoxicological data using the *in silico* toolbox in WP3 and an evaluation on how the LCIA toxicity impact assessment modelscould best be used within the case study.

In the case study with H&M, a life cycle based impact mapping of silicones in personal care products has been performed to identify possible concerns with silicones in production-, use- and end-of-life phase. A modelling approach was used to approximate the extent of silicone emissions and environmental accumulation for the European population. In addition, a list of 120 possible alternatives

to the targeted silicones have been compiled and a first screening has been done in terms of human and ecotoxicity using *in silico* models from WP3. A small perception study has been performed to investigate perceptual differences between commercial foundations with and without silicones.

Four new case studies were launched during 2021, in collaboration with WP3, 4 and 5.

One of them has the aim to compare conventional synthesis with bio-catalysis for the production of amide containing substances. Another of the case studies is working on a sustainability assessment of a novel hydrogenation reaction process. In this case study hazard and exposure assessment, material flow analysis and life cycle assessment are combined to explore the environmental and human health performance of the novel process. These two case studies are further described on page 8.

The third is focusing on engine oils, in which an assessment is performed of reference values with respect to toxicity and biodegradability to subsequently apply biobased substitutes. This will be done using green chemistry metrics.

And in the fourth case study, the different raw materials and process routes in making nanocellulose from recycled textiles will be compared in terms of toxicity and environmental impacts estimated using a screening LCA from cradle-to-gate.

Progress has also been made on the planning of the third of the larger case studies in collaboration with Perstorp. This will be started in 2022 and will focus on including green chemistry principles early in the development of a new chemical process, covering the modelling of chemical processes for upscaling, the generation of toxicological and ecotoxicological parameters for the chemical of interest and potential breakdown products and prospective LCA under different scenarios.

Interaction with other WPs

Interaction with the other WPs is essential for WP6. In 2021, as the initial case studies progressed and new needs and possibilities were identified, the interaction increased further. Now each of the case studies has a core team in which representatives from WP3, 4 and 5 are included to ensure input from all work packages.

The interaction with WP4 has also increased significantly in 2021 with the launch of the four new case studies. Here, WP3 and WP5 use their toolbox to help analyse the sustainability of the processes and new scenarios developed in WP4. This enables WP3 and WP5 to use and develop their tools and workflows further in new scenarios. WP6 plays a coordinating role in this work.

FACTS ABOUT WP6

Case studies

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 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.

Activities

- Case study 1: Indoor air quality – materials inside the car that do not cause health effects. In collaboration with Volvo Cars: Task development, initial sampling campaign of the car cabin, mapping of alternative plasticizers, data generation using WP3 toolbox, start of work on USEtox and ProScale from WP5.
- Case study 2: Cyclosiloxanes and silicones in cosmetics. In collaboration with H&M: life-cycle-based impact mapping of silicones in personal care products, modelling of silicone emissions and environmental contamination in Europe, mapping of alternatives to targeted silicones, initial screening for human and ecotoxicity using the WP3 toolbox, perception study of foundations with and without silicones.
- Development of a new case study in collaboration with Perstorp focusing on including green chemistry principles early in the development of a new chemical process
- Development and launch of four new case studies focusing on the research topics in WP4, in which WP6 plays a coordinating role.

WP leaders

Dämien Bolinius, IVL Swedish Environmental Research Institute

Lisa Skedung, RISE

We asked some of the Mistra SafeChem industry partners why they decided to join the programme.

MISTRA SAFECHEM INDUSTRY PARTNER

AC2T research GmbH

The recent progress in tribology-related research demonstrated a significant positive influence on the environmental impact of numerous chemo-mechanical machinery parts and technologies. Significant energy losses due to friction process and wear formation stay in the focus of the system optimisation, circularity principles and progressive pollution reduction practices.

Participation in the Mistra SafeChem gives us a unique opportunity to be a part of an interdisciplinary team working on a deeper understanding of the wear mechanisms and impacts of the particle-related issues onto stability and life cycle of mechano-chemical transformations. Expected results will help us to formulate the crucial issues towards green tribology and improve the overall sustainability of the materials and processes.

AC2T research participates in a case study related to the formation of degradation products over the operation period of the lubricant operation at the same time trying to evaluate environmental and toxicity aspects as an important part of life cycle assessment.

Serhiy Budnyk
Senior Scientist,
Sustainable Lubrication,
AC2T research GmbH

MISTRA SAFECHEM INDUSTRY PARTNER

Cytiva

Cytiva has substantial out-reach in the biotech industry and the flexibility of Mistra SafeChem's platform can both meet national demands and add to long-term stability. Bringing green and sustainable approaches to Cytiva's chemical processes will have a considerable impact on an entire web of biotech infrastructure.

By imparting the approaches from the Mistra SafeChem platform into the workings of Cytiva, particularly in terms of coupled hazard screening and LCA aspects, the company will be able to propagate the approaches internally for maximum effect and sustainability.

Cytiva wants to further reduce the toxicity of some of the chemicals used in our manufacturing processes. One of the first steps is to identify alternative "green" chemicals. The requirement that the substitutes remain "green" in the future is crucial for the initiative. Therefore, the development of a framework for early prediction and verification of potentially dangerous properties is of utmost interest to Cytiva.

Ismet Dorange
Research and Development Manager,
Cytiva

MISTRA SAFECHEM INDUSTRY PARTNER

IKEM

Chemistry is used in all value chains. More than 96 percent of the products placed on the market depend on chemicals. The chemical industry has a large responsibility, but also a huge possibility to help value chains throughout the society to become climate neutral, circular and sustainable. Only by means of chemistry can we reach our highly ambitious climate targets.

The most effective way to substitute chemicals of concern is to facilitate the development of new, safe and sustainable chemicals. To succeed, there is a need for a holistic approach where the chemical industry, downstream users and academia collaborate to increase the use of renewable carbon stock, make production processes more energy and atom efficient, reduce costs and increase speed and accuracy for non-animal testing methods, as well as increase uptake in the value chains.

IKEM gather Swedish companies that are producing or using chemistry in a wide sense. We believe Mistra SafeChem is well equipped to contribute to the development of safe and sustainable chemistry in Sweden, and IKEM is committed to contributing to this common goal through our engagement in WP2.

Kristina Neimert Carne
Head Chemicals Policy,
IKEM,
Innovation and Chemical Industries in Sweden

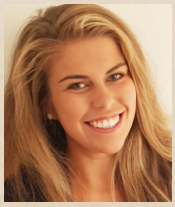
MISTRA SAFECHEM INDUSTRY PARTNER

RenFuel

RenFuel is a small and innovative company dedicated to developing green and sustainable solutions to the plastics industry and refinery industry. As a start-up within green chemistry and technology, we believe that Mistra SafeChem is an excellent programme to participate in to develop strategic connections and collaborate regarding the challenges and opportunities as a smaller player in the green transition of society.

Mistra SafeChem provides us with a useful platform to accelerate the development of our technology on the topic of sustainability. RenFuel is currently drafting a case study of our lignin-based polymer Lignisol®. The purpose of the case study is to enable early-stage screening for eco-toxicological effects of potential formulations using tools under development within the programme.

As a participant in Mistra SafeChem, we see that there are multiple valuable opportunities of collaboration in a network of both highly competent academic groups and companies in various industries.



Clara Pierrou
Business Development Manager,
RenFuel

DELIVERABLES 2021

Scientific publications 2021

Work package 4

• **Thersleff, T., Jenei, I. Z., Budnyk, S., Dörr, N., Slabon, A.** (2021) Soot Nanoparticles Generated from Tribofilm Decomposition under Real Engine Conditions for Identifying Lubricant Hazards. *ACS Applied Nano Materials*, 4, 220

• **Budnyak, T. M., Onwumere, J., Pylypchuk, I. V., Jaworski, A., Chen, J., Rokicińska, A., . . . Slabon, A.** (2021) LignoPhot: Conversion of hydrolysis lignin into the photoactive hybrid lignin/Bi4O5Br2/BiOBr composite for simultaneous dyes oxidation and Co2+ and Ni2+ recycling. *Chemosphere*, 279, 130538

• **Budnyak, T. M., Vlasova, N. N., Golovkova, L. P., Markitan, O., Baryshnikov, G., Ågren, H., & Slabon, A.** (2021) Nucleotide Interaction with a Chitosan Layer on a Silica Surface: Establishing the Mechanism at the Molecular Level. *Langmuir*, 37, 1511

• **Weis, E., Hayes, M. A., Johansson, M. J., & Martín-Matute, B.** (2021) Iridium-catalyzed C− H methylation and d3-methylation of benzoic acids with application to late-stage functionalizations. *Iscience*, 24, 102467

• **Bermejo-López, A., Carrasco, S., Tortajada, P. J., Kopf, K. P., Sanz-Marco, A., Hvid, M. S., ... & Martín-Matute, B.** (2021) Selective Synthesis of Imines by Photo-Oxidative Amine Cross-Condensation Catalyzed by PCN-222 (Pd). *ACS Sustainable Chemistry & Engineering*, 9, 14405

• **Martín-Matute, B., Meier, M. A., Métro, T. X., Koenig, S. G., Sneddon, H. F., Sudarsanam, P., & Watts, P.** (2021) Sustainable Chemistry and Engineering in Pharma. *ACS Sustainable Chemistry & Engineering*, 9, 13395

• **Weis, E., Johansson, M. J., & Martín Matute, B.** (2021) Late Stage Amination of Drug Like Benzoic Acids: Access to Anilines and Drug Conjugates through Directed Iridium Catalyzed C–H Activation. *Chemistry–A European Journal*, 27, 18188

• **Li, M. B., Yang, J., Yang, Y., Xu, G. Y., Luo, G., Yang, J., & Bäckvall, J. E.** (2021) Amino Supported Palladium Catalyst for Chemo and Stereoselective Domino Reactions. *Angewandte Chemie*, 133, 680

• **Li, M.-B., & Bäckvall, J.-E.** (2021) Efficient Heterogeneous Palladium Catalysts in Oxidative Cascade Reactions. *Accounts of Chemical Research*, 54, 2275

• **Deiana, L., Rafi, A. A., Naidu, V. R., Tai, C. W., Bäckvall, J. E., & Córdova, A.** (2021) Artificial plant cell walls as multi-catalyst systems for enzymatic cooperative asymmetric catalysis in non-aqueous media. *Chemical Communications*, 57, 8814

• **Posevins, D., Bermejo López, A., & Bäckvall, J. E.** (2021) Iron Catalyzed Cross Coupling of Propargyl Ethers with Grignard Reagents for the Synthesis of Functionalized Allenes and Allenols. *Angewandte Chemie*, 133, 22352

• **Hilker, S., Posevins, D., Unelius, C. R., & Bäckvall, J. E.** (2021) Chemoenzymatic Dynamic Kinetic Asymmetric Transformations of β Hydroxyketones. *Chemistry–A European Journal*, 27, 15623

• **Kong, W. J., Reil, M., Feng, L., Li, M. B., & Bäckvall, J. E.** (2021) Aerobic Heterogeneous Palladium-Catalyzed Oxidative Allenic C–H Arylation: Benzoquinone as a Direct Redox Mediator between O2 and Pd. *CCS Chemistry*, 3, 1127

• **Schriever, K., Saenz-Mendez, P., Rudraraju, R. S., Hendrikse, N. M., Hudson, E. P., Biundo, A., . . . Syrén, P.-O.** (2021) Engineering of Ancestors as a Tool to Elucidate Structure, Mechanism, and Specificity of Extant Terpene Cyclase. *Journal of the American Chemical Society*, 143, 3794

• **Stamm, A., Öhlin, J., Mosbech, C., Olsén, P., Guo, B., Söderberg, E., ... & Syrén, P. O.** (2021) Pinene-Based Oxidative Synthetic Toolbox for Scalable Polyester Synthesis. *JACS Au*, 1, 1949

• **Muangmeesri S., Li, N., Georgouvelas, D., Ouagne, P., Placet, V., Mathew, A. P., Samec, J S. M. S.** (2021) Holistic Valorization of Hemp through Reductive Catalytic Fractionation. *ACS Sustainable Chem. Eng.* 9, 51, 17207

Work package 5

• **Holmquist, H., Roos, S., Schellenberger, S., Jönsson, C., & Peters, G.** (2021) What difference can drop-in substitution actually make? A life cycle assessment of alternative water repellent chemicals. *Journal of Cleaner Production*, 329, 129661

• **Aurisano, N., Huang, L., Milà i Canals, L., Jolliet, O., & Fantke, P.** (2021). Chemicals of concern in plastic toys. *Environment International*, 146, 106194

• **Fantke, P., Chiu, W. A., Aylward, L., Judson, R., Huang, L., Jang, S., . . . McKone, T.** (2021) Exposure and toxicity characterization of chemical emissions and chemicals in products: global recommendations and implementation in USEtox. *The International Journal of Life Cycle Assessment*, 26, 899

• **Fantke, P., Cinquemani, C., Yaseneva, P., De Mello, J., Schwabe, H., Ebeling, B., & Lapkin, A. A.** (2021) Transition to sustainable chemistry through digitalization. *Chem*, 7, 2866

• **Aurisano, N., Weber, R., & Fantke, P.** (2021) Enabling a circular economy for chemicals in plastics. *Current Opinion in Green and Sustainable Chemistry*, 31, 100513.

PhD Thesis

• **Valiente Sánchez, A**. (2021) Catalytic and Electrocatalytic Transformations with Palladium and Nickel : Scope and mechanistic investigations *(Department of Organic Chemistry, Stockholm University)*

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