Toxikologiska rådet
– expertorgan för rådgivning och samråd i toxikologiska frågor

The Toxicological Council
– body of experts for advice and consultation on toxicological issues

REPORT 1/24

Toxicological Council Annual report 2024

Preface

The Toxicological Council is an expert organization whose task is to facilitate rapid identification of chemical substances that may be harmful to human health or the environment. The Toxicological Council identifies and evaluates signals of new and emerging potential chemical risks and reports the findings to the Coordination Group for New and Emerging Chemical Threats, SamTox. Together with SamTox, the Toxicological Council forms a systematic approach at the national level for early detection, prioritization and management of chemical risks, an Early Warning and Action System.

The Toxicological Council is organized by the Swedish Chemicals Agency and consists of representatives from Swedish authorities responsible for chemical-related regulation and several universities that cover scientific areas related to chemical risks. The members of the Toxicological Council contribute with scientific and regulatory information on potential risk chemicals from their respective authorities and research areas.

The Toxicological Council's task is to strengthen the systematic monitoring and use of scientific information to identify and evaluate new or emerging potential chemical risks. The council has also decided to include known but insufficiently managed chemical risks in its evaluations. The council annually provides SamTox with updated and relevant information.

This annual report was produced by the Toxicological Council in 2024 and contains a consolidated assessment of the situation regarding new and emerging potential chemical risks. The conclusions presented are based on relevant scientific evidence, authority reports and expertise. The report represents the Toxicological Council's assessment and does not necessarily reflect the positions of individual authorities or academic institutions.

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Svensk sammanfattning

Toxikologiska rådet har under 2024 fortsatt arbetet med att identifiera nya potentiella kemikalierisker baserat på ledamöternas expertkunskap och information från deras respektive myndigheter och forskningsområden.

Under 2024 identifierade Toxikologiska rådet ökad förekomst och exponering för trifluorättiksyra (TFA) som en potentiell kemisk risk. Toxikologiska rådet anser att ämnen som bryts ner till TFA ska identifieras och att de viktigaste källorna till TFA ska regleras. Dessutom bör ytterligare information om (eko)toxiciteten hos TFA tas fram för att fastställa en säker nivå.

De ökande koncentrationerna av mono-*n*-hexylftalat i human urin identifierades som ett prioriterat område för vidare undersökning. Toxikologiska rådet har identifierat ett behov av att göra ytterligare insatser för att klargöra exponeringskällan, även utanför den kosmetiska sektorn (t.ex. importerade produkter och varor).

Toxikologiska rådet har under året arbetat med att vidareutveckla metoder för tidig identifiering av kemikaliehot. Ett examensarbete som syftade till att undersöka tillförlitligheten av att använda QSAR-baserade (både traditionella och AI-baserade) metoder för att identifiera kemikaliehot i stora databaser har genomförts. Toxikologiska rådet har även fortsatt att utveckla samarbetet med de arbets- och miljömedicinska klinikerna, den Hälsorelaterade miljöövervakningen vid Naturvårdsverket för bättre samverkan vid identifiering av kemikaliehot.

Toxikologiska rådet har även arrangerat en workshop för att diskutera hur nya metoder inom förutsättningslös screening (suspect och non-target screening) med hjälp av högupplöst masspektrometri kan användas för regulatoriska ändamål.

Vidare har Toxikologiska rådet samlat och diskuterat ny information för tidigare identifierade nya kemikaliehot och prioriterade områden för uppföljning (3D-skrivare, sensibiliserande ämnen, 1,4-dioxan, fluorerade ämnen i litiumjonbatterier och ämnen i LCD-skärmar (LCM)).

English summary

The Toxicological Council has continued its work throughout 2024 to identify new potential chemical risks based on the members' expertise and information from their respective authorities and research areas.

In 2024, the Toxicological Council identified increased occurrence and exposure to trifluoroacetic acid (TFA) as a potential chemical risk. The Council considers that substances that break down into TFA should be identified and that the main sources of TFA should be regulated. Additionally, further information on the (eco)toxicity of TFA should be obtained to establish a safe level.

The increasing concentrations of mono-*n*-hexyl phthalate in human urine were identified as a priority area for further investigation. The Toxicological Council has identified a need for additional efforts to clarify the source of exposure, including beyond the cosmetic sector (e.g., imported products and articles).

During the year, the Toxicological Council has worked on further developing methods for early identification of chemical threats. A thesis project aimed at investigating the reliability of using QSAR-based methods (both traditional and AI-based) to identify chemical threats in large databases was conducted. The Council has continued its work on developing collaboration between occupational and environmental medicine clinics, the health-related monitoring at the Swedish Environmental Protection Agency, and the Toxicological Council for better cooperation in identifying chemical threats.

The Council has also organized a workshop to discuss how new methods in non-targeted screening can be used for regulatory purposes.

Furthermore, the Toxicological Council has gathered and discussed new information for previously identified new chemical threats and priority areas for follow-up (3D-printers, sensitizing substances, 1,4-dioxane, fluorinated substances in lithium-ion batteries and substances in LCD screens (LCM)).

1 Identified new potential chemical risks

During 2024, the Toxicological Council identified increasing presence and exposure to trifluoroacetic acid as a potential chemical risk.

1.1 Trifluoroacetic acid (TFA)

1.1.1 Uses and sources

Trifluoroacetic acid (TFA) belong to the group of ultra-short chain per- and polyfluoroalkyl substances (PFAS) comprising a carboxylic acid group connected to a fully fluorinated carbon (chemical formula: CF_3CO_2H). It is used primarily in organic synthesis as a solvent, catalyst and reagent. It is generally believed that the highly persistent TFA found in the environment mainly comes from degradation of other perfluorinated substances.

TFA is registered under REACH as manufactured and/or imported to the EU in volumes of 100-1000 t/year. However, there are other use categories, e.g. 'intermediate', that do not require registration, so the actual total volume is unknown. There is also widespread use of chemicals that can degrade to TFA in the environment, for example fluorinated gases used as refrigerants (hydrofluoroolefines e.g., HFO-1234-yf), pesticides, pharmaceuticals and many other PFAS.

There may be many potential sources to TFA, but it is believed that degradation of fluorinated gases used as refrigerants, and especially HFO-1234-yf, are the most important[1]. Pesticides and industrial uses of TFA may lead to locally increased concentrations. Pesticides containing a fully fluorinated methyl group attached to a carbon (-C-CF_3) may be degraded to TFA[2]. It has been estimated that the German use of fluorinated gases results in emissions of TFA of about 2000 tonnes/year and the use of pesticides results in 457 tonnes/year[3]. It is speculated that some destructive degradation methods used for long-chain PFAS (including fluoropolymers) may be a source of TFA (e.g., oxidation, incineration, and electrolysis).[4] [5] [6]

1.1.2 Monitoring and exposure

TFA was measured above detection limits in 90% of Swedish groundwater samples taken from background areas. The median concentration was 190 ng/L and the maximum concentration in one sample was 2 700 ng/L (limit of detection 50 ng/L) [7]. German

[1] Persistent degradation products of halogenated refrigerants and blowing agents in the environment: type, environmental concentrations, and fate with particular regard to new halogenated substitutes with low global warming potential (UBA Texte 73/2021). Dessau-Roßlau; 2021 May

[2] Chang An et al. Application note. Identification of trifluoroacetic acid as polar metabolite from pesticides containing a trifluoroacetic (CF3) moiety using 14C tracer technology. M-032717, EAG Laboratories, 2017

[3] UBA. Reducing the input of chemicals into waters:trifluoroacetate(TFA) as a persistent and mobile substance with many sources (UBA Background November 2021), Dessau-Roßlau 2021

[4] Freeling and Björnsdotter Assessing the environmental occurrence of the anthropogenic contaminant trifluoroacetic acid (TFA). Vol. 41, Current Opinion in Green and Sustainable Chemistry. 2023

[5] The Global Threat from the Irreversible Accumulation of Trifluoroacetic Acid (TFA)
Hans Peter H. Arp, Andrea Gredelj, Juliane Glüge, Martin Scheringer, and Ian T. Cousins. Environ. Sci. Technol. 2024, 58, 19925−19935

[6] Garavagno et al., Trifluoroacetic Acid: Toxicity, Sources, Sinks and Future Prospects. Sustainability 2024, 16(6), 2382; https://doi.org/10.3390/su16062382

[7] SGU 2024, Inledande screening av PFAS i grundvatten i områden utan kända lokala föroreningskällor. PM. 133 s. https://www.sgu.se/globalassets/grundvatten/pfas/inledande-screening-av-pfas-i-grundvatten-i-omraden-utan-kanda-lokala-fororeningskallor.pdf

researchers[8] have observed higher levels of TFA in groundwater in areas with a higher proportion of agricultural land (>50%). In Sweden, SGU has observed the same trend (personal communication). SGU is planning additional statistical analyses in 2025 within a limited geographical area, based on samples collected in 2024, to verify that the observed higher levels are connected to agricultural land use and not population density (i.e. refrigerant use).

TFA is also present in Swedish and Norwegian drinking water[9] (70-720 ng/L), Swedish surface water (380-2 400 ng/L)[10] [11], groundwater near the surface (130-5 400 ng/L) in Swedish areas with intense agricultural use[12], sewage effluent water (about 1 000 ng/L) [13] and runoff water from landfills[14].

TFA may also be enriched in plants and fruits. Mean concentrations of 34 000 ng/L and 6 200 ng/L[15] were reported for orange juice and apple juice bought in Swedish food stores. Similar concentrations have previously been reported in Europe.

1.1.3 Risks to human health and the environment

TFA is classified for aquatic toxicity (chronic 3, H412, may be hazardous to aquatic organisms) and Germany has submitted a classification proposal for reproductive toxicity based on evidence of developmental toxicity in rats[16].

Only three EU Member States (the Netherlands, Denmark and Germany) have national maximum limits for TFA in drinking water (2 200, 9000 and 60 000 ng/L respectively). There is uncertainty concerning safe levels of TFA, both for humans and the environment due to lack of data.

The increasing use of substances degrading to TFA as well as the persistence of TFA, will likely lead to increased concentrations and exposure. It is alarming and there is a clear risk that concentrations will reach harmful levels. There is no cost-effective method available to remove TFA from water and it will be too late to react when harmful concentrations have been reached.

[8] Joerss et al. 2024. Pesticides can be a substantial source of trifluoroacetate (TFA) to water resources. Environment International 193 (2024) 109061.
[9] Eurofins 2023. Ultrashort PFAS in Swedish and Norwegian drinking water.
[10] Björnsdotter et al. 2022. Mass Balance of Perfluoroalkyl Acids, Including Trifluoroacetic Acid, in a Freshwater Lake | Environ Sci Technol. 2022; 56(1):251-259
[11] Boström, G., Tröger, R., Jonsson, O. & Gönczi, M. 2024. Identifiering av metaboliter från växtskyddsmedel relevanta att analysera i svenska yt- och grundvatten. CKB rapport 2024:1. Sveriges lantbruksuniversitet.
[12] Boström, G., Tröger, R., Jonsson, O. & Gönczi, M. 2024. Identifiering av metaboliter från växtskyddsmedel relevanta att analysera i svenska yt- och grundvatten. CKB rapport 2024:1. Sveriges lantbruksuniversitet.
[13] Golovko et al. 2022. Spread of organic micropollutants and per-and polyfluoroalkyl substances (PFAS) to farmlands when irrigated with municipality wastewater, Nationell miljöövervakning 2022urn:nbn:se:naturvardsverket:diva-10292
[14] Björnsdotter et al. 2019. Ultra-Short-Chain Perfluoroalkyl Acids Including Trifluoromethane Sulfonic Acid in Water Connected to Known and Suspected Point Sources in Sweden | Environ. Sci. Technol. 2019, 53, 11093−11101
[15] Eurofins 2024. Trifluoroacetic acid (TFA) and trifluoromethane sulphonic acid (TFMS) in juice and fruit/vegetable purees. Access 2024-09-02 https://cdnmedia.eurofins.com/european-east/media/uxcnaa2c/eurofins_tfa_tfms_juice_24_final.pdf
[16] Registry of CLH intentions until outcome - ECHA (europa.eu)

1.1.4 Regulatory activities

EFSA will assess the toxicity of TFA and the potential environmental contamination of TFA from pesticide use. It is currently discussed if Sweden should act on pesticides containing fluorinated carbons already before EU introduces measures. An EU proposal under REACH to ban all but essential uses of PFAS, including several potential sources of TFA, is under discussion.

There is a regulation for fluorinated gases (EU 2024/573) intended to decrease the use of gases that contribute to global warming. However, as HFOs have a low potential for global warming, it is therefore likely that HFOs rather will substitute refrigerants with a high potential for global warming. Under the Montreal Protocol, there is a requirement to report the use of HFOs but no restriction of use. The use of HFO is, with current measures, not likely to decrease and concentrations of TFA are expected to increase steadily. The current estimate is that TFA emissions due to use of fluorinated gases will increase by a factor of 7 from 2020 to 2050[17].

1.1.5 Further needs

Potentially important precursors to TFA should be identified, and the major sources of TFA should be regulated. HFO is likely one major source of TFA and therefore the use of HFO-1234-yf and other HFOs should be decreased where possible, e.g. limited to essential uses. Regulatory initiatives are needed as HFO use is not regulated today. For example, the formation of TFA could be included as a negative aspect in the current regulation (today only based on global warming potential) of fluorinated gases. The extent of degradation of different fluorinated gases to TFA needs to be investigated further, and regulatory initiatives to encourage substitution of these should be taken.

Furthermore, additional information on the (eco)toxicity of TFA should be generated to establish a safe threshold value.

2 Priority areas for further investigation

During 2024, the Toxicological Council identified increasing presence and exposure to mono-*n*-hexyl phthalate as a priority area for further investigation

2.1 Mono-*n*-hexyl phthalate

German authorities have reported an increase in mono-*n*-hexyl phthalate concentrations in urine samples from children and adults in Germany. The relevance for Swedish conditions was further examined by the Toxicological Council and it was concluded that this is a priority area for further investigation.

2.1.1 Use and exposure

Mono-*n*-hexyl phthalate (MnHexP) is not in itself used in products but is primarily a metabolite of dihexyl phthalate (CAS 84-75-3) (DnHexP), and also of various phthalate mixtures. DnHexP is primarily used as a plasticizer in PVC but does not have an active

[17] Persistent degradation products of halogenated refrigerants and blowing agents in the environment: type, environmental concentrations, and fate with particular regard to new halogenated substitutes with low global warming potential (UBA Texte 73/2021). Dessau-Roßlau; 2021 May

registration as substances in use in the EU under REACH[18]. According to the Nordic product registers, there has been no import of DnHexP to Nordic countries for several years. According to information from the Swedish Product Register, 1,2-benzenedicarboxylic acid, di-C6-10-alkyl ester (CAS 68515-51-5), which can be metabolized into mono-*n*-hexyl phthalate, was previously used in PVC, as well as in modelling clay. Even though there is no known use of these phthalates, they may possibly occur in imported products or as unintended contaminant in products.

The reason for the presence of MnHexP in urine samples of adults and children is unknown. UV-filters contaminated with DnHexP in sunscreen, and other consumer products, are considered possible sources [19]. DnHexP is not an allowed ingredient in cosmetic products but might be introduced as an impurity.

2.1.2 Occurrence in humans

DnHexP is rapidly metabolized by hydrolysis followed by oxidation reactions and excreted in urine. MnHexP and its metabolites have previously been identified in human urine in many countries.

In Germany, measurable amounts have recently been reported in increasing concentrations and in an increasing number of young children (2-6 years old), with an increase from 26% in 2017/2018 to 61% in 2021/2022[20] [21] [22]. The link between sunscreen products and increasing levels of mono-*n*-hexyl phthalate in young children is currently being investigated in Germany.

In Swedish young children, even slightly higher levels than in Germany of MnHexP have been measured in urine (Riksmaten småbarn, Swedish Food Agency, unpublished communication), and, as in Germany, the concentration in young children's urine exceeds that of older children and adults.

2.1.3 Health and environmental risks

Dihexyl phthalate has been identified as a SVHC (Substance of Very High Concern) due to its reproductive toxicity. Pirow et al.[23] conducted a risk assessment for MnHexP concentrations measured in urine in Germany, based on the assumption that the amount of excreted MnHexP constitutes 69% of orally administered dihexyl phthalate (calculated for dibutyl phthalate by

[18] Pirow R. et al. 2024. Mono-n-hexyl phthalate: exposure estimation and assessment of health risks based on levels found in human urine samples. Archives of Toxicology 98:3659–3671.
[19] Pirow R. et al. 2024. Mono-n-hexyl phthalate: exposure estimation and assessment of health risks based on levels found in human urine samples. Archives of Toxicology 98:3659–3671.
[20]LANUV (2021) Determination of pollutants and pollutant metabolites in the urine of 2- to 6-year-old children from North Rhine-Westphalia, report on the 3rd cross-section (2017/18), module 1 (plasticisers)—in German. Landesamt fur Natur, Umwelt und Verbraucherschutz Nordrhein-Westfalen.
[21] LANUV (2022) Determination of pollutants and pollutant metabolites in the urine of 2- to 6-year-old children from North Rhine-Westphalia, report on the 4th cross-section (2020/21), module 1 (plasticisers)—in German. Landesamt fur Natur, Umwelt und Verbraucherschutz Nordrhein-Westfalen.
[22] LANUV (2024) Determination of pollutants and pollutant metabolites in the urine of 2- to 6-year-old children from North Rhine-Westphalia—LANUV follow-up study on the plasticiser metabolite mono-n-hexyl phthalate (MnHexP)]—in German. Landesamt fur Natur, Umwelt und Verbraucherschutz Nordrhein-Westfalen, V.01/2024.
[23] Pirow R. et al. 2024. Mono-n-hexyl phthalate: exposure estimation and assessment of health risks based on levels found in human urine samples. Archives of Toxicology 98:3659–3671.

Anderson et al. 2001[24] and Koch et al. 2007[25]) and a TDI value for dihexyl phthalate (63 µg/kg/day) calculated by Pirow et al.[23] They concluded that exposure is well below the calculated TDI value and that a health risk is unlikely. We note that the calculation is based on many assumptions, one of which is that exposure comes from dihexyl phthalate, which has not been demonstrated.

2.1.4 Regulatory measures

No regulatory measures are planned.

2.1.5 Identified needs

Although the levels in young children are still relatively low, it is concerning that the levels and the proportion of exposed children are increasing, especially since the source remains unknown. The Toxicological Council has identified a need to carry out further efforts to clarify the source of exposure, also beyond the cosmetic sector (e.g. imported products and articles).

A similar request has been submitted under the Rapid Response Mechanism (RRM) to PARC[26] by the European Environment Agency (EEA) and the European Chemicals Agency (ECHA). The request is to identify the possible sources of exposure and the parent compound of MnHexP. The requestors wish to have the data by March 2025. Further analysis of MnHexP in urine from young children in Swedish sampled in 2024 is planned during 2025. Within PARC, Sweden will sample urine from adolescents (15-17 years) during 2025-2026, were also MnHexP will be analyzed. These samples will be collected from south, middle and north of Sweden and cover three different seasons of the year. The Toxicological Council will follow this work, and members will also contribute to the work.

3 Method development for systematic identification and prioritization of new potential chemical risks

The members of the Toxicological Council identify signals from the outside world that indicate new potential chemical risks. The signals are analyzed and prioritized jointly with the aim of identifying further needs for investigation or measures. The Toxicological Council's method for identifying and prioritizing potential chemical risks is largely based on the members' expert knowledge. The Toxicology Council considers that a more systematic approach is needed as a complement to identify new potential chemical risks and is taking initiatives to develop and improve additional methods.

[24] Anderson WA, Castle L, Scotter MJ, Massey RC, Springall C (2001) A biomarker approach to measuring human dietary exposure to certain phthalate diesters. Food Addit Contam 18(12):1068–1074.
[25] Koch HM, Becker K, Wittassek M, Seiwert M, Angerer J, Kolossa-Gehring M (2007) Di-n-butylphthalate and butylbenzylphthalate—urinary metabolite levels and estimated daily intakes: pilot study for the German Environmental Survey on children. J Expo Sci Environ Epidemiol 17(4):378–387.
[26] Partnership for the Assessment of Risks from Chemicals | Parc

3.1 Method development for increased coordination and identification of potential chemical risks based on exposure-health-related data at the OEM clinics and within HÄMI

During 2023 and 2024, the Toxicological Council has initiated a project on the possibilities to increase the coordination between the seven regional Occupational and Environmental Medicine (OEM, also well known as AMM in Swedish) clinics in Sweden, the health-related environmental monitoring (HÄMI) at the Swedish EPA, the Toxicological Council and other relevant actors. With an increased collaboration between HÄMI and the OEM clinics, an infrastructure for knowledge exchange about potential chemical risks as well as collection of biological samples of relevance for health-related exposure analysis at a national level could be developed. Increased coordination could also have positive effects on preparedness for crisis.

The OEM clinics evaluate chemical risks to human health in work environments and general outdoor and indoor environments. Thus, they are a key source of information and knowledge about (new) potential chemical risks to human health. This information can be further handled within the framework of the Toxicological Council. In turn, feedback from the Council can provide the OEM clinics with information and knowledge about new potential chemical risks identified through other channels. The need for coordination between agencies on environment-related adverse health outcomes has previously been highlighted at national HÄMI meetings and forms part of the Environmental Objectives Council's program "Health as a driving force for the environmental objectives and sustainable development"[27]. For information on the initial discussions and the assignments of the OEM clinics and HÄMI, see the Toxicological Council annual report 2023.[28]

Representatives from the OEM clinics, HÄMI, and the Toxicological Council presented the identified needs at the annual OEM clinic's spring meeting 2024. The presentation was well received and was followed up at the HÄMI meeting in October 2024.

During the HÄMI meeting, all seven OEM clinics were represented and were asked to provide information on their practical challenges. They also presented what needs and opportunities they had identified with an increased coordination in environmental health in general as well as between the clinics and the agencies. The needs are in accordance with the needs identified earlier by the different national agencies.

The needs and opportunities as identified by the OEM clinics include e.g.:

- Increased possibilities for preventive work to reduce adverse health effects of chemicals
- Targeted efforts for effective and efficient monitoring, analysis, and risk assessment of chemicals
- Support for laboratory infrastructure
- Targeted efforts (rapid response) to assess the extent and magnitude of unforeseen workplace and environmental incidents, accidents, and disasters
- Increased awareness of current activities at the agencies, e.g.
    - Legislation and new rules; recommendations and guidance
    - Clarify roles to find synergies and address gaps
- Knowledge exchange, e.g.

[27] Hälsa som drivkraft för miljömålen — Folkhälsomyndigheten (In Swedish)
[28] Toxikologiska rådets årsrapport 2023 (PDF, 453 kB) (In Swedish)

    - Establish expert networks; forum for faster identification and information sharing of new potential risk chemicals
    - Shared data collection; national infrastructure for collection of samples
    - Quality assurance
    - On-going and planned research project, including analysis and data sharing
- Increased collaboration, e.g.
    - Between the OEM clinics and with national agencies
    - Between the areas of environmental and occupational medicine
    - Large-scale national investigations to increase the possibilities to identify associations between exposure and adverse health effects
    - Preparedness for crisis and war, speed up decision-making and communication, identify efficient management options

The work on method development for increased coordination is planned to continue in 2025. The format of the coordination will need to be explored e.g. to what extent it is possible to further develop the already existing forums and networks or if there is a need to establish additional structures. It will also be further explored if the collaboration should mainly include contact points between actors or also web-based tools and databases as well as if additional areas should be included. Notably, the missions and assignments for the OEM clinics, as well as their resources, are given by the respective regional healthcare authorities and are not nationally uniform.

3.2 Improved regulatory screening of chemicals

The Toxicological Council has discussed deficiencies in non-target and suspect screening methods (high resolution mass spectrometry) for use in regulation. Specifically, the experience from regulatory authorities is that it is rarely possible to demonstrate the presence of substances that are not already known in the investigated matrix using advanced methods for non-target or suspect screening. The Council's conclusion is that there is a need for enhanced preparations before the analytical screening to increase the regulatory usefulness of the methodology and of the results. Therefore, the Toxicological Council took the initiative to organize a workshop to discuss how to improve communication between researchers, laboratories and authorities to facilitate the adaption of screening methodologies to the needs and prerequisites for regulatory measures (e.g. for early warning systems, restriction proposals and the regulatory screening). A full day workshop took place October 24, 2024, and was hosted by Stockholm University. The goals of the workshop were to produce a straightforward guide for both authorities and analytical laboratories (e.g. university or consultant labs) for an improved preparation phase before screening (e.g. structuring data, defining needs), a clearer communication about what is possible to analyze and an improved communication of the derived results.

The workshop was attended by 21 representatives from regulatory authorities and 17 representatives from the academia. SLU is responsible for summarizing the conclusions and recommendations from the workshop in a short report/guidance (funding from "myndighetsstöd") during 2025.

3.3 Systematic analysis and prioritization of large data sets

In 2020, the Toxicological Council initiated the development of a methodology that will facilitate identification and prioritization of substances with potentially hazardous properties

for human health and the environment based on large data sets, such as the Swedish product register or large-scale mapping of chemicals in various materials. [29] [30] The project was financed by the Swedish Chemicals Agency. During 2022, the methodology was further developed by researchers at Umeå University and Gothenburg University. In 2020 and 2021, the focus was on method development and automation, but calculations were also made on health and environmental data to be able to identify potential risk chemicals. The focus in 2022 was on quality assessment of estimated data and to describe the range of validity of models and data with the objective to deliver more reliable lists of suspected risk chemicals.

During 2024, the Swedish Chemicals Agency co-supervised (together with the Swedish Environmental Research Institute) a master thesis study at Karolinska Institute to further develop the approach and to investigate the reliability of computational methods for hazard identification and prioritization of chemicals. For this purpose, the VEGA toolbox QSARs (already applied in 2020) and the new AI-based Mistra SafeChem computational toolbox were tested and evaluated for the effects carcinogenicity, mutagenicity, reproductive and developmental toxicity, and skin sensitization. It was concluded that further research is needed to extract reliable lists of potential NERCs using these methods.

4 New information and follow up of priority areas for continued investigation

4.1 3D Printers and Consumer Exposure

In 2022, the Toxicological Council identified 3D printers and consumer exposure as a priority area for continued investigation. Technological development regarding 3D printers and additive manufacturing has been ongoing for a relatively long time, but in recent years there has been rapid development. For the industrial use of 3D printers, methods have been developed that effectively reduce exposure to particles, including nanoparticles, and other emissions.

The techniques and materials used by consumers are similar to those in the industrial setting; however, it is likely more difficult to reduce exposure in home and school environments. In these environments, children and other sensitive groups will also be exposed. As 3D printers are relatively cheap, and thus becoming more available to the public, including schools and other public spaces, the emissions and exposures in such environments are increasing. Some preventive measures, including enclosures and filters, can result in increased costs which in turn can result in such improved printers not being used. Small-scale consumer use and use in schools, apartments, and public premises such as libraries and leisure facilities, can thus be problematic from an exposure point of view.

During 2024, national agencies represented in the Toxicological Council together with experts in the field have published recommendations for consumer use at home, in schools, or other public spaces.[31]

[29] Toxicological Council (2021). Research report 2021. Methods for early identification of chemicals that have the potential to harm human health or the environment. Report 1/21

[30] Toxicological Council (2022). Research report 2022. Methods for early identification of chemicals that have the potential to harm human health or the environment. Improvement of workflow and application for identification of NERCs in the Danish EPA database on articles. Report 1/22.

[31] 3D-skrivare - Kemikalieinspektionen

As the recommendations are only published on agency webpages, the consumer coverage is likely low and additional efforts related to information on safe use are needed to ensure that it reaches consumers.

3D printers are normally considered as machines, and the Swedish Work Environment Authority performs market surveillance on machines. This also includes 3D printers used at home or in public spaces.

The Council concludes that there is a need to ensure that consumers receive the necessary information for safe use of 3D printers. Information on safe use is also needed for small-scale producers using 3D printers, including compliance with applicable legislation depending on the object printed and intended use.

4.2 Exposure to Sensitizing Substances

The Toxicological Council has previously identified exposure to sensitizing substances as a priority area for continued investigation. Sensitizing substances are present in everyday products and items, including e.g. detergents, paints, and cosmetics. Preventive work should be focused on reducing the development of dermal and respiratory problems due to sensitization, mainly through decreasing the use and exposure to sensitizing substances.

Sensitizing substances are regulated through different legislations depending on the intended use, and these substances and risks are hence not managed in a harmonized way. The Council has previously identified a need to increase the coordination between relevant agencies and ongoing activities as well as harmonization of legislation[32]. One important regulatory tool for identification and information on sensitizing substances is classification under the Classification, Labelling and Packaging (CLP) Regulation[33]. Classification is often also the basis for further regulation.

The Swedish Food Agency and the National Board of Health and Welfare will in a government assignment until April 2026 analyze the need for actions related to allergies, including a national strategy and action plan and national support in terms of expertise, recommendations, and guidelines. The analysis was initially focused on food, but additional areas are now included. The Council follows and contributes to the analysis. Depending on the outcome of the work, additional actions might be called for.

4.3 1,4-Dioxane

1,4-dioxane was identified in 2022 by the Toxicological Council as a priority area for continued investigation. In Europe, environmental monitoring shows that the levels are constant and not decreasing. The substance is classified as carcinogenic (category 1B), has a high persistence and mobility in water, and has been added to the candidate list of substances of very high concern (SVHC) under REACH[34].

The Swedish Geotechnical Institute has carried out a screening study of 1,4-dioxane during 2023 and 2024, financed by the Swedish Environmental Protection Agency (a report will be published 2025). Nine sites in Sweden with known contamination by chlorinated solvents

[32] Toxicological Council, Annual report 2018–2019, in Swedish. Toxikologiska rådets årsrapport 2018-2019 (PDF 933 kB)
[33] Regulation (EC) no 1272/2008 of the European Parliament and of the Council of 16 december 2008 on classification, labelling and packaging of substances and mixtures
[34] ECHA, 2021. Member State Committee support document for identification of 1,4-dioxane. https://echa.europa.eu/documents/10162/ce76bdd9-006a-19fc-05eb-4bb60daa0256

known to contain 1,4-dioxane as a stabilizer (either TCE or TCA and TCE) were investigated. At each site groundwater and, when possible, surface water was sampled. 1,4-Dioxane was found at all TCA-contaminated sites in concentrations ranging from 12 to 105 µg/L. At sites with only TCE contamination, levels above the LOQ (limit of quantification) for 1,4-dioxane were found at two out of five sites. 1,4-Dioxane was not measured above the LOQ in surface water at any site, while chlorinated solvents were detected in surface water at all sampled sites. The result from this study is consistent with international results reported in literature.

Based on the findings of this study and international literature data, it is recommended that investigations at sites contaminated with TCAs should include analysis of 1,4-dioxane in groundwater. In the case of sites with only TCE contamination a corresponding recommendation is not justified based on the results of this study. However, investigation of 1,4-dioxane at such sites could be recommended in specific cases depending on possible distribution pathways between the source area and water supplies.

In a screening study of effluent water from municipal wastewater treatment plants and receiving surface waters low levels of 1,4-dioxane was found in all samples (0.04-0.4 µg/L)[35]. Further, in a Swedish screening study of river outlets 1,4-dioxane was found in all 32 analysed river outlets (0.03 – 0.4 µg/L)[36].

There are no limit or target values for 1,4-dioxane in drinking water, groundwater or surface water in Sweden. This is something that need to be developed if the recommendation of including 1,4-dioxane in sampling and monitoring protocols is enforced in the work with remediation in Sweden. To enable recommendations on sampling strategies for 1,4-dioxane, it could also be motivated to investigate characteristics of the distribution pattern as well as the persistence of 1,4-dioxane in soil and groundwater. However, for the moment, no follow up study is planned. The Toxicological Council will follow and analyze new information and further discuss the risks.

5 Follow up of identified new chemical risks

5.1 Fluorinated substances in lithium-ion batteries

Fluorinated substances in lithium (Li)-ion batteries were considered in the Toxicological Council's annual report 2021 as an identified new potential chemical risk. Fluorine plays an important role in the development of Li-ion batteries in terms of cathode materials (transition metal fluorides, fluorinated polyanionic compounds), electrolytes, and interfaces. In 2023 the Toxicological Council concluded that there is a risk that PFAS can be released during the manufacture, waste handling and recycling of Li-ion batteries. Since battery factories and facilities for the recycling of batteries are established in Sweden, there is a need to further investigate emissions of PFAS and other substances and investigate what should be monitored and controlled. The Swedish EPA has commissioned Stockholm University to undertake an environmental screening study on fluorinated substances used in Li-ion batteries during 2024-2025. At Lund University, PFAS known to be present in Li-ion batteries will be analyzed in urine and serum from workers in recycling industries during 2025. Results from these pilots

[35] Malnes m.fl., 2024. urn:nbn:se:naturvardsverket:diva-11125

[36] Golovko O. et al. 2024. Environmental monitoring of organic micropollutants, PFAS and pesticides in Swedish river outlets 2023. Report to the Swedish Agency for Marine and Water Management (Havs- och vattenmyndigheten).

will be used to point out specific substances of concern and provide data to set relevant cut-off values for emissions. The Toxicological Council will follow this work.

5.2 Liquid Crystal Monomers (LCM)

Substances in LCD (Liquid Crystal Display) screens were identified in the Toxicological Council's annual report 2020 as a prioritized group of substances for further investigation and as an identified new potential chemical risk in 2023.

During 2024 the Swedish Chemicals Agency has financed a retrospective study investigating the possible presence of LCM (Liquid Crystal Monomers) in human blood in a non-target screening data set. The study was performed by the Department of Environmental Science at Stockholm University and found in contrast to Chinese data no clear indications of presence of LCM in blood. In 2025, the Swedish EPA will finance a follow up study to further investigate the validity of the method.

6 Other discussions

6.1 Deformed fish

The County Board representatives in Norrbotten contacted the Toxicological Council for advice after discovering deformed fish in their region. The Council discussed the issue and confirmed that these deformities are rarely seen in uncontaminated waters and the County Board is correct to demand remediation action. The Toxicological Council established contact between the County Board representatives and relevant researchers and governmental agencies to determine which substances are likely responsible for the observed deformities. Based on this, the County Board representatives have prepared a detailed and research-based plan for remediation to discuss with the responsible polluting company.